Volume 6 / Number 8 / 2012 ISSN 1840-2291

HealthMED

Journal of Society for development in new net environment in B&H

HealthMED journal with impact factor indexed in:
Thomson Reuters ISI web of Science,
Science Citation Index-Expanded, Scopus,
EBSCO Academic Search Premier, Index Copernicus, getCITED

THOMSON REUTERS

embase

SCOPUS

INDEX COPERNICUS INTERNATIONAL

design by Mirza Bašić

Volume 6 / Number 8 / 2012

HealthMED

Journal of Society for development in new net environment in B&H

Address of theSarajevo, Bolnicka BB
Editorial Board healthmedjournal@gmail.com
http://www.healthmedjournal.com
Published by DRUNPP, Sarajevo
Volume 6 Number 8, 2012
ISSN 1840-2291

HealthMED journal with impact factor indexed in:

- Thomson Reuters ISI web of Science,
- Science Citation Index-Expanded,
- Scopus,
- EBSCO Academic Search Premier,
- EMBASE
- Index Copernicus,
- getCITED, and etc.

Sadržaj / Table of Contents

Sadržaj / Table of Contents

Sadržaj / Table of Contents

Efficacy and tolerability of miconazole nitrate ovules in pregnants with vaginal candidiasis

Ahmet Uysal[1], Cuneyt Eftal Taner[2], Semih Mun[2], Murat Oztekin[2]

[1] Ministry of Health, Seferihisar Necat Hepkon State Hospital, Izmir, Turkey,
[2] Ministry of Health, Aegean Maternity and Teaching Hospital, Turkey.

Abstract

Objective: Try to evaluate the efficacy and tolerability of miconaole nitrate in pregnant women with vaginal candidiasis.

Material and Methods: Pregnant women with 13 to 28 weeks of gestation and complaining of vaginitis symptoms were enrolled to the study. Women with clinical and microbiological diagnosis of vaginal candidiasis were administered a single 1200 mg miconazole nitrate ovul intravaginally. Symptom scores, clinical and microbiological cure rates and treatment pleasure of the patients were noted, a week and a month after treatment.

Results: Sixty-nine pregnant women completed the study protocol. Mean age was 22 ±0,4 year and mean gestational age was 21,04 ± 4,90 weeks. Symptom scores significantly decreased after treatment. Clinical cure rates were 42, 02 % and 82.61 %, and microbiological cure rates were 47.8 % and 79.7%, a week and a month after treatment, respectively. We had 14 cases resistant to theraphy but had no recurrence in cured cases.

Conclusion: We concluded that intravaginal single dose of 1200 mg miconazole nitrate ovul is efficacious and well tolerated in the treatment of vaginal candidiasis in pregnant women.

Key words: Miconazole Nitrate Ovul, Pregnancy, vaginal candidiasis

Introduction

Candidal vaginitis is extremely common with most women experiencing this infection at some time in life. The most common cause of vulvovaginal yeast infection is candida albicans, but a significant proportion of yeast vaginitis is produced by non albicans candida. The significance of non-albicans candida lies in the greater difficulty in its identification microscopically in vaginal secretions and the frequent resistance of these forms to conventional therapies (1). Pregnancy is the most common predisposing factor with the incidence and severity of micotic infection increasing with the duration of gestation. The high hormone levels in pregnancy and increased glycogen content of the vagina constitute a favorable environment for the growth of candidal organisms. High levels of estrogen and progesterone may have direct virulance enhancing effects as well via the fungal cytoplasmic receptors spesific for these hormones (2). In this study we tried to evaluate the efficacy and tolerability of miconazole nitrate ovules in pregnant women with vaginal candidiasis.

Material and Methods

Pregnant women with 13 to 28 weeks of gestations and complaining of vaginal discharge and symptoms of vaginal itching, burning, dyspareunia, and dysuria were evaluated for the diagnosis of common vaginal infection. At the first visit detailed history of the pregnants were taken. Obstetrical and ultrasonographic examinations were done and symptom scores were evaluated. Amount of vaginal discharge, burning, itching, dyspraunia and dysuria symptoms were evaluated by scores as none: 0, mild: 1, moderate: 2 , severe: 3.

Vaginal secretions were analyzed by a wet mount preparation. A sample of vaginal secretion was suspended with a drop of saline solution on slide and covered with a slip then assessed by microscopy, 10 % KOH was added to another slide and suspended with vaginal secretions for evidence of fungal elements and for the assessment of Whiff test. Vaginal PHS of the secretions was evaluated with a standart pH meter.

Women with clinical diagnosis of vaginal candidiasis were enrolled to the study. Clinical diagnosis of vaginal candidiasis were based on the following criteria, normal vaginal pH, cottage cheese appearance of vaginal discharge, no odor

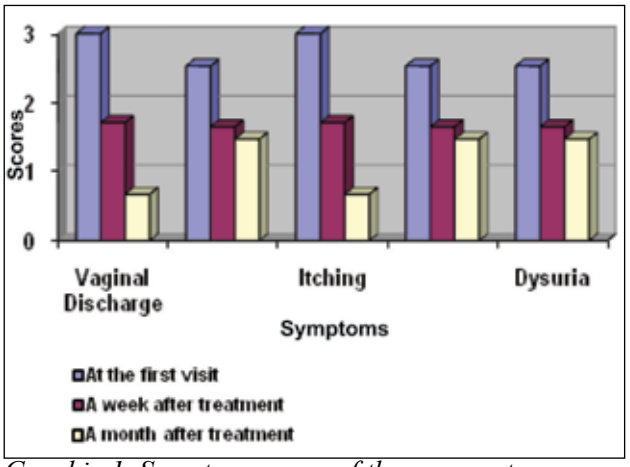
in Whiff test, pseuodophyhaes in wet mount examinations after adding a drop of 10 % KOH.

Pregnant women in the first trimester, or pregnant with premature rupture of membranes, vaginal bleeding, preterm labor, vaginitis other than candida infection and mix infections and severe vulvitis were excluded. Diabetic pregnants and pregnant women with urinary tract infections and women using any kind of antibiotics during the study or in the last 15 days were also excluded.

Sabourand dextrose agar cultures for microbiological diagnosis of candida infections were performed in the microbiology laboratory. Laboratory personel were blinded to clinical results. Pregnants with clinically diagnosed vaginal candidiasis were administered a single 1200 mg dose of miconazole nitrate ovul (Mikopenotran Embil Pharmaceutical Co, Ltd., Istanbul). Treatment response of patients were scored as not effective : 0, fair : 1, good : 2, excellent : 3.

Symptom scores, clinical and microbiological examinations and treatment response scores of the pregnants were repeated a week and a month after the treatment. Women who were lost during the follow up were excluded.

This study was approved by the ethic committee of our hospital and signs of the pregnants were taken for their approvels. For statistical analyses Conchran, Pearson, Chi-square, Mc Nemar and Friedman tests were used. P values < 0.05 were accepted as significant.



Graphic 1. Symptom scores of the pregnant women

Results

Sixty nine pregnant women completed our study protocol. Mean age of the women was 22 ± 0.4 (range 17-37) years. Mean gestational age was 21.04 ± 4.90 (range 13-28) weeks.

Mean symptom scores of the pregnant women at the first visit, a week and a month after treatment were shown in Table I.Mean symptom scores significantly decreased a week and a month after treatment as shown in Table I and Graphic 1.

In the study group 65 (94.2 %) of the 69 pregnant women had Candida albicans and 4 (5.8 %) women had Candida Glabrata infection in vaginal cultures. After treatment with intravaginal single dose of 1200 mg miconazole nitrate, in 33 (47.8 %) women candida infection disappeared in vaginal cultures at the first week. Candida albicans was detected in 22 (31.9 %) women and C.Glabrata in 14 (20.3 %) women, a week after treatment. After a month Candida infection was disappeared in 55 (79.7 %) women in vaginal cultures. C.albicans was detected in only 14 (20.3 %) cases. These cases were accepted as resistant to therapy. We had no case with relapse a month after treatment in vaginal cultures. Up to clinical examinations, clinical cure rates of the 69 women was 42.02 % (29 cases) at the first week and was 82.61 % (57 cases) a month after treatment. Microbiological cure rates were 47.8 % (33 cases), and 79.7 % (55 cases), respectively. Both clinical and microbiologic cure rates significantly increased a month after treatment as shown in Graphic 2.

Mean treatment pleasure of the pregnants was 2.30 ± 0.83 at the first week and it was 2.59 ± 0.73 a month after treatment (Graphic 3).

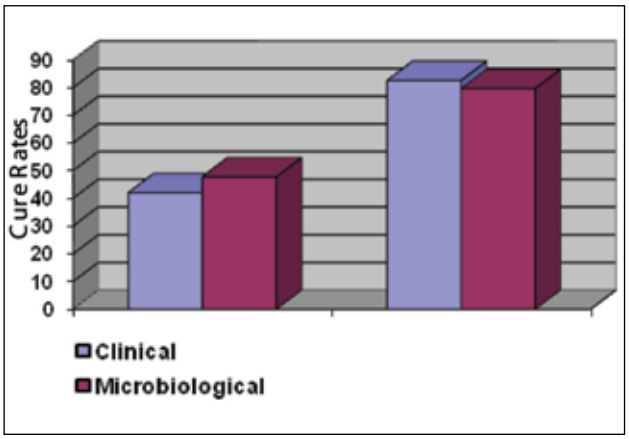
Table 1. Mean symptom scores of the pregnants

Symptom	At the first visit	A week after treatment	A month after treatment
Vaginal discharge	3.00 ± 0.00	1.71 ± 0.69	0.67 ± 0.58
Burning	2.53 ± 0.50	1.65 ± 0.58	1.47 ± 0.72
Itching	3,00 ± 0.00	1.71 ± 0.69	0.67 ± 0.58
Dysparaunia	2.53 ± 0.50	1.65 ± 0.58	1.47 ± 0.72
Dysuria	2.53 ± 0.50	1.65 ± 0.58	1.47 ± 0.72

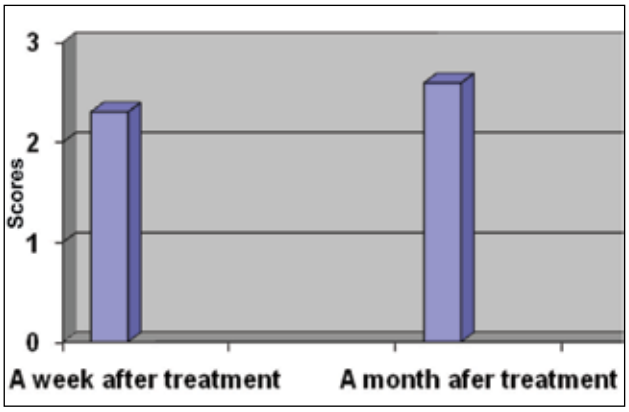
Mean treatment pleasure of the pregnants increased a month after treatment, but it was not significantly different then the mean treatment scores of the first week.

Discussion

Point prevalence studies; indicate that Candida may be isolated from the genital tract of approximately 20 % of asymptomatic healthy women of childbearing age. Giraldo et al reported that vaginal candidiasis could be detected in 28.8 % of symptomatic women by polymerase chain reaction technique and 6.6 % by culture (4). Several factors are associated with increased rates of asymptomatic colonization with Candida. Pregnancy is the most common prediposing factor with high hormone levels and with increased glycogen content of the vaginal environment. World wide studies showed that approximately one third of all pregnant women yield Candida infection on any particular day (2). C.albicans is responsible for 80 to 92 % of episodes of vulvovaginal candidiasis (5). An increased frequency of other Candida species particularly C.glabrata has been reported possible due to widespread use of over the counter drugs, long term use of suppressive azoles and the use of short courses of antifungal drugs (6). In our study we found C.albicans in 94.2 % and C.glabrata in 5.8 % of pregnant women with candidiasis.



Graphic 2. Clinical and microbiological cure rates after treatment



Graphic 3. Treatment response of the pregnants

The use of medication in pregnant women requires careful consideration of benefit to the mother versus risk posed to the fetus. Many of the antimycotic agents are capable of penetrating the placental barrier and entering fetal blood, therefore adverse effects of these agents on the fetus are a valid concern. The use of topical azoles for the treatment of superficial fungal infections is safe and efficacious (7, 8).

Miconazole, a synthetic imidazole antifungal agent is absorbed poorly from the gut, skin and buccal mucoza in human. Absorption from the vagina is also thought to be negligicible. Daneshmend investigated the serum concentrations of miconazole in "females for 72 hours following a single 1200 mg vaginal pessary. He reported the mean peak serum miconazole concentration as 10.4 μg and calculated mean systemic bioavailability of the vaginal pessery as 1.4 % (9). This low absorption rate may provide a safer use in pregnant women.

Dinsmore and Granger investigated the effectiveness of miconazole 1200 mg single ovule in the treatment of acute vaginal candidiasis. They reported the cure rate at day 7 as 88 % with a recurrence rate at day 28 as 16 % of those cured (10). In our study symptom scores of the patients significantly decreased after treatment. Our clinical cure rates were 42.02 % and 82.61 % and microbiological cure rates were 47.8 % and 79.7 % a week and a month after treatment respectively.We had 14 cases resistant to therapy but we had no case with relapse a month after treatment in vaginal culture. This result may be regarded with some caution since recurrence rates were reported as 10-16 % (10, 11) in non-pregnant females.

Odds and Macdonald (13) reported that miconazole persisted in biodetecable concentrations for at least 48 hours after insertion of a single 100 mg miconazole vaginal pessary. Retrospective analysis of cure rates in clinical trials of vaginal antifungal agents has suggested that the total dose

applied topically has more effect on the outcome of therapy than the duration of treatment (14). Up to those suggestions 1200 mg miconazole ovules may have longer effect than expected and this may discribe why we had better cure rates a month after treatment.

We concluded that intravaginal single dose of 1200 mg miconazole ovul is efficacious and well-tolerated in the treatment of vaginal candidiasis in pregnant women.

Disclosure

In this manuscription about ''Efficacy and Tolerability of Miconazole Nitrate Ovules in Pregnants with vaginal candidiasis'' is submitted for publication. All authors have no financial relationship (within the past 12 months) with a biotechnology manufacturer, a pharmaceutical company, or other commercial entity that has an interest in the subject matter or materials discussed in the manuscript. For this manuscription, all authors have contributed significantly, and that all authors are in agreement with the content of the manuscript.

References

1. *Edwards L. The diagnosis and treatment of infectious vaginitis. Dermatologic Therapy 2004, 17: 102-110*
2. *Faro S. Candida In Kaufman RH, Faro S, Brown D, eds, Benign diseases of the vulva and vagina 5 th edition, Elsevier Mosby, Philadelphia, 2005*
3. *DrakeTE. Maibach HI. Candida and candidiasis. Cultural conditions, epidemiology and pathogenesis Postgrad Med, 1973, 53: 83-87*
4. *Giraldo P, von Nowaskonski A, Gomes FA, Linhares I, Neves NA, Witkin SS. Vaginal colonization by Candida in asymptomatic women with and without a history of recurrent vulvovaginal candidiasis. Obstet Gynecol 2000, 95: 413-416*
5. *Candidiasis of the genitalia. In: Odds FC. Candida and candidiasis, a review and bibliography, 2nd ed. London: Bailliere Tindoll, 1988, 124-35*
6. *Horowitz BJ, Giaquinta D, Ito S. Evaluating pathogens in vulvovaginal candidiasis, implications for patient care. J Clin Pharmacol 1992, 32, 248-55.*
7. *Moudgal W, Sobel JD. Antifungal drugs in pregnancy: a review. Expert Opin Drug Saf. 2003, Sep: 2(5): 475-83*
8. *Sobel JO. Use of antifungal drugs in pregnancy: a focus on safety. Drug Saf. 2000, Jul 23(1): 77-85*
9. *Daneshmend TK. Systemic absorption of miconazole from the vagina. Journal of Antimicrobial Chemotheraphy. 1986, 18, 507-511*
10. *Dinsmore WW, Granger SE. An open study to assess the acceptability and effectiveness of miconazole 1200 mg single ovule in the treatment of acute vaginal candidiasis. B J C P, 1989; 43: 238-241*
11. *Sian AYL, Vendeputte E, Arien J, Cartrysse V, Deeters T, Vulvovaginal candidiasis, effectively treated with one miconazole ovule. Mykosen 1980; 23: 373-377*
12. *Upmalis DH, Cone FL, Lama CA, Reisman H, Rodriquez Gomes G, Gilderman L, et al. Single dose miconazole nitrate vaginal ovule in the treatment of vulvovaginal candidiasis: two single blind controlled studies versus miconazole nitrate 100 mg cream for 7 days. J Womens Health Gend Based Med. 2000, 9: 421-9*
13. *Odds FC, Macdonald F. Persistence of miconazole in vaginal secretions after single applications. Br J Vener Dis, 1981, 57: 400-1*
14. *Gough D. The influence of dosage and duration of administration of miconazole on the cure and relapse of candidal vaginitis. R Soc Med Symp Ser 1979; 7: 15-20.*

Corresponding Author
Ahmet Uysal,
Seferihisar Necat Hepkon Devlet Hastanesi,
Bashekimi Seferihisar,
Izmir,
Turkey,
E-mail: medicoexpert@gmail.com

An assessment of emergency and disaster preparedness in high schools in Istanbul-Turkey

Aysel Kokcu[1], Sema Kuguoglu[2], Ayse Ergun[3]

[1] Turkish Red Crescent Society, Istanbul Directorate, Turkey,
[2] Marmara University, Health Sciences Faculty, Division of Nursing, Department of Pediatric Nursing, Istanbul, Turkey,
[3] Marmara University Health Sciences Faculty, Division of Nursing, Department of Community Health Nursing, Istanbul, Turkey.

Abstract

This study was carried out as a descriptive study; to determine the most probable hazards/ emergencies in high schools in Istanbul and; to evaluate the preparedness for disasters and emergencies and; to find out the differences between school types in regards to disaster and emergency preparedness. The research was conducted with 2500 school employees and administrators working in 150 public and private high schools in Istanbul. Data were collected through "A Questionnaire Form for Emergency and Disaster Preparedness in Schools", developed by the researcher of this study. While Public High Schools covered in the study were found to be unprepared for disasters and emergencies, Private Turkish High Schools were found to be more prepared for disasters and emergencies than the other school types. Findings show that students and employees working in schools, and school buildings and education will be negatively affected in a probable major disaster/emergency situation in Istanbul.

Keywords: Emergency, Disaster Preparedness, High School.

Introduction

A disaster or emergency situation in Istanbul is likely to cause major damages and casualties in schools where 32 % of population of Istanbul live (Kocak, 2004). Thus, for the protection of the children- future of the society, for the safety of schools, and for raising healthy generations and creating a healthy future, it is quite important for authorities to take all protective pre-disaster precautions; to provide an effective disaster and emergency service; to make multidisciplinary plans and preparations in schools where children under 19 - the densest population in the city - spend most of their day.School emergency preparedness related to natural hazards, technological hazards or human induced hazards covers before all else, which precautions need to be taken first. Despite several studies and researches are available about individuals and groups related to disasters and disaster risks in our country, quite a few researches have been carried out about institutions involving schools and disaster preparedness of these institutions. Those few researches are about the types of plans and procedures and inventories of the materials a school keeps at school in case of a probable disaster or emergency (Ozmen, 2006; Ocal, 2007).

Schools in Istanbul are considerably at risks caused by disasters and emergencies. It is very important to develop separate plans and prepare for all emergencies from school based activities to district and community level emergencies (Duff, 2006).

As schools and school community surrounding it will be affected in major disasters, aid to schools will be late and schools will have to cope with the disaster with their own supplies for 3 or more days (Hosseini, 2006). After the trauma experienced at schools, out of students; school facilities, school staff and organizational structure may also be affected from emergencies and disasters. Among the consequences are partial damage, collapse of school buildings, death of students or school staff, and important disruptions in school procedures, and school order (Curtıs, Mıller & Berry, 2000).

So, community members, educators and school administrators should be well informed about how to behave, *before disasters*, *during disasters,* and *after disasters*. Making our schools "disaster resistant institutions" and education "a disaster resistant task" requires establishing chain of

command and order in schools, cooperating with local authorities, forming a board for disasters, making plans, making risk and threat analysis, determining available preparedness and resources, rating risks, determining high risk areas, evaluating emergency exits, fire evacuation situations, storing emergency supplies, (sheltering, nutrition, dressing, first aid, rescue, etc) determining critical tasks and critical personnel for critical tasks, training school emergency service teams, and disaster response teams, adopting periodical drills, and plans and renewing them (Duff, 2006). As technology changes and plans are renewed and updated, nurses – members of school health teams- need to adopt to novelties, new protocols, new units and new emergency and disaster plans (Psychological First Aid: Field Operations Guide, 2005). In disaster and emergency preparedness, among the roles of school nurses are; surveying, tracking, defining the disaster, participating in school activities, being informed about school activities, assessing probable emergency risks, initiating procedures, evaluating the efficiency of ongoing activities and emergency trainings, responding to emergencies when occur, being well informed about children with special medical needs, making plans for the needs of these students during emergencies, cooperating with psychiatrists, psychologists, health professionals , and volunteers working with children and families.

Method

This study was carried out as a descriptive study to determine; the probability of disasters / emergencies in high schools in Istanbul; disaster and emergency preparedness in high schools; and differences between schools in regards to disaster and emergency preparedness. After necessary permissions from Istanbul Provincial Directorate of Education, research was carried out in 150 high schools. Data were collected in the period between 30.12.2008 and 30.05.2009.

Universe of the research consisted of employees of five different high school categories in Istanbul: Public High Schools, Anatolian High Schools, Commerce Vocational High Schools, Industrial Vocational High Schools, and Private High Schools. Sample group was designated according to quota sampling in which a population is stratified according to particular categories relevant to the search being carried out. Total number of schools in Istanbul in above-mentioned five categories was stratified into categories. Then the number of schools in each category in each stratum to reflect relative proportion of the schools in that category was calculated. About 30 per cent of the schools in Istanbul Province were included in the research coverage. According to the relative number of employees reflecting the number of employees in the schools in the research coverage, 7000 questionnaire forms were distributed by the researcher to the schools. 2900 of 7000 questionnaire forms were returned. 400 of the forms were not analyzed as all or some of the questionnaire items were not checked by the samples. Rate of the returned questionnaires was 41.4%. The research was conducted with 2500 voluntary administrators and employees (teacher and school personnel).

Instruments

Data for the research were collected with *A Questionnaire Form for Disaster and Emergency Preparedness in High Schools (QFDEPHS)*, a 232 item questionnaire developed by the researcher based on literature review and experts' opinions.

While developing an instrument to collect data, field experts' opinions related to the instrument help provide content validity of the data collection instrument. For the content validity of the questionnaire form, academics related to this field and specialists working for institutions playing a role in state/district, province Disaster Management Units contributed to the questionnaire form with their critiques and suggestions. Pilot study was conducted in two phases. In the first phase, two groups consisting of 6-8 employees from randomly selected schools were given the questionnaire to answer the questions to determine whether the questionnaire was understood by the employees. In the second phase, redesigned questionnaire form was given to the employees in three different schools (these schools were not included in the later sampling group) to see whether the questionnaire was understandable enough or not before the research. Questionnaire form consisted of three parts.

1. Demographic information; consists of 7 descriptive questions, like; age, gender, education level, etc of samples.

2. Frequency of hazards consists of responses on 5 point Likert type scale of 43 questions, about disasters that may occur in schools like natural disasters (earthquake, etc), technological disasters (power cuts, etc) human induced disasters (fire at the school building, etc). Responses for each question were:0= there are no risks, 1=there are rarely risks, 2= there are sometimes risks, 3= highly risky. Cronbach's Alpha was 0.987.

3. A Scale for Disaster and Emergency Preparedness in High Schools, (SDEP) consists of total 182 questions and three sub-dimensions related to disaster and emergency preparedness in the schools where employees work (Cronbach's Alpha 0.988). Respondents were asked to rate their responses for the questions on a 3 point Likert type scale as 1 (I am not sure), 2(No, unprepared), 3 (yes, prepared) Average point for three sub dimensions was the point for general preparedness. Sub-dimensions of the scale were as follows:

3.1. Disaster and Emergency Preparedness Checklist; contains 38 questions indicating preparedness activities before probable disasters and emergencies in schools. (Cronbach's Alpha 0.976). Sample question: In *your school, is there a Board for Disasters aiming to develop disaster and emergency policies and strategies?*

3.2. Institutional Preparedness Checklist; contains 100 questions indicating the activities that should be done against disasters and emergencies at schools (Cronbach's Alpha: 0.983). There are 13 sub-sections as: General Measures (3 questions), Emergency Exit (7 questions), Measures for Fire (9 questions), First Aid (3 questions), Coordination (13 questions), Emergency Services (9 questions), Communication (9 questions), Logistics (11 questions), Drills (14 questions), Disaster Response (9 questions), Post-Disaster Improvement (4 questions), students' and parents' participation in institutional preparedness activities (4 questions), teachers' participation in institutional preparedness activities (5 questions). Sample question: Is your school building reliable against earthquakes?

3.3. Individual Checklist; consists of 44 questions indicating individual preparedness activities that should be done against disasters and emergencies in schools (Cronbach's Alpha 0.969). There are four sub sections as: Emergency Procedures (10 questions), Emergency Telephones (5 questions), Training (15 questions), Roles in Emergency Response (14 questions). Sample question: In disasters and emergencies, have you got a role in overall management of the incident? After demographic information and open-ended questions, alpha value for the remaining 242- item *(QFDEPHS) questionnaire* was calculated as 0.976. When Alpha value for each question was checked , no value was detected to decrease reliability. So, no question was deleted from the form.

Statistical Analysis

To analyzee data collected for the research, NCSS (Number Cruncher Statistical System) 2007 & PASS 2008 Statistical Software (Utah, USA) program was used. Besides descriptive statistical methods (mean, standard deviation), One-way Anova Test was used to compare quantitative data for between groups comparisons of normal distribution parameters, and Tukey HSD test was used to determine the group causing the difference. For between groups comparisons of parameters not giving normal distribution Kruskal Wallis test was used, and Mann Whitney U test was used to determine the group causing the difference. Cronbach Alpha quotient was used for reliability and validity. Significance was determined at $p<0.05$.

Results

Findings obtained from this research that was conducted to evaluate disaster and emergency preparedness in high schools in Istanbul were analyzed in four aspects: ***descriptive characteristics***; ***frequency of occurrence*** of natural disasters, technological disasters, human induced disasters, and emergency situations; ***individual opinions*** about disaster and emergency preparedness; and ***preparatory activities against disasters and emergencies*** (disaster and emergency aid planning preparations, institutional preparation activities, individual preparation activities).

22.3 % of repsondents were employees in Private High Schools, 16 % were in Public High Schools,

17.5 % were in Commerce Vocational High Schools, 14.7% were in Anatolian High Schools, and 29.5% were in Industrial Vocational Schools. Age of respondents varied between 17 and 67, and average age for respondents was 36.55±8.14. 48.6% of respondents were women, and 51.4% were men. Majority of respondents, 78 % were university graduates. 14.2 % of respondents had master's degree. 85.3 % of respondents were teachers, 3.9 % were deputy principals, and 1.2 % were school principals.

Hazards, employees said, most probably would occur in a year were, in order ; among natural hazards, earthquakes was (6%); among technological disasters, power cut was (4.9%); among human induced hazards, tobacco-alcohol related incidents was(12.8%). When employees' opinions related to Frequency of Occurrence of Hazards were compared in regards to school they work in, difference between all natural, technological and human induced disasters and emergencies was significant (Table 1). When the school causing the difference was analyzed, dual comparisons were made between Private High Schools and other school types, for nearly all variables the difference between Private High Schools and other school types was statistically significant.

Table 2 shows The Comparison of schools according to employees' scores. Difference between average score for Private High Schools and the average scores for other school types was significant and higher for private high schools. Average score for Industrial Vocational Schools was higher than Anatolian High Schools; difference was statistically significant (Table 2).

When respondents' responses for disaster and emergency preparedness plans were analyzed, we found that 77% of respondents said that their schools had civil defense plans, plans for protection and defense against sabotages, and plans for disasters and emergency situations like fires. We found that 33.1% of respondents said that hazard and risk analyses were done before plans; 50% said the plans contained all hazards; 55.8% said school plans were updated regularly. 63.9% employees expressed that there was a board for disasters in their schools. 34.7% of respondents said that school plans were made collaboratively with local emergency units, and 37.9% indicated that there was a shelter at their schools. For several issues related to the topics that should be included in school plans, employees gave *"I am unsure"* responses.

Points for Private High Schools' disaster and emergency aid preparedness plans were significantly higher than the scores for all other school types; and scores for Commerce Vocational High School and Industrial Vocational High Schools were found to be statistically, significantly higher than the score for Anatolian High Schools ($p<0.001$) (Table 3). For opinions related to institutional preparedness, 12.9 of respondents said the school buildings were not reliable, and 30.9% said they were not informed about the reliability of the school buildings. 35 % of respondents indicated that hazard mitigation procedures like fixing furniture or cupboards etc to the walls were not performed, and 26.9 indicated they had no idea about this procedure. 29.4 % of sample group said there wasn't a fire exit or fire escape in their school buildings.

39.3 of employees expressed that there wasn't an infirmary in their school buildings, and 28.3 % said there wasn't enough first aid material in their schools. On emergency preparedness at schools, 47.6% of employees said they worked with Provincial Directorate of National Education, 44.5% said they worked with Fire Department, 42.8 % with Directorate of Civil Defense, 40.4% with Health Organizations, and 40% with Security Units. Respondents were asked whether there were emergency services in their schools, respondents said that they had Control Center, Headquarters Service: 27.5%, Safety and Guidance Service: 26%, Fire Department Service: 26.5, Rescue Service: 23.4%, First Aid Service:21.5 %,Social Aid Service: 22.3%. 22.4% of respondents said they didn't have Technical Repair Service, and 45% of respondents indicated that there weren't any specialized personnel for disasters or emergencies in their schools. 31.4 % of employees said there weren't trained personnel to use spare communication systems at school, and 36.1% said there wasn't a satellite phone in their schools to communicate, 13.1% said there wasn't announcement system at school, 25.1% said there wasn't a bleeper at school, 30.1% said they didn't have walkie-talkies in their school, 33.7% said they didn't have long distance two-way radios in their schools, and 12.4% said there wasn't an emergency alert system in their schools.

For logistical preparations to be made before disasters, 9.2 % of employees indicated that emergency supplies were not controlled and cared in a year. We determined that: 13.8 % of employees thought flashers and batteries were not stored enough, 32.6% thought food storage was not enough, 26.1% thought water storage was not enough, 22.8% thought search and rescue equipment

Table 1. In Regards to School Type, Comparison of Employees' Opinions About Frequency of Occurrence of Hazards

Hazard		Private High School	Public High School	Commerce Vocational High School	Anatolian High School	Industrial Vocational High School	*p*
		mean±SD	mean±SD	mean±SD	mean±SD	mean±SD	
Natural	Heart Attack	0.19±0.47	0.28±0.60	0.32±0.58	0.22±0.48	0.32±0.63	***0.001***
	Epileptic Fit	0.26±0.52	0.60±0.68	0.71±0.72	0.42±0.63	0.56±0.66	***0.001***
	Faint	0.78±0.74	1.27±0.89	1.47±0.89	1.04±0.79	1.07±0.80	***0.001***
	Allergic Reactions	0.76±0.80	0.84±0.87	0.90±0.88	0.86±0.79	0.85±0.82	***0.112***
	Heat/Sunstroke	0.40±0.67	0.67±0.80	0.68±0.81	0.54±0.72	0.61±0.77	***0.001***
	Animal Bites (dog, insect, snakeetc.)	0.23±0.56	0.32±0.64	0.38±0.65	0.25±0.55	0.41±0.69	***0.001***
	Earthquake	0.80±0.85	0.98±0.92	0.88±0.89	0.86±0.93	0.98±0.88	***0.001***
	Freeze/Hail/Icy conditions	0.64±0.75	0.78±0.83	0.89±0.84	0.69±0.78	0.89±0.85	***0.001***
	Strong winds/Storms	0.72±0.75	0.87±0.85	0.99±0.84	0.75±0.80	1.06±0.86	***0.001***
	Snow/Blizzard	0.75±0.76	0.93±0.80	1.02±0.79	0.90±0.82	1.17±0.82	***0.001***
	Drought/Heat Wave	0.50±0.72	0.68±0.81	0.82±0.93	0.65±0.80	0.93±1.01	***0.001***
	Land Slides	0.12±0.43	0.22±0.56	0.27±0.58	0.19±0.52	0.29±0.66	***0.001***
	Torrens/Floods	0.18±0.48	0.38±0.68	0.39±0.67	0.29±0.61	0.42±0.69	***0.001***
	Lightning	0.15±0.44	0.26±0.61	0.33±0.65	0.18±0.47	0.29±0.59	***0.001***
Technological	Dam break/Pipeline Explosions	0.20±0.52	0.30±0.59	0.38±0.64	0.30±0.59	0.31±0.62	***0.001***
	Power Outage	0.80±0.77	1.03±0.79	1.20±0.82	1.08±0.82	1.12±0.82	***0.001***
	Gas Cut	0.31±0.64	0.51±0.73	0.65±0.77	0.48±0.71	0.65±0.75	***0.001***
	Water Shortage	0.56±0.74	0.93±0.81	1.09±0.83	0.89±0.81	0.97±0.82	***0.001***
	Communication Failure	0.40±0.67	0.57±0.75	0.68±0.77	0.55±0.72	0.66±0.78	***0.001***
	Nuclear Radiation	0.08±0.36	0.16±0.51	0.24±0.62	0.11±0.44	0.21±0.58	***0.001***
	Chemical/ Explosive Substance Hazards	0.11±0.42	0.23±0.61	0.30±0.66	0.18±0.49	0.33±0.68	***0.001***
Human induced	Sudden / Extreme Psychological Reactions	0.54±0.72	1.07±0.86	1.08±0.88	0.86±0.81	0.93±0.91	***0.001***
	Suicide Attempts	0.14±0.44	0.40±0.64	0.50±0.72	0.33±0.60	0.36±0.64	***0.001***
	Broken bones (arm,leg, etc.)	0.85±0.70	1.06±0.78	1.05±0.78	0.97±0.76	1.04±0.75	***0.001***
	Burns	0.39±0.62	0.62±0.77	0.64±0.78	0.52±0.75	0.72±0.77	***0.001***
	Bleeding (skin,nose,etc.)	0.81±0.73	1.09±0.83	1.14±0.82	1.02±0.84	1.17±0.85	***0.001***
	Tobacco and alcohol related incidents	0.48±0.74	1.27±1.04	1.35±1.0	1.06±0.92	1.41±1.09	***0.001***
	Boycott/Occupying/Strikes	0.12±0.45	0.34±0.68	0.34±0.66	0.20±0.53	0.29±0.65	***0.001***
	Food Poisoning/Food Related Hazards/Mass Food Consumption Areas	0.24±0.55	0.42±0.68	0.54±0.73	0.38±0.63	0.48±0.76	***0.001***
	Epidemics (Hepatitis,mumps,etc.)	0.23±0.55	0.45±0.69	0.52±0.72	0.36±0.61	0.48±0.70	***0.001***
	Terrorist Attacks and Activities	0.09±0.34	0.26±0.65	0.35±0.69	0.17±0.47	0.27±0.65	***0.001***
	Angry Parents	0.55±0.69	1.12±0.91	1.08±0.83	0.78±0.75	1.05±0.85	***0.001***
	Criminal Activity in the Neighborhood (robbery, murder,etc.)	0.19±0.47	0.84±0.85	0.95±0.89	0.55±0.75	0.83±0.86	***0.001***
	Gang Activity (at school or neighborhood)	0.13±0.41	0.78±0.87	1.02±0.90	0.49±0.74	0.96±0.88	***0.001***
	Detecting Strangers in School	0.19±0.55	0.71±0.82	0.80±0.83	0.44±0.70	0.89±0.86	***0.001***
	Detecting Weapons in School	0.09±0.42	0.22±0.52	0.35±0.65	0.14±0.41	0.29±0.62	***0.001***
	Violence by Students or School Staff	0.14±0.44	0.69±0.78	0.74±0.78	0.41±0.63	0.84±0.79	***0.001***
	Detecting Drugs and Drug Use in School	0.07±0.32	0.29±0.59	0.39±0.66	0.16±0.45	0.39±0.68	***0.001***
	Work-Related Accidents (electric schock, falling, etc.)	0.32±0.55	0.47±0.64	0.47±0.68	0.32±0.58	0.74±0.77	***0.001***
	Forest/Bush Fires	0.13±0.42	0.27±0.66	0.29±0.62	0.15±0.46	0.27±0.61	***0.001***
	Major Motor-Vehicle Accidents in/ near School Building	0.26±0.53	0.38±0.62	0.49±0.70	0.34±0.59	0.47±0.69	***0.001***
	Bombs (Including threats)	0.10±0.42	0.18±0.52	0.22±0.52	0.18±0.45	0.20±0.56	***0.001***
	Fire at School	0.15±0.46	0.21±0.54	0.29±0.60	0.18±0.49	0.25±0.59	***0.001***

Kruskal Wallis test ***p<0.01*

Table 2. Comparison of Schools According to Their Average Scores for QFDEPHS

High School	Mean± SD	P*	Dual comparisons***
Private High School	66.18±20.93	0.001**	L1>L2, L3, L4, L5**
Public High School	52.26±19.67		
Commerce V. H.S	51.19±21.16		
Anatolian High School	48.75±19.46		
Industrial Vocational H.S	53.87±21.54		L5>L4**

**Oneway ANOVA test **p<0.01 ***Post-Hoc Tukey HSD test*
L1: Private High School, L2:Public High School, L3: Commerce Vocational High School, L4:Anatolian High School, L5:Industrial Vocational School

Table 3. Comparison of Preparation Scores for Disaster and Emergency Aid, According to School Types

School	mean±SD	median	P***	Dual Comparison****
Private High School	70.28±29.81	81.57	***0.001***	L1>L2,L3,L4,L5**
Public High School	47.86±30.70	48.68		
Comerce Vocational School	48.21±31.84	48.68		L3>L4*
Anatolian High school	43.89±33.21	39.47		
Industrial Vocational School	48.57±32.46	50		L5>L4*

**p<0.05 **p<0.01 ***Kruskal Wallis test, ****Mann-Whitney U test*
L1: Private High School, L2:Public High School, L3: Commerce Vocational High School, L4:Anatolian High School, L5:Industrial Vocational Schools

was not enough, and 26.6% thought that medical supplies for students with special medical needs were not stored enough. When employees were asked if copies of important documents were stored, 13% answered "No".

It was also found that in schools where respondents worked; in 33.5 % search and rescue drills, in 30.4% first aid drills, in 16.7% fire drills, in 16.7% internal and external evacuation drills, in 13.4% earthquake drills were not performed, and in 18.9% of respondents' schools drills were performed twice a year. In respondents' schools, it was also determined that; Incident Command Center" was not designated for emergencies: 16.9%, there was not an appointed disaster and emergency response team: 13.8%, mechanisms to switch off gas, electric or water automatically did not exist: 14.8%, 24.7% of respondents didn't have emergency bags, and in 30.6 of schools a staging area for emergencies was not designated. 24.7% of respondents indicated that they did not have agreements signed with institutions or organizations capable of giving psychological support to students and parents to improve after disasters. 42.2 % of employees said that they wouldn't have an alternative education program if they couldn't return to their school buildings in a short period of time after a disaster or emergency. According to the findings; 16.5 % of employees indicated that parents did not involve in Disaster Planning Committee, 18.5% of employees did not assist to provide emergency supplies, 25.2 % of employees did not participate in emergency exercises, and trainings. In addition, 12.7 % of respondents indicated that students at their schools were not informed about how to behave in an emergency.

10.8% of respondents said that teachers at their schools didn't know how to do "kneel, cover, hold" actions when earthquakes began. 11% of respondents said teachers didn't know when to evacuate classes after disasters and emergencies, 14.8% said they didn't know how to apply triage, and 15% said they didn't know how to apply first aid, and 13.5% said they didn't know how to give psychological first aid.Table 5 shows two group comparisons of the average institutional preparedness points by schools. Difference between total points and average points of Private High Schools for all sub dimensions and points of all other school types were statistically significant and higher than the points for all other school types. Statistically significant difference was determined between the total points and points for some sub-dimensions, between Anatolian High schools and Public

Table 4. Assessment of Institutional Preparedness Scores According to School Types

Institutional Preparedness Scores		Private High School	Public High School	Commerce Vocational High School	Anatolian High School	Industrial Vocational High School	p
		mean±SD (median)	mean±SD (median)	mean±SD (median)	mean±SD (median)	mean±SD (median)	
Total points		66.16±23.67	49.35±22.86	48.17±24.59	44.40±24.19	50.78±26.89	0.001**
Sub dimensions	General Precautions	81.26±26.97	59.45±28.66	63.74±30.59	62.30±30.73	61.69±28.92	0.001**
	Emergency Exit	86.98±21.07	66.23±25.55	65.22±26.58	66.01±27.79	68.51±26.86	0.001**
	Precautions Against Fire	83.54±21.97	62.86±26.86	63.25±29.63	59.49±30.86	65.79±30.65	0.001**
	First Aid	88.53±24.21 (100)	49.25±29.91 (50)	48.74±31.94 (50)	50.13±31.42 (50)	52.41±34.25 (50)	0.001**
	Coordination	54.66±40.09 (61.53)	40.46±37.07 (38.46)	40.07±38.13 (34.61)	33.03±38.38 (11.53)	41.53±40.56 (34.61)	0.001**
	Emergency Services	64.88±32.38 (77.77)	47.64±29.93 (50)	46.25±32.12 (50)	43.50±32.05 (50)	51.01±34.84 (50)	0.001**
	Communication	61.06±29.89 (66.67)	47.25±25.28 (50)	43.54±28.58 (44.44)	41.12±27.69 (44.44)	47.81±30.36 (50)	0.001**
	Logistics	59.63±35.02 (68.18)	38.68±28.83 (38.63)	37.08±31.74 (36.36)	33.10±30.93 (27.27)	39.61±34.82 (36.36)	0.001**
	Exercises	71.07±28.84	57.76±27.34	56.17±30.32	52.32±30.80	59.11±31.14	0.001**
	Disaster Response	54.32±33.27	39.79±29.93	35.69±31.70	32.54±28.75	39.62±33.44	0.001**
	Post-Disaster Improvement	45.01±40.77 (37.5)	36.0±32.61 (37.5)	32.77±35.05 (25)	27.21±30.98 (12.5)	35.80±36.88 (25)	0.001**
	Students and Parents	55.52±39.09 (50)	41.43±34.08 (37.5)	41.37±36.94 (37.5)	35.76±35.35 (25)	43.50±38.68 (37.5)	0.001**
	Teachers	71.97±32.32 (80)	59.57±33.62 (60)	61.16±34.49 (60)	54.63±35.08 (60)	59.53±34.80 (60)	0.001**

Kruskal Wallis test was used ***p<0.01*

High Schools; between Anatolian High Schools and Industrial Vocational High Schools (Table 4).

As for **individual preparedness** at schools; respondents said they didn't know procedures about earthquakes: 21.3%, gas leak: 39.5%, terror and sabotage: 42.1%, freeze and icy conditions: 40.5%, HAZMAT (chemical and hazardous materials, etc): 50.5%, emergency health procedures and food poisoning :39%, school site based environmental risks: 46.3%, fire and explosions: 37.3%, how to deliver children to their parents: 38%, emergency procedures to be applied during a work related accident: 37.5%. Rate of respondents who didn't know useful numbers: emergency telephone number 112 (911 for USA), telephone number of fire department; the telephone number of police/gendarme, telephone number of electrical services department was: 24.6%, telephone number of gas services department: 25.2%. 55.1 of employees didn't know how to apply heart massage/cardiopulmonary resuscitation, (artificial respiration/heart massage), 44.5 of employees didn't know basic first aid, 63.7% of employees didn't know system of emergency management, 68.1% didn't know search and rescue procedures, 54.2% didn't know how to evacuate, and 61.1% said they weren't trained on many skills like extinguishing fires.

When employees were asked what their roles in disaster/emergency response were, 52.7 % of employees indicated that they didn't have roles specified by the law and more than half of them said they didn't have any roles about many aspects of disaster response procedures in their schools.

When general total points for individual preparedness and average points for all sub-dimensions analyzed; differences between points of Private High Schools and other school types were found to be statistically significant, and points of Private High Schools were significantly higher than that of other school types (Table 6). Average general

Table 5. Two Group Comparisons of Points for Institutional Preparedness By School Type

Sub-Dimensions of Institutional Preparedness	L1-L2	L1-L3	L1-L4	L1-L5	L2-L3	L2-L4	L2-L5	L3-L4	L3-L5	L4-L5
Total points	L1>L2**	L1>L3**	L1>L4**	L1>L5**	AD	L2>L4*	AD	AD	AD	L5>L4**
General Precautions	L1>L2**	L1>L3**	L1>L4**	L1>L5**	AD	AD	AD	AD	AD	AD
Emergency Exit	L1>L2**	L1>L3**	L1>L4**	L1>L5**	AD	AD	AD	AD	AD	AD
Precautions Against Fire	L1>L2**	L1>L3**	L1>L4**	L1>L5**	AD	AD	AD	AD	AD	L5>L4**
First Aid	L1>L2**	L1>L3**	L1>L4**	L1>L5**	AD	AD	AD	AD	L5>L3**	AD
Coordination	L1>L2**	L1>L3**	L1>L4**	L1>L5**	AD	L2>L4**	AD	L3>L4**	AD	L5>L4**
Emergency Services	L1>L2**	L1>L3**	L1>L4**	L1>L5**	AD	AD	AD	AD	L5>L3*	L5>L4**
Communication	L1>L2**	L1>L3**	L1>L4**	L1>L5**	AD	L2>L4**	AD	AD	L5>L3*	L5>L4**
Logistics	L1>L2**	L1>L3**	L1>L4**	L1>L5**	AD	L2>L4**	AD	AD	AD	L5>L4**
Exercises	L1>L2**	L1>L3**	L1>L4**	L1>L5**	AD	AD	AD	AD	AD	L5>L4**
Disaster Response	L1>L2**	L1>L3**	L1>L4**	L1>L5**	L2>L3*	L2>L4**	AD	AD	AD	L5>L4**
Post Disaster Improvement	L1>L2**	L1>L3**	L1>L4**	L1>L5**	AD	L2>L4**	AD	L3>L4*	AD	L5>L4**
Students and Parents	L1>L2**	L1>L3**	L1>L4**	L1>L5**	AD	L2>L4**	AD	L3>L4*	AD	L5>L4**
Teachers	L1>L2**	L1>L3**	L1>L4**	L1>L5**	AD	L2>L4*	AD	L3>L4**	AD	L5>L4*

Mann-Whitney U test ***p<0.01* **p<0.05*

L1: Private High School, L2:Public High School,L3: Commerce Vocational High School, L4:Anatolian High School, L5:Industrial Vocational Schools, AD: not significant

total points of Industrial Vocational High Schools are statistically significant and higher than the points of Public High Schools and Commerce Vocational High Schools, Anatolian High Schools (p<0.001), (Table 7).

Discussion

When the results of this research are considered in general, research shows that Public or Private, all High Schools are unprepared for disasters and emergencies. Private High Schools were found to be more prepared than other school types. These results emphasize the importance of preparations for disasters and emergencies for all schools. One of the most basic conditions for schools to reach its academic goals and provide a desired level of education is a learning environment where students and school staff feel themselves safe (Ozer & Donmez, 2007). In his research, Afyouni (2007) determined that disaster preparedness of educational institutions was not enough for major natural disasters but schools were prepared well enough to struggle minor disasters.

In respondents' schools, among all natural disasters, earthquakes were rated the most **probable to occur** in a year. Kano, Ramirez, Ybarra, Frias& Bourke (2007), in their research they conducted

Table 6. Assessment of the Points for Individual Preparedness by School Type

Individual Preparedness Points	Private High School	Public High School	Commerce Vocational High School	Anatolian High School	Industrial Vocational High School	p
	mean±SD (median)	mean±SD (median)	mean±SD (median)	mean±SD (median)	mean±SD (median)	
Total Points	69.47±20.51 (70)	60.41±20.52 (60)	58.84±23.43 (60)	58.98±19.29 (8.33)	63.19±21.08 (61.67)	0.001**
Emergency Procedures	69.61±29.13 (75)	57.75±27.26 (50)	56.39±29.36 (50)	54.51±27.82 (50)	60.26±30.79 (50)	0.001**
Emergency Telephone Numbers	87.73±24.74 (100)	77.27±29.30 (90)	76.99±31.44 (90)	80.59±26.93 (90)	82.72±26.25 (100)	0.001**
Training	63.29±20.99 (60)	56.58±20.03 (53.3)	54.44±23.84 (53.3)	54.76±18.83 (53.3)	58.63±19.77 (53.3)	0.001**
Roles in Emergency Response	58.80±24.92 (57.14)	51.40±22.87 (50)	49.52±25.77 (50)	47.71±22.91 (50)	52.95±25.0 (50)	0.001**

Kruskal Wallis test ***p<0.01*

Table 7. Dual Comparisons of Individual Preparedness Points by School Type

Individual Preparedness Points	L1-L2	L1-L3	L1-L4	L1-L5	L2-L3	L2-L4	L2-L5	L3-L4	L3-L5	L4-L5
Total Points	L1>L2**	L1>L3**	L1>L4**	L1>L5**	AD	AD	L5>L2*	AD	L5>L3*	L5>L4**
Emergency Procedures	L1>L2**	L1>L3**	L1>L4**	L1>L5**	AD	AD	AD	AD	AD	L5>L4*
Emergency Telephone Numbers	L1>L2**	L1>L3**	L1>L4**	L1>L5**	AD	AD	L5>L2**	AD	L5>L3**	AD
Training	L1>L2**	L1>L3**	L1>L4**	L1>L5**	AD	AD	AD	AD	L5>L3**	L5>L4**
Roles in Emergency Response	L1>L2**	L1>L3**	L1>L4**	L1>L5**	AD	L2>L4**	AD	AD	AD	L5>L4**

Mann-Whitney U test ***p<0.01* **p<0.05* *AD: Not Significant*
L1: Private High School, L2:Public High School,L3: Commerce Vocational High School, L4:Anatolian High School, L5:Industrial Vocational Schools,

with school employees in Los Angeles, found that the most damaging disaster among natural disasters was earthquakes. It was determined that earthquake hazard was considered less probable in Private High Schools than it is felt in the other school types. After Marmara Earthquakes in 1999, Many of the high schools in Turkey were reinforced by the government against natural disasters. Despite this reinforcement, as public buildings were highly damaged after the earthquake in 1999, research showed that teachers' and school employees' worries had not been relieved yet. Besides this, old school buildings, crowded schools and level of training at schools, and insufficient number of exercises and drills can be ascribed to this result (Urkmez, 2002). In our research, from Technological Disasters, power failure was rated the most probable to occur in a year. Kano, Ramirez, Ybarra, Frias & Bourque (2007), in their research, found that power failure at schools was rated as "highly probable" (75.8%). In Kano & Bourque's (2007), research conducted in California, among the hazards at school, power cut was rated the third most probable hazard to occur.

Rate of considering power cut as a hazard is much higher in state schools than the rate for private schools. Absence of generators in state schools, and canceling lessons when electricity is off, may have caused employees to perceive power cut a more probable hazard to occur. Power cut in state schools, during a disaster, will cause all possibilities of communication, heating, lighting to lose. This fact shows that it is inevitable to prepare regulations for schools to keep generators at schools in case of emergencies.

It was determined that, for Private Schools, rate of smoking and drinking alcohol at school was much less than the drinking and smoking rate for four other school types, and it was rated the most probable hazard to occur in Industrial Vocational Schools. Kara, Hatun, Aydogan, Babaoglu & Gökalp (2003), in their research conducted in Province of Kocaeli with High School students, found that the rate of students who had tried smoking, once at least was 66.5%, rate of students who had drunk one glass of alcoholic drink at least, in his/her life was 54.4%, rate of students who had smoked everyday regularly last 30 days was 15.4%. In a study on prevalence of alcohol and drug use conducted with tenth grade high school students in Istanbul by Ogel, Taner & Eke (2006), prevalence of smoking at least once in life was found to be 37%, prevalence of alcohol use was 51.2%. In the same research, it was also found that prevalence of smoking and alcohol use was higher among children from lower socio-economic classes than that was for other children. That most of children from lower socio-economic classes go to public high schools supports the findings of our research.

Our research results show that, at schools in general, there are **plans for disasters and emergencies**. It was determined that, approximately in two thirds of schools, there were plans for disasters and emergencies like, civil defense, defense against sabotages, and fire, and there was a board for disasters. In a research carried out by Ashby (2007) in USA, it was determined that most schools had emergency plans. Burling & Hyle (1997), in their study, investigated the disaster preparation plans of schools in

different regions controlled by United Nations, and they found that most schools had different plans for hazards, especially the schools in regions experiencing unexpected disasters had more comprehensive disaster preparation plans than the schools in regions experiencing seasonal disasters. In the study conducted by Olympia, Wan & Avner (2005) to investigate the preparedness of schools to respond to emergencies in children, it was determined that 418 of 573 schools had made plans for disasters. In their study carried out in Arkansas, Graham, Shirm, Liggin, Aitken & Dick (2006) found that 95 % of schools had evacuation plans, 80% of schools had disaster plans against gunmen attacks, bombs, or biological attacks. In the research on Los Angeles by Kano, Ramirez, Ybarra, Frias & Bourque (2007), school employees indicated that, their schools were very well prepared for disasters and emergencies, and their schools were capable of looking after students 24 hours continuously in emergencies. In the research conducted in state schools in California by Kano & Bourque (2007), most school districts were found to have emergency aid plans and evacuation plans, on the other hand it was found that those schools did not include children who need special care.

According to the research carried out by Öcal (2007) on earthquake preparations in primary schools in Province of Kırıkkale, 74.1% of schools had disaster response plans. Our research results show that level of disaster and emergency plans made at schools in Turkey is lower than the similar plans made at schools abroad.

Our research results show that disaster and emergency aid plans made at private schools are better than the plans made at other schools. This case is thought to have stemmed from such characteristics of private schools as having less number of students, employing experienced staff, employing professional health and security personnel. More than half of the members of sample group indicated that there was A Board for Disasters in their schools, and rest of the members indicated either they didn't know about it, or there wasn't A Board for Disasters in their schools. Our research results are aligned with Afyouni's (2007) research findings in which he indicates that 52% of schools in the sample group had Boards for Disaster Improvement. According to the research conducted by Graham, Shirm, Liggin, Aitken & Dick (2006) in Arkansas, it was reported that all schools had a Crisis Management Team.

Nearly one third of our sample group said that their school plans were made after a hazard and risk analysis process. Öcal (2007), in his study, indicate that many school principals had the risk of their school buildings analyzed. According to a research by Ashby (2007), 99.6% of schools had disaster plans against many hazards

In our research, half of the employees indicated that plans made at their school included all hazards. While approximately one third of respondents said that school plans were made in coordination with, local emergency units, Ashby (2007) in her research, indicated that more than half of schools cooperated with stakeholders to prepare in regards to disaster plans. In the research conducted by Graham, Shirm, Liggin, Aitken & Dick (2006) in Arkansas, schools worked in coordination with the police departments, fire departments, and hospital personnel in their district.

More than half of the respondents of our research indicated that their school plans were updated every academic year. Similarly, in a research conducted by Ashby (2007), more than half of schools (52%) are reported to update their emergency management plans regularly. Though shelters should be included in the disaster plans, only one third of our respondents indicated that their schools had shelters. Parallel to our research, in the research conducted by Ocal (2007), only 31.5% of schools in Kirikkale were found to have a shelter. Delibalta (2005) found that 24% of schools in Kecioren-Ankara didn't have a shelter, and 64% of schools with a shelter didn't comply with the rules and regulations about shelter, and were not up to the standards defined. Our results show that employees find the institutional preparations at their schools insufficient. Half of employees working in private schools think their schools are prepared for disasters and emergencies, whereas this rate is much lower in state schools.

For the scope of general precautions, employees working in state schools indicated that they did not find their schools strong and reliable and indicated that goods and furniture in school buildings were not fixed to the walls enough. Delibalta (2005), in his research in Kecioren-Ankara, reported that school administrators thought that the school

buildings were not built in accordance with the standards described for earthquakes. He also found that in 25% of schools precautions were not taken against materials/goods probable to fall, and 19% of school buildings were over 30 years old. In the research conducted by Ocal (2007) with employees working in primary schools in Kirikkale Province, fixing goods and furniture to the walls to mitigate unstructural damages at primary schools, similar to the findings of our research, was found to be insufficient (63%). In the research by Hosseini (2006) on earthquake risk management planning in schools in Iran, it was declared that International Institute of Earthquake Engineering and Seismology investigated resistance of school buildings in Tahran and most of the school buildings were not found to be earthquake resistant. Milutinovic & Trendafiloski (2005), indicated in their research that, when major natural disasters and human induced disasters The Republic of Macedonia had experienced were considered, 69.4% of school buildings weren't built in accordance with any seismic and security conditions. In the scope of "Istanbul Seismic Risk Mitigation and Emergency Preparedness Project"(ISMEP), until 14 January 2010, 302 schools had been reinforced against earthquakes, and feasibility studies for reinforcement of 673 schools had been completed. In addition, reinforcement process still continues in 12 schools. 22 schools were destroyed and rebuilt in its old location. It is continued to rebuild 23 schools. In 2010 it was planned; to destroy and rebuild 136 schools; to reinforce 100 schools; and to complete feasibility studies of 197 schools. (İstanbul Seismic Risk Mitigation and Emergency Preparedness Project (ISMEP), 2010).

Our research results showed in general that a significant number of schools either did not have emergency exits and fire exits, or employees working at those schools were not aware of the exits. It was found that preparations related to emergency exits in private schools were better those in other school types. Precautions against fire were seen to be the best prepared of the preparations in schools in general. Exercises performed at schools from time to time, are thought to contribute positively to preparations. It was seen that employees working in state schools thought their schools were less prepared for fires than other schools. Similar to the results of our research, the research conducted by Kano &Bourke (2007) in state schools in California, showed that majority of schools had fire extinguishers, and the materials and school buildings were checked for safety. In his research on schools in Kecioren-Ankara, Delibalta (2005) found that fire escape did not exist in 59% of schools, and fire escapes were not usable in the schools in which fire escape existed. Research showed that majority of schools (89%) had equipment to put out fires.

When employee's opinions related to first aid preparations were analyzed, the schools were found to be not prepared enough, but private schools were found to be relatively more prepared than other school types. According to the findings tenured health personnel do not work in nearly all of state schools. Private schools employ health professionals on the other hand. Presence of health professionals at schools is thought to make school staff feel confident about their school and affect the data results positively for private schools. Similar to our research, in a research conducted by Kano & Bourque (2007) in California, it was indicated that there were not sufficient emergency supplies at schools. Ocal (2007) reported that 40.7% of classrooms in primary schools in Kirikkale did not have a first aid kit. In a research carried out by Sapien & Allen (2001), especially insufficiency of advanced emergency equipment at schools was emphasized. In our research, it was seen that not all schools were coordinating with authorities and related organizations about disasters and emergencies. Just as for other sub dimensions and sub sections, for this topic too, average points for state schools are lower than the points for private schools. Results of the research conducted by Kano, Ramirez, Ybarra, Frias & Bourque (2007), Kano & Bourque (2008) in Los Angeles and California parallel with the results of this research.

As for Communications; though private schools were seen to be better prepared, all schools were found to be quite inefficient about communications. It was found that during probable disasters and emergencies, when communication equipment and possibilities were out of use, educational institutions, and schools at first, would be bereft of communications. Parallel with our findings, Ocal (2007), in his research in primary schools in Kirikkale, concluded that although va-

rious communications equipment was needed in schools, there was not internal communication systems in most of the schools (51.9%)

In the study conducted by Olimpia (2005) to investigate preparedness of schools to respond to emergencies in children, 68% of schools were determined to be bereft of communication systems. In the research by Kano, Ramirez, Ybarra, Frias & Bourque (2007), conducted in schools in Los Angeles, nearly all employees indicated that bells and two-way radios were used to communicate during emergencies at their schools.

When logistical preparedness levels of schools considered, half of private school employees indicated that their schools were prepared, this rate fell by half to 24.7% in state schools. While some supplies and materials were stored in private schools as a way of preparedness against disasters, these supplies were not stored in state schools. In the research by Kano, Ramirez, Ybarra, Frias & Bourque, (2007) conducted in Los Angeles with school employees, 70% of schools were found to have torches, batteries, and equipment and materials for children with special medical needs, and less than half of the respondents of the research indicated that their schools had rescue materials. In a research by Kano & Bourque (2007) conducted in California, school employees indicated that logistical materials at their schools were insufficient. For exercises and drills, which are sub-group activities of Institutional Preparedness, schools were seen to be inefficient in general. On the other hand, more exercises were performed in private schools then they were done in state schools. When compared to private schools, more crowded school size and limited exercise areas made exercises in state schools difficult to evaluate, prepare and perform. On the other hand, in a research by Graham, Shirm, Liggin, Aitken & Dick (2006) conducted in Arkansas, it was determined that most schools did not test their school plans with drills and exercises. In the research by Kano, Ramirez, Ybarra, Frias & Bourque, (2007), school employees in California said that exercises for earthquakes were performed the most frequently and after that fire exercises were performed the second most frequently in schools. According to the research conducted by Kano & Bourque (2007) in California, though most schools had emergency aid plans and evacuation plans, majority of those schools did not do the exercises regularly. According to the findings of the research by Ocal (2007) on disaster preparations at primary schools in Kırıkkale, in the vast majority of schools (75.5%), first aid exercises, damage evaluation exercises, fire-extinguishing exercises were performed.

In this research we found that all preparations for post-disaster improvement our schools were quite insufficient. It was seen that aftermath of the disasters had not been considered, and all efforts and planning at schools had targeted to survive from disasters. Altun-Akbaba (2005), in their research, indicated that school principals should develop action plans for disasters at schools and make preparations at schools before disasters.

In the present research, the student and parent participations in disaster and emergency preparedness activities at schools was found to be insufficient. Similarly, Barata, et.al., (2004), Kano, Ramirez, Ybarra, Frias & Bourque (2007), Ocal (2007), Kano & Bourque (2008), also noted that parent and student participation in preparatory activities was inadequate.

As for teachers' level of disaster preparedness, though it was insufficient, teachers working at private schools were found to be more prepared against disasters than their colleagues working in state schools. This result shows that teachers need training on disasters on emergencies. Ocal (2007) also obtained similar results with the present research.

Though its level was higher in private schools our research showed that individual preparedness was quite insufficient in all schools. Employees working in private schools were better informed about the emergency procedures of Individual Preparedness topic than the personnel working in state schools are. To make sure that school emergency plans are performed timely and effectively, tenured personnel should be trained according to emergency response procedures. Procedures are required parts of emergency planning. Based on exercises performed, plans, procedures and training programs need to be renewed every year (Alexander, 2005). Parallel with our research findings, in their research they conducted with school employees in Los Angeles, Kano, Ramirez, Ybarra, Frias & Bourque (2007), also concluded that school staff was inefficient about emergency procedures.

According to research results, it was determined that all school employees did not get enough training on disasters and emergencies. Parallel with our results, Kano, Ramirez, Ybarra, Frias & Bourque's (2007) research also concluded that the school staff were inefficient about first aid training and CPR training. In their research, Olympia, Wan & Avner, (2005) reported that majority of teachers and school administrators (75%) were trained on CPR (Cardiopulmonary Resuscitation). In their research, conducted in California, Kano & Bourque (2007), reported that employees were having training on especially first aid and search and rescue. It was seen that people had not yet developed adequate awareness about individual preparedness training against disasters and emergencies. These training activities should be organized for all school employees and parents.

According to the results of the research, points for teachers working at private schools related to disaster and emergency preparedness is higher than the points for teachers working at state schools. In parallel with our research results, in the research by Shiwaku & Shaw (2007) private school teachers were found to have higher level of information on disasters than their colleagues working in state schools. In the research carried out by Jhangiani (2001) on self-efficacy, previous experience and expectations, significant difference was determined between the individuals who had previously experienced disasters and taken emergency preparedness courses and the individuals who had experienced disasters.

Separately, previously joining emergency preparedness courses was determined to be positively relevant to taking first aid courses and CPR courses. This research showed that the expectation of a disaster in near future increased the interest in emergency preparedness courses, and also enhanced a person's trust in his/her own skills positively. In Ozmen's (2006) research, for questions related to the training of crisis response teams, school principals expressed their opinions as "almost no one in the team had received any training in this field". Sapien & Allen (2001) reported that approximately a third of school personnel (35%) had not received any emergency training.

Though the point for private schools is higher, it is seen that all employees working at schools have low points for emergency response roles to be taken on in a disaster.

Awareness of these roles and fulfilling their requirements will give a chance of surviving to people to experience disasters and other people together with them not only at schools but also anywhere they get caught in a disaster. Higher points for emergency response roles at Private Schools are thought to have stemmed from employing health professionals at private schools. This situation not only raises the psychological level of school employees, but it also motivates them to work more efficiently. In the research conducted by Ocal (2007) in Kirikkale with employees at primary schools, it was determined that: 35.2% of employees were aware of their roles and responsibilities in disaster plans; 31.5% were unaware, and 33.3% were unsure about their roles and responsibilities in disaster plans. In Kano, Ramirez, Ybarra, Frias & Bourque's (2007) research, school employees were asked about their roles in emergency and most employees indicated that they would be responsible for at least one activity in an emergency.

Limitations

This research is limited with voluntary respondents working in Anatolian High Schools, Public High Schools, Commerce Vocational High Schools, Industrial Vocational High Schools, and Private High Schools in Province of Istanbul, and collected data are based on personal information.

Conclusion

In this research designed to evaluate the disaster and emergency preparedness at high schools in Istanbul, disaster and emergency preparedness at high schools was determined to be insufficient, though it was insufficient, preparedness level of private schools was found to be better than other school types.

In addition, A Questionnaire Form for Emergency and Disaster Preparedness in Schools, which was the first form developed for this purpose in Turkey, enabled to evaluate disaster and emergency preparedness objectively, and it was found to be a statistically reliable and valid instrument and included in the literature.

For school administrators and employees, this form is also a guide covering all preparations that should be performed at schools against disasters and emergencies.

In the direction of research findings; with share holder institutions and organizations, it is required: to make risk analyses against disasters and emergencies; to make necessary plans for this aim; to employ qualified health professional in all educational institutions; to make new regulations, practices and institutional changes in order to complete institutional and individual preparedness at all schools in Istanbul, that is under risk of a major natural disaster, earthquake.

Acknowledgements

This research was supported by Marmara University Scientific Research Projects Unit (SAG-C-DRP-250608-0176).

For their contributions to our research; we thank Prof. Dr Mikdat Kadioglu, Director of Center of Excellence for Disaster Management, Research and Applications, Istanbul Technical University and, Prof. Dr. Mustafa Sukru Senocak, Head of Biostatistics and Medical Informatics Department, Cerrahpasa Medical Faculty, Istanbul University.

References

1. *Afyouni, HA., (2007). Perceptions of United States East Coast Higher Education Leaders on Natural Disaster Recovery, Johnson &Wales University, Degree of Doctor of Education, Rhode Island.*
2. *Alexander, D., (2005). Towards the development of a standard in emergency planning,Disaster Prevention and Management, Vol.14, No. 2.*
3. *Altun-Akbaba, S., (2005). Turkish school principals' earthquake experiences and reactions, International Journal of Educational Management, Vol.19. No.4.*
4. *Ashby, M., (2007). Emergency Management, Status of School Districts' Planning and Preparedness, United States Government Accountability Office.*
5. *Barata, IA., Liovera, I., Ward, M., Miele, D., Sama, A., Falitz, S., Rapaport, A., Ayan, J., (2004). Are There Differences Between Households With Children Regarding the Degree of Household Preparedness for a Disaster Such as Fire Flood Earthquake, Blackout or Devastating Act Such as a Terrorist Attack in the Community. Annals of Emergency Medicine, 44:4.*
6. *Burling, WK., Hyle, AE., (1997). Disaster preparedness planning: policy and leadership issues, Disaster Prevention and Management, V 6, N 4, pp.234-244.*
7. *Curtıs, T., Mıller, BC., Berry, H., (2000). Changes in reports and incidence of child abuse following natural disasters, Child Abuse & Neglect, Vol. 24, No. 9, pp. 1151–1162.*
8. *Duff, D., (2006). Disasters and Emergency Management, Forensic Nursing, Jones and Barlett Publishers, London.*
9. *Graham, J., Shirm, S., Liggin, R., Aitken, M.R., Dick, R., (2006). Mass-Casualty Events at Schools: A National Preparedness Survey Pediatrics 2006;117;e8-e15.*
10. *Hosseini, M., (2006). Earthquake disaster risk management planning in schools, Disaster. Prevention and Management, Vol.15. No.4. pp649-661.*
11. *Istanbul Sismik Riski Azaltma ve Acil Durum Hazirlik Projesi (ISMEP), T.C. Istanbul Valiligi Yonlendirme Komitesi IX. Toplantisi Karar Tutanagi. (2010).*
12. *Jhangiani, R., (2001) Predicting earthquake preparedness: The roles of self-efficacy, previous experience and expectations, Report to the Neighborhood Emergency Preparedness Program (NEPP) Workshops, Columbia.*
13. *Kano, M., Bourque, LB., (2007). Experiences With and Preparedness for Emergencies and Disasters Among Public Schools in California, National Association of Secondary School Principals. NASSP Bulletin, Vol. 91, N.3. pg. 201.*
14. *Kano, M., Bourque, LB., (2008). Correlates of school disaster preparedness: main effects of funding and coordinator role, Natural Hazards Review, ASCE.*
15. *Kano, M., Ramirez, M., Ybarra, WJ., Frias, G., Bourque, LB., (2007). Are Schools Prepared for Emergencies? A Baseline Assessment of Emergency Preparedness at School Sites in Three Los Angeles County School Districts, Education and Urban Society, Volume 39 Number 3, 399-422.*
16. *Kara, B., Hatun, S., Aydogan, M., Babaoglu, K., Gokalp, A. S., (2003). Kocaeli Ilindeki Lise Ogrencilerinde Saglik Acisindan Riskli Davranislarin Degerlendirilmesi, Cocuk Sagligi ve Hastaliklari Dergisi, 46: 30-37.*
17. *Kocak, H., (2004). Bir Dogal Afet Olarak Depreme Hazirlikli Olma Bilinci ve Katilim: ABD, Japonya ve Turkiye (Afyon Ili Ornegi), Ankara Univ. Sosyal Bilimler Enstitusu, Ankara, (Danisman: Prof. Dr. A. Mengi).*

18. *Milutinovic, Z., Trendafiloski, G.S., (2005). Open Partial Agreement on the Preventions of, Protection Against and Organization of Relief in Major Natural and Technological Disasters, International Workshop on Regional Co-Operation in the Field Of Risk Mitigation and Emergency Management, Yugoslav Republic of Macedonia.*

19. *Olympia, RP., Wan, E., Avner, JR., (2005). The Preparedness of Schools to Respond to Emergencies in Children: A National Survey of School Nurses. Pediatrics Vol. 116 No. 6.*

20. *Ozmen, F., (2006). The level of preparedness of the schools for disasters from the aspect of the school principals. Disaster Prevention and Management, Vol. 15 No. 3, 2006 pp. 383-395, Emerald Group Publishing Limited 0965-3562.*

21. *Ocal, A., (2007). Ilkogretim okullarında deprem hazirliklari: Kirikkale Il ornegi. Kastamonu Egitim Dergisi, Cilt:15 No:1 1-12.*

22. *Ogel, K.,Taner, S., Eke, C.Y., (2006). Onuncu Sinif Ogrencileri Arasinda Tutun, Alkol ve Madde Kullanim Yayginligi: Istanbul Orneklemi, Bagimlilik Dergisi 2006; 7: 18-23.*

23. *Ozer, N., Donmez, B., (2007). Okul guvenligine iliskin kurumsal etkenler ve alinabilecek onlemler. Milli Egitim, Sayı:173.*

24. *Psychological First Aid: Field Operations Guide, (2005). National Child Traumatic Stress Network and National Center for PTSD.*

25. *Sapien, R., Allen, A., (2001). Emergency preparation in school: A snapshot of a rural state. Pediatric Emergency Care, Vol 17, No 5.*

26. *Shiwaku, K., Shaw, R., (2007). Future perspective of school disaster education in Nepal, Disaster Prevention and Management, Vol. 16, No.4.*

27. *Urkmez, N., (2002). Okullari Acil Durumlara Hazirlama. YORET Postasi, 17.*

Corresponding Author
Aysel Kokcu,
Turkish Red Crescent Society,
Istanbul Directorate,
Turkey,
E-mail: healthmedjournal@gmail.com

Cross-cultural validation of the diabetes self-management scale in Iranian patients

Rahim Tahmasebi[1,2], Azita Noroozi[3]

[1] Department of Biostatistics, Bushehr University of Medical Sciences, Bushehr, Iran,
[2] The Persian Gulf Marine Biotechnology Research Center, Bushehr University of Medical Sciences, Bushehr, Iran,
[3] Department of Health, Bushehr University of Medical Sciences, Bushehr, Iran.

Abstract

Objective: The purpose of this study was to evaluate the validity and reliability of the Diabetes Self-Management Scale (DSMS) translated within the Iranian population. Method: Design of this study had two-stage. Preliminary stage consisted of process of forward and backward translation of Taiwanese version, content validity, and item analysis. Second stage performed to evaluation of psychometric properties by testing the construct validity (by exploratory and confirmatory factor analysis), and internal consistency. Results: Data for psychometric stage were collected from 410 women who referred to a diabetes outpatient clinic in Iran through convenience sampling procedure. Through exploratory factor analysis, 35 items of the scale converged to seven factors with 3 items omission. Construct validity was determined by confirmatory factor analysis through which modified model of DSMS was supported with deleting one factor (interaction with significant others factor). Cronbach's alpha coefficient for the whole scale was obtained as .92, which indicates the reliability of the scale. Conclusion: DMSES with 29 items was reliable and valid for using in Iranian diabetic patients, and cultural factors appeared to play a role in the formation of factors structure in this scale.

Key words: Diabetes self- management, Scale, Validity, Reliability, Cross Cultural

Introduction

Diabetes is becoming a pandemic in the world (Sigurdardottir, 2005). According to the recent estimates of the World Health Organization (WHO), by the year 2030 there will be 366 million diabetic patients in the world (Wild, Roglic, Green, Sicree, & King, 2004). Diabetes complications afford a significant public health burden. Despite developments in medicine and pharmacology, in clinical practice optimal diabetes control remains difficult (Clark, 2008). This incoherence reflects the central role that individuals play in determining their health status. Self-management in diabetes is necessary to keep the illness under control, as much as 95% of the self-care is usually provided by the ill persons (Sigurdardottir, 2005). Self-management behaviors, including physical inactivity, high calorie intake, inadequate blood glucose self-monitoring, and low adherence to medication regimens are risk factors for development of acute and chronic complications (Clark, 2008). Self-management is important in diabetes management because the most important self-management choices affecting the health and well-being of a person with diabetes are made by the person and not by health care practitioners ("Training in flexible, intensive insulin management to enable dietary freedom in people with type 1 diabetes: dose adjustment for normal eating (DAFNE) randomised controlled trial", 2002).

Diabetes self-management is complex behavior and various factors influence it. Whereas diabetes is a life-long challenge, it needs behavioral change in different area of the patient's life, such as work, recreation, meals, and relationships (Lin, Anderson, Chang, Hagerty, & Loveland-Cherry, 2008). Also, self- management of diabetes involved a serial of physiological and psychosocial subjects, including interaction with health care practitioners, self regulation, and adherence to treatment (Lin, Anderson, Hagerty, & Lee, 2008).

Instruments designed to measure self-management should reflect the underlying model upon which they are based (Whittemore, 2000). Lin and et al. designed diabetes self- management scale (DSMS) for Chinese patients. Originally, 74 items were in the DSMS. A pilot study was conducted

to test and refine scale and 20 items were deleted in this stage. Based on principle axis factoring, a shorter instrument with 35 items was attained. The 35 items loaded in five factors model named self- integration, self- regulation, interaction with health professionals and significant others, self-monitoring of blood glucose, and adherence to recommendation regimen. The final DSMS is a 4-point likert type scale, from 1= not relevant to 4= very relevant (Lin, Anderson, Chang, et al., 2008).

Because the DSMS was originally developed for Chinese diabetic patients, it should translate into Persian and carefully reviewed for cultural applicability. Although it might have been established that an instrument has psychometric properties in the original version, it's necessary to evaluate the validity and reliability in the translated version (Polit-O'Hara & Hungler, 1999). Therefore, given the apparent cultural discordance, the large prevalence of diabetic patients, and difference in self-management performance in diabetic patients, it is necessary to confirm whether this scale can be used in Iranian diabetic patients and to see whether the Persian version of this scale is unbiased relative to the Chinese version that exist in English language.

This study aimed to provide evidence for the content, and construct validity and internal consistency of the Iranian version of diabetes self-management scale (DSMS) which could help researchers and health professionals in their potential research and practice in the future.

Method

Preliminary Stage

Cross- cultural evaluation of the DSMS was preceded by a preliminary stage. Because of cultural and language differences, it was necessary to ensure the accuracy and appropriateness of the newly translated instruments to apply it in Iranian diabetic patients. The preliminary stage consisted of translating the Chinese version (published in English language) of the DSMS based on Brislin method (Brislin, 1970), reviewing the instrument with panel of expert for content validity, and conducting a pilot study for item analysis.

1) Translation and back-translation

In cross-cultural research, a critical problem is translation of questionnaire into the language of the population being studied (E. Jones, 1987). Back-translation is needed to confirm meaning equivalence of the original with translated versions (E. G. Jones & Kay, 1992). Therefore, the process of forward–backward translation was used to obtain both semantic and cultural equivalences (Brislin, 1970).

At first, the principal researcher and a bilingual person translated the original scale into Persian. Second, a health education specialist who was fluent in both Farsi and English back-translated the questions from Persian into English. Two faculty members and researchers evaluated the meaning equivalency between the initial translation and the back-translated version of the questionnaire. Due to differences in the structure of two languages, minor adaptations were made to the wording of items during the translation process. Item 1, "managing food portions and choices when eating out" was modified to "managing food amounts and choices when eating out". Item 3, "managing diabetes and participating in social activity" was modified to "participating in social activity despite disease". In item 17, "situations" was converted to "situations and factors". Item 19, "monitoring blood sugar levels and A1c to reach goals" was modified to "monitoring blood sugar levels and A1c to optimal disease control". In item 24 "out-of-range" was changed to "abnormal range".

2) Panel of expert for content validity

The researcher invited 7 Iranian experts, including six health education specialists, and one faculty member in nursing who was an expert in instrument development to evaluate the content of each item. The panel assessed each item using a 3-point Likert-type scale: 1 = essential, 2 = useful but unessential, and 3 = unessential. If each item was rated as option 3, the expert who rated was asked to provide his or her suggestions for modifying it. In this study, no experts rated items as "unessential." A CVR score of .80 or higher indicates good content validity (Lawshe, 1975). CVR score for each question was equal to or more than .78 and total CVR score of 35 items was calculated .89 that was acceptable.

3) Pilot study for item analysis

The newly translated instrument was administered with using a convenience sample of 40 diabetic patients who were fluent in Persian to assess the each item. An item analysis enables researchers to decide which items can be retained and which items should be deleted (Ferketich, 1991; Nunnally & Bernstein, 1994). In this regard, the mean and variance scores of each item were examined through descriptive statistics. An item was dropped if its mean greatly diverged from the total item mean, or if its variance was near zero. In this study, the range of the mean score for the scale was from 1.52 to 3.42 and the range of variance score was from 0.09 to 0.717. Item–total correlation was examined in the next stage. Items 26, 27, and 28 had correlations <.3 (.037, 0.079 and .005, respectively) did not contribute sufficiently to the total score but mean and variance were adequate. Therefore, to avoid possible omission of items that could be clinically significant in a larger sample, we did not delete these items from the pilot study.

Psychometric Testing of Instrument

Exploratory and confirmatory factor analysis performed for construct validity. Exploratory factor analysis (EFA) was used to generate a model. This method is a data-driven approach through which no specifications are made with regard to the number of latent factors (initially) or to the pattern of relationships between the common factors and the indicators.

Confirmatory factor analysis (CFA) as suggested by others was used to confirm the model. CFA can determine how well the proposed model fits the data. In this study, CFA was used to examine and modify the model that emerged from the EFA. For this purpose, several alternative models were tested.

According to Noar, four types of statistical models were used (Noar, 2003):

(a) A one-factor model tested whether DSMS could measure one overall factor, rather than separate factors.

This model would suggest that self-management represent by a one-dimensional construct.

(b) An uncorrelated factors model tests that separate factors are independent. This model would suggest that what is being measured are independent constructs.

(c) A correlated factors model tests that separate factors of DSMS are related to one another. This model would suggest the possibility of a hierarchical model.

(d) A hierarchical model tests the idea that a second-order factor can account for relations between individual factors. Support for this model would suggest that all factors are related to a higher-order factor. Retention of such a model would suggest that summing the total of the entire scale is appropriate and represents a meaningful and interpretable score.

The EFA was done through SPSS version 16 and CFA was completed with LISREL 8.8. Chi-square (χ^2), the adjusted goodness-of-fit index (AGFI), and the root-mean-square error of approximation (RMSEA) were used as model fit criteria. Model was considered fit if AGFI values was greater than .8 and RMSEA less than .06. The comparative fit index of Bentler-Bonett Non Normed Fit Index (NNFI) was selected. Value of .90 or greater for NNFI is recommended as acceptable values for this measure. The Akaike Information Criterion (AIC) was selected as measures of model parsimony. There are no generally accepted cut-off values for the AIC. When comparing models, those with lower AIC values are considered more parsimonious and better models. T value was used for elimination of parameters in CFA, and Modification Index (MI) was used for inclusion of additional parameters (Schumacker & Lomax, 2004).

Also in this stage, internal consistency reliability of the total scale and each factor was assessed with Cronbach's coefficient.

Results

Sample Characteristics

A total of 410 Iranian diabetic patients were recruited in this study through convenience sampling procedure. Median age of diabetic patients was 53 years with range of 15 to 85years old. Median disease duration was 6 years (range: 1 to 40 years). Of these, 21.7% (111) were male and 72.9% (299) were female. Of 410 responder, 76.6 percent (n=314) were educated to primary/secondary level of education, 16.6 percent (n=68) were

graduated to high school level and 6.8 percent of them (n=28) had obtained college degrees.

Of all, 21% (n= 86) were used insulin, 67.6 percent (n= 277) were treated by oral drugs, 3.6 percent (n=15) had nutritional diet and 7.8 percent of them (n=32) were used mixed treatment. Most of the patients in this study had family history of diabetes (63.7 percent).

Construct validity

Exploratory Factor Analysis: Data of 410 patients were used to analyze the factors of the 35-item DSMS. Factors were extracted using Principal axis Factoring Analysis with a promax rotation. The following criteria were used in order to obtain the best fitting structure and the correct number of factors: (1) Eigenvalues greater than 1.0, (2) Cattell's scree test, (3) the percentage of total variance explained by each factor, and (4) factor loading cut-off of .40. The Kaiser–Meyer–Olkin measure of sampling adequacy was .905, showing the sample was large enough to perform a satisfactory factor analysis. Bartlett's test of Sphericity was significant (χ^2 =7893, df = 595, p= 0.000) indicating that there were some relationships among the items (Field, 2000).

The principal axis factoring analysis for DSMS revealed seven factors with an Eigenvalue >1, explaining 65.7% of the total sample variance. After inspecting the scree plot, factor solutions ranging from one to seven factors (Eigenvalue: 10.95, 3.16, 2.80, 2.12, 1.57, 1.31, and 1.06) were considered. These seven components accounted for 31.30%, 9.04%, 8.01%, 6.07, 4.48, 3.73, and 3.03% of variance, respectively. However, factors 8 and 9 with an Eigenvalue <1 (Eigenvalue: .85, and .82) only accounted for 2.44% and 2.34% of variance, respectively.

The results of the factor analysis showed in Table 1. Seven factors emerging from a total of 35 items all loaded above .40, but three items were cross loaded in several factors. Item 18 was loaded in 5 factors and items 19 and 33 were loaded in four factors, therefore these items were deleted (Field, 2000). Seven factors (subscales) related to nutrition and healthy lifestyle (Items 1, 2, 4, 5, 7), illness adaptation (Items 3, 6, 8, 9, 10), self- regulation (Items 11, 12, 13, 14, 15, 16, 17), interaction with health professionals (Items 20, 21, 22, 23, 24, 25), interaction with significant others (Items 26, 27, 28), self- monitoring blood glucose (Items 29, 30, 31), and adherence to recommended regimen (Items 32, 34, 35).

Confirmatory factor analysis: In CFA, the researcher examined whether the model identified by EFA fit the data. Mardia's coefficients for multivariate skewness were 46.16 and for kurtosis were estimated to be 22.6. As these values were significant, robust maximum likelihood estimation procedures were used in this study. A covariance matrix and asymptotic covariance matrix were applied to estimate model.

Several alternative models included one-factor model, uncorrelated factor model, correlated factor model, and hierarchical model were examined against the proposed seven-factor model identified through EFA.

As expected, the correlated model compared to other models fitted more properly. However, the overall fit indices did not reach the criteria of proper fit. The fit indices for the models showed in Table 2. To improve the correlated model, the modification index and t values were applied. According to the highest modification index and conceptual meaning, one pair of correlated-error terms added to the correlated model. Error correlations were between items 1 and 2 based on conceptual meaning. For

Table 2. Fit index confirmatory factor analysis of DMSES

Model	χ^2	df	RMSEA (90% CI)	NNFI	GFI	AIC	AGFI	$\frac{\chi^2}{df}$
One-factor	4629.59	464	.15 (.14- .15)	.76	.53	4754.59	.46	9.98
Uncorrelated	1823.78	464	.085 (.08- .o9)	.92	.74	1951.78	.71	3.93
Correlated	990.25	443	.055 (.05- .06)	.97	.84	1160.25	.81	2.23
Hierarchical	916.54	442	.051 (.05- .06)	.97	.85	1088.54	.82	2.07
Final hierarchical	724.04	361	.05 (.04- .05)	.98	.86	872.04	.84	2

Abbreviation: df, degrees of freedom; RMSEA, root mean square error of approximation; NNFI, non-normed fit index; AIC, Akaike Information Criterion; AGFI, adjusted goodness-of-fit index;

Table 1. Rotated factor analysis of DMSES

No	Items	F1	F2	F3	F4	F5	F6	F7
	F1: Nutrition & healthy lifestyle							
1	Managing food amount and choices when eating out	.832						
2	Managing disease to stay healthy	.788						
4	Considering effect on blood sugar when making food choices	.618						
5	Lifestyle healthier because of diabetes	.603						
7	Managing food choices to control blood sugar	.734						
	F2: Illness adaptation							
3	Participating in social activity despite disease		.424					
6	Managing weight effectively		.502					
8	Exercising to control blood sugar and weight		.803					
9	Merging diabetes into daily life successfully		.729					
10	Adjusting diabetes routine to fit new situation		.741					
	F3: Self- regulation							
11	Understanding reasons for changes in my blood sugar levels			.560				
12	Recognize which signs and symptoms of high and low blood sugar			.848				
13	Acting in response to symptoms			.747				
14	Attending to symptoms of high and low blood sugar			.704				
15	Making decisions based on experience			.502				
16	Treating low blood sugar reactions.			.437				
17	Attending to situations and factors that may affect blood sugar levels			.541				
	F4: Interaction with health professionals							
20	Comfortable discussing degree of flexibility in treatment plan with health care provider and physician				.833			
21	Comfortable suggesting treatment plan changes to health care provider or physician				.886			
22	Comfortable asking health care provider or physician questions				.807			
23	Collaborating with health care provider or physician to identify reasons for poor control				.696			
24	Comfortable discussing abnormal range of blood sugar tests with health care provider or physician				.857			
25	Comfortable asking health care provider or physician about diabetes care resources				.783			
	F5: Interaction with significant others							
26	Asking others for help with high blood sugar					.873		
27	Asking others for help in controlling diabetes					.849		
28	Comfortable asking others for diabetes management tips					.576		
	F6: Self- monitoring blood glucose							
29	Testing blood sugar when experiencing symptoms of high blood sugar						.793	
30	Testing blood sugar when feeling sick						.919	
31	Testing blood sugar when experiencing symptoms of low blood sugar						.761	
	F7: Adherence to recommended regimen							
32	Taking prescribed amount of medication							.792
34	Taking medications at the prescribed times							.946
35	Seeing health care provider or physician every 1-3 months							.469

example, manage food amount when eating out was considered effective to stay healthy. The correlations between factor of interaction with significant others (F5) with Nutrition & healthy lifestyle factor (.05), Illness adaptation factor (-.16), Self- regulation factor (0), interaction with health professionals

factor (.04), and Adherence to recommended regimen factor (.14), were not significant. Therefore, in according to item–total correlation, we deleted this factor with three items (items 26, 27, and 28) and conducted the CFA again. The fit of the DSMS with 29 items especially in AIC was better: $\chi^2 = 724.04$, df = 361, RMSEA = 0.050 (90 per cent CI 0.044, 0.055), NNFI = 0.98, GFA= .86, AGFI = 0.84, AIC = 872.04. Based on the improvement in the χ^2:df ratio, the constancy of the RMSEA value, and the reduction of the AIC value, we determined this scale with 29 items had stronger factorial validity. Fit indices after and before omission of this factor are shown in Table 2.Standardized factor loading in all factors of DSMS ranged from .56 to .89 which were statistically significant ($p<0.001$). Furthermore all residual or error variances ranged from .20 to .70 and were statistically significant ($p<0.001$). The correlations between the factors, were significant ($p<0.001$), suggesting that an oblique solution was appropriate for this proposed model.

Reliability

After confirming factors structures, Cronbach's coefficient alpha was used to assess internal consistency reliability of the total scale and each factor separately in total sample (n = 410). In this regard, Cronbach's coefficient alpha was .92 for the final version of the DSMS. Additionally, these coefficients were .86, .70, .84, .91, .87, and .77 for factors nutrition & healthy lifestyle, illness adaptation, self- regulation, interaction with health professionals, self- monitoring blood glucose, and adherence to recommended regimen respectively.

Discussion

In preliminary stage, for Adapting of existing instrument for cross-cultural use, Brislin's model was used which includes simultaneous translations and back-translations followed by the bilingual experts (Brislin, 1970), and extent of expert agreement in translated items was assessed with CVR. Item analysis is an additional means of finding weaknesses in the measurement and assessment of how well each item contributes to the overall measure (Kim & Han, 2004). In this study, the items were homogenous to the scale, as the mean and variance scores of each item and item-total correlation confirmed its. Therefore, we used a spacious approach to increase efficiency, and to achieve the goals of cultural and functional equivalence. In psychometric stage, results show that the DSMS accounted for 65.7% of the variance in the total DSM scores. This rate was better than 45.66% reported in Lin's study (Lin, Anderson, Chang, et al., 2008). Investigators identified seven factors from the EFA. These seven factors represent concepts that are somewhat different from Lin's (2008) five dimensions. For example, self- integrating factor separated in two factors, including nutrition & healthy lifestyle and illness adaptation. Interaction with health professionals and significant others divided in two factors, because received instruction of health care provider or physician is quite different of significant others. Other factors were similar to Lin's study (Lin, Anderson, Chang, et al., 2008). In EFA, items 18, 19, and 33 were deleted. These items imply to decision making based on blood sugar level, but in Iranian culture, most of the patients attend to physical symptom and act in response to symptoms. This subject was confirmed by factor loading of several items related to physical symptom importance (items 12,13, and 14 with factor loading .848, .747, and .704 respectively). As Nunnally and Bernstein demonstrated, EFA should not be used to confirm factor structure because EFA is a data-driven method for exploring the factor structure of a set of variables (Nunnally & Bernstein, 1994). Therefore, CFA was applied to confirm factor structure. In CFA, a modified correlated factors model with one pair of correlated errors (between item 1 and 2) showed better-fit indices. This model showed interaction with significant others factor was exactly uncorrelated to other factors. By deleting this factor, the AIC and other indicators became better in the modified model. In Lin study, the factor loading of these items (.49, .51, and .51 respectively for item 26, 27, 28) were less than other items in interaction with health professional and significant others factor. Totally, these items are not coordinate to self-management behavior, because self management is personal ability to manage illness and adherence to health care provider directions (Barlow, Wright, Sheasby, Turner, & Hainsworth, 2002). However, diabetic patients need to support of families, fri-

ends, and significant others in the management of their disease. Reliability of the Iranian version of DSMS was high with a value of .92 for the total scale and ranged from .70 to .91 for the subscales, which is appropriate (Jacobson, 2004). Devellis suggested that alpha coefficients greater than .90 may indicate the need to shorten the instrument length (DeVellis, 1991), and Lin suggested further study for it (Lin, Anderson, Chang, et al., 2008). Despite deletion of 6 items, Cronbach's a coefficients in DSMS (.92) especially interaction with health professionals factor (.91) still need further studies to examine whether some more items can be combined or deleted.Notwithstanding use of convenience sampling maybe thought to limit generality of the findings, but the results are of major importance and significances to the diabetic patients in Iran. This study showed that DSMS is valid and reliable scale and could be used to measure self- management among Iranian patients who are suffering from diabetes.

Acknowledgments

This work financially supported by Bushehr University of Medical Science, Bushehr, Iran. The authors are grateful for the participation of all the diabetic patients in this study.

References

1. *Barlow, J., Wright, C., Sheasby, J., Turner, A., & Hainsworth, J. (2002). Self-management approaches for people with chronic conditions: a review. Patient Educ Couns, 48(2), 177-187.*
2. *Brislin, R. W. (1970). Back-translation for cross-cultural research. Journal of Cross Cultural Psychology, 31, 185-216.*
3. *Clark, M. (2008). Diabetes self-management education: a review of published studies. Prim Care Diabetes, 2(3), 113-120.*
4. *DeVellis, R. F. (1991). Scale development : theory and applications. Newbury Park ; London: Sage.*
5. *Ferketich, S. (1991). Focus on psychometrics. Aspects of item analysis. Res Nurs Health, 14(2), 165-168.*
6. *Field, A. (2000). Discovering Statistics Using SPSS for Windows. London: Sage.*
7. *Jacobson, S. F. (2004). Evaluating instruments for use in clinical nursing research. In F. Marilyn & J. O. Sharon (Eds.), Instruments for Clinical Health-Care Research (pp. 73–80). London: Jones and Bartlett.*
8. *Jones, E. (1987). Translation of quantitative measures for use in cross-cultural research. Nurs Res., 36(5), 324-327.*
9. *Jones, E. G., & Kay, M. (1992). Instrumentation in cross-cultural research. Nurs Res, 41(3), 186-188.*
10. *Kim, M. T., & Han, H. R. (2004). Cultural considerations in research instrumentation development. In F. Marilyn & J. O. Sharon (Eds.), Instruments for Clinical Health-Care Research. London: Jones and Bartlett.*
11. *Lawshe, C. H. (1975). A quantitative approach to content validity. Personnel Psychology, 28(4), 563-575.*
12. *Lin, C. C., Anderson, R. M., Chang, C. S., Hagerty, B. M., & Loveland-Cherry, C. J. (2008). Development and testing of the Diabetes Self-management Instrument: a confirmatory analysis. Res Nurs Health, 31(4), 370-380.*
13. *Lin, C. C., Anderson, R. M., Hagerty, B. M., & Lee, B. O. (2008). Diabetes self-management experience: a focus group study of Taiwanese patients with type 2 diabetes. J Clin Nurs, 17(5A), 34-42.*
14. *Noar, S. M. (2003). The role of structural equation modeling in scale development. Structural Equation Modeling, 10(4), 622-647.*
15. *Nunnally, J. C., & Bernstein, I. H. (1994). Psychometric Theory. New York: McGraw-Hill Inc.*
16. *Polit-O'Hara, D., & Hungler, B. P. (1999). Nursing research : principles and methods (6th ed. ed.). Philadelphia: Lippincott.*
17. *Schumacker, R. E., & Lomax, R. G. (2004). A Beginner's Guide to Structural Equation Modelling (2nd ed.). London: Lawrence Erlbaum Associates.*
18. *Sigurdardottir, A. K. (2005). Self-care in diabetes: model of factors affecting self-care. J Clin Nurs, 14(3), 301-314.*
19. *Training in flexible, intensive insulin management to enable dietary freedom in people with type 1 diabetes: dose adjustment for normal eating (DAFNE) randomised controlled trial. (2002). BMJ, 325(7367), 746.*
20. *Whittemore, R. (2000). Strategies to facilitate lifestyle change associated with diabetes mellitus. J Nurs Scholarsh, 32(3), 225-232.*
21. *Wild, S., Roglic, G., Green, A., Sicree, R., & King, H. (2004). Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. Diabetes Care, 27(5), 1047-1053.*

Corresponding Author
Azita Noroozi,
Department of Health Education,
College of Health,
Bushehr University of Medical Sciences,
Bushehr,
Iran,
E-mail: azitanoroozi@yahoo.com

Detection prevalence of inducible clindamycin resistance in Coagulase-Negative Staphylococci (CoNS) isolates in an Iranian 1000-bed tertiary Care Hospital Using D Test

Mohammad Rahbar[1], Mona Mohammad-Zadeh[2], Hossein Masoumi Asl[3], Leila Azimi[4] , Abdolaziz Rastegar Lari[4]

[1] Deparment of Microbiology, Iranian Reference Health laboratory, Ministry of Health and Medical Education, Tehran, Iran,
[2] Department of Microbiology, Milad Hospital, Tehran, Iran,
[3] Center for Communicable Disease Control, Ministry of Health and Medical Education, Tehran, Iran,
[4] Antimicrobial Resistance Research Center, Tehran University of Medical sciences, Tehran, Iran.

Abstract

Background and objectives: Clindamycin is an antibiotic which usually can be used for treatment of infection of skin and soft tissue infection caused by staphylococci. The aim of this study was to determine prevalence of inducible clindamycin resistance among coagulase-negative staphylococci that were isolated in Iranian 1000-bed tertiary care hospital.

Methods: A total of 114 strains of coagulase-negative staphylococci were isolated from clinical specimens. All isolates were identified by conventional microbiological methods. Inducible clindamycin resistance was performed by double disk diffusion method as recommended by Clinical Laboratory Standards Institute (CLSI).

Results: Of 114 isolates coaagulase –negative staphylococci, 107(93.8%) strains were isolated from blood cultures. Of the 114 CoNS isolates 61(53.50%) were resistant to both erythromycin and clindamycin. 10 (8.77%) isolates were resistant to erythromycin but susceptible to clindamycin. Of 114 CoNS 32 (28.07%) isolates were susceptible to both erythromycin and clindamycin. The rate of inducible clindamycin resistance was 9.64%. All inducible clindamycin were methicillin resistant.

Conclusion: Resistance to antimicrobial agents such as macrolides might not be readily apparent by routine testing. It is recommended to implement of the D-test or the Disk induction test as a simple, practical method with routine antibiotic susceptibility testing, for detection inducible and constitutive clindamycin resistance among staphylococci isolates.

Key words: clindamycin, inducible resistance, Coagulase-Negative Staphylococci

Introduction

Coagulase-negative staphylococci (CoNS) are recognized to be an important causing nosocomial and community –acquired infections in worldwide (1,2,3,4). The increasing prevalence of methicillin resistance among CoNS is an increasing therapeutic problem. Vanocmycin is a antibiotic choice for treatment of methicillin resistant CoNS isolates. However vancomycin is an expensive drug and there are many reports regarding increasing reduced susceptibility among CoNS isolates to vancomycin(5,6,7). It is of interest to determine which of alternative antibiotics to vancomycin are suitable for therapy. There are many reports in vitro susceptibility of methicillin resistant CoNS isolates to clindamycin, co-trimoxazol, erythromycin quinolones and tetracycline.

Macrolides (e.g., erythromycin, lincosamid, clindamycin and streptogramin (e.g.,quinupristin-dalfopristin) antimicrobial agents that collectively are named MLS agents. These antibiotics are widely used in the treatment of staphylococcal infections (6, 8).

Resistance to MLS_b antibiotics occurs either through target site modification, efflux of antibiotics, or drug modification. Inducible MLS_b resistance cannot be determined using standard susceptibility test methods, including standard broth-based or agar dilution susceptibility tests (8,9). Clinical laboratory Standard Institutes (CLSI) recently descri-

bed a practical disk diffusion method for detection of inducible clindamycin resistance (D-Zone test). It is involves placing standard erythromycin and clindamycin disks in adjacent position from 15- to 26 mm apart on a Muueller Hinton agar plate when performed standard disk diffusion method. Inducible resistance to clindamycin is manifested by a flattening or blunting of clindamycin zone inhibition adjacent to the erythromycin disk giving a D shape to zone of inhibited growth (Figure 1). It is very important to determine if there is any resistance to clindamycin, when it is candidate for therapy. Antimicrobial susceptibility pattern are important for treatment of infections, however false susceptibility results may be achieved if staphylococci are not tested for inducible resistance by a simple tests known as D-test.

The aim of this study was to determine the prevalence of inducible clindmycin resistance among clinical isolates of CoNS using D-test. We also determined prevalence of all isolates against commonly used antibiotics.

Methods

Clinical isolates of CoNS from different specimens including blood cultures and other specimens between January 2009 and December 2009 in Milad hospital of Tehran were subject of our study. Milad hospital is a 1000-bed non- teaching tertiary care hospital. In total, one hundred and fourteen strains of CoNS isolated from different specimens of patients admitted to our hospital. Duplicate isolates were not included in our study. Out of 114 CoNS 107(93.85%) strains were isolated from blood cultures. The CoNS were identified using standard microbiological procedures. All CoNS were tested by routine disk diffusion method as recommended by CLSI for following antibiotics-erythromycin (15μg), clindamycin (2 μg), ciprofloxacin(5 μg), Penicillin (10U) gentamycin (10 μg), trimethoprim/ sulfamethoxazole (1.25 μg/23.75 μg), oxacillin (1 μg),vancomycin (30 μg), Chloramphenicol (30 μg), Tetracycline (30 μg), Ceftriaxone (30 μg) and Azithromycin (30 μg). All erythromycin-resistant and clindamycin – sensitive CoNS were further tested by D-test for finding inducible clindamycin resistance. Briefly an erythromycin disk was placed 15-26 mm (edge to edge) from a clindamycin disk in a standard disk diffusion test which has been recommended by CLSI (10). Following overnight incubation at 37C, interpretation was done as follows: The disk diffusion test, based on the D test, showed four phenotypes. 1-D test Positive (iMLSB Phenotype): Inducible resistance to clindamycin was manifested by flattening or blunting of the clindamycin zone adjacent to the erythromycin disk, giving a D shape. 2-D-test Negative (MSB Phenotype): No flattening of the Clindamycin zone; Resistant to erythromycin but susceptible to Clindamycin. 3-Constitutive Resistance (cMLSB Phenotype): Resistant to both erythromycin and. Clindamycin (Sensitive (Phenotype): Sensitive to both erythromycin and clindamycin. Quality control (QC) of the erythromycin and clindamycin disks was performed with *Staphylococcus aureus* ATCC 25923 according to the standard disk diffusion QC method. Additional quality control was performed with another in house selected *S.aureus* that showed positive and negative D-test reaction.

Results

During our study in total 408 staphylococcus spp. were isolated from clinical specimens. Of 408 stapylococcal isolates 114 (28%) isolates were CoNS. *S warnery* with 74 isolates were the predominant isolates. Of 114 isolates 107 (93.8%) strains were isolated from blood cultures. Patient age range between nine month to 88 years old and the majority of patents were children. We observed a high rate of resistance among CoNS isolates. The erythromycin and clindamycin resistance

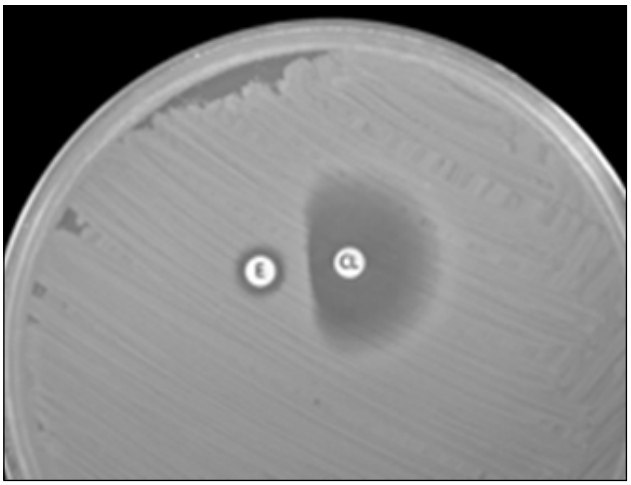


Figure 1. Inducible clindamycin resistance

patterns of CoNS based on disk diffusion method are shown in table 1.

Of the 114 CoNS isolates 61 (53.50%) were resistant to both erythromycin and clindamycin.10 (8.77%) isolates were resistant to erythromycin but susceptible to clindamycin. Of 114 CoNS 32 (28.07%) isolates were susceptible both erythromycin and clindamycin. The rate of inducible clindamycin resistance is shown in table 1. In our study all inducible clindamycin resistance were methicillin resistant and we did not observe any inducible clindamycin among methicillin susceptible CoNS isolates. The antibiotic susceptibility patterns of CoNS isolates are summarized in table 2. All isolates were susceptible to vancomycin except two isolates with intermediate susceptibility. Cholramphenicole was the second most effective antibiotic against CoNS.

Discussion

Coagulase-negative staphylococci are the major causative agents of nosocomial infections, particularly blood stream infections. Nosocomial infections caused by CoNs account nearly 9% of hospital acquired infections[11]. The performance of susceptibility testing remains an important duties of microbiology laboratory for detection methicillin resistance among staphylococci spp [12]. Resistance to methicillin among CoNs is very important due to cross resistance to virtually all beta lactam and other antibiotics. For reason of emergence methicillin resistance among CoNS only a few antibiotics are available to treat infections caused by CoNS. The macrolide-lincosamide – streptogramin B (MLS_b) family are one the alternative, with clindamycin being the preferred antibiotic [11, 13].

Accurate susceptibility data are important for appropriate therapy decisions. However, false in vitro susceptibility results may be obtained by the microdilution method and disk diffusion testing with erythromycin and clindamycin disk is nonadjacent positions. Hence, the routine testing of Staphylococcal isolates for inducible clindamycin resistance is recommended by the CLSI guidelines.[10]

Meticillin resistance among CoNS isolates in comparison with *S.aureus* is prevalent In our study among the 114 CoNS isolates we found 103 (90.35) to be resistant to methicillin which is resemble that reported by other investigators.[14] In study by Sharma in India more than 80% isolates of CoNS were methicillin resistant[15]. A multi center study in China by Sun et al the rate MRCoNS was 89.5% .[16]

Table 1. MLS resistance of CoNS isolates using D-test

Susceptible to Er and CC	phenotype MS	Inducible MLS	Constitutive MLS_b	Total	Organism
21	10	11	61	103	MR-CoNS
11	0	0	0	11	MS-CoNS

MR-CoNS : Methicillin Resistant Coagulase-negative Staphylococci,
MS-CoNS : Methicillin Sensitive Coagulase-negative Staphylococci
Er :Erythromycin,CC: Clindamycin

Table 2. Drug resistance pattern of CoNS isolated from clinical specimens

Resistant (%)	Intermediate (%)	Susceptible (%)	Antibiotic
110(96.49)		4(3.50)	Penicillin
76(29.25)	0(0.0)	38(33.33)	Co-trimoxazole
0(0.00)	0(0.00)	114(100)	Vancomycin
78(68.42)	0(0.00)	36(31.57)	Gentamycin
21(18.42)	0(0.00)	93(81.57)	Chloramphenicol
65(57.01)	0(0.00)	49(42.98)	Tetracycline
94 (82.45)	1(0.08)	19(16.66)	Ceftriaxone
90(70.76)	0(0.00)	24(21.05)	Azithromycin
60 (52.63)	0(0.00)	54(47.36)	Ciprofloxacin

In our study of 114 CoNS isolates,11(9.64%) were iMLSb phenotype which is similar those reports by other investigator from other countries [17] .Studied in our country regarding prevalence of inducible clindamycin resistance among staphylococci spp limited to *S.aureus* [8,18]. However we have only a few reports that describe prevalence of inducible clindamycin among CoNS. In a study by Naderinasb and et al from north east of Iran the rate of inducible clindamycin resistance among CoNs was 5 % [19]. In other study by Shoja et al in north west of Iran only 1% isolates of CoNs was inducible clindamycin resistant[20].

Most of the studies have indicated a higher prevalence of constitutive resistance than inducible resistance in CoNS. In our study the rate of constitutive resistance was 53.50% .The true incidence depends on the patient population studied, the geographical region, the hospital characteristics and Methicillin susceptibility [1].

Conclusion

It is recommended to implement of the D-test or the Disk induction test as a simple, practical method with routine antibiotic susceptibility testing, for detection inducible and constitutive clindamycin resistance. The high rates of occurrence of inducible resistance especially in MRCoNS strains raise concerns that clindamycin failures may occur in treatment of infections caused by these strains. Finally, early detection helps in the use of clindamycin only in infections caused by truly clindamycin susceptible CoNS isoltes and thus helps to avoid treatment failures.

Acknowledgment

This study was supported by a grant No. 504 M/T of Tehran University of medical sciences Tehran, Iran. The author wish to tank for all staff of Microbiology laboratory in Milad hospital of Tehran for technical supports.

References

1. *Kumar S., Umadevi S., Joseph N., Kali A., Easow J., Srirangaraj S., Kandhakumari G., Singh R., Charles P. and Stephen S. Detection of inducible clindamycin resistance in Staphylococcus aureus and coagulase-negative staphylococci - a study from South India. The Inter J Microbiology 2011.9 :(Online)*

2. *Bhat Y R, Lewis LE, Ke V. Bacterial isolates of early-onset neonatal sepsis and their antibiotic susceptibility pattern between 1998 and 2004: an audit from a center in India. Ital J Pediatr. 2011; 37:32-*

3. *Coutinho Vde L, Paiva RM, Reiter KC, de-Paris F, Barth AL, Machado AB. Distribution of erm genes and low prevalence of inducible resistance to clindamycin among staphylococci isolates. Braz J Infect Dis. 2010; 14: 564-8.*

4. *Oğuz VA, Yapar N, Sezak N, Cavuş SA, Kurutepe S, Peksel H, Cakir N, Yüce A. The rate of inducible clindamycin resistance and susceptibilities to other antimicrobial agents in staphylococci Mikrobiyol Bul. 2009; 43 37-44.*

5. *Stuart JI, John MA, Milburn S, Diagre D, Wilson B, Hussain Z.Susceptibility patterns of coagulase-negative staphylococci to several newer antimicrobial agents in comparison with vancomycin and oxacillin. Int J Antimicrob Agents. 2011; 37 248-52. Epub 2011 Feb 4.*

6. *Ciraj AM, Vinod P, Sreejith G, Rajani K. Inducible clindamycin resistance among clinical isolates of Staphylococci. Indian J Pathol Microbiol. 2009; 52:49-51.*

7. *Hemels MA, van den Hoogen A, Verboon-Maciolek MA, Fleer A, Krediet TG. A Seven-Year Survey of Management of Coagulase-Negative Staphylococcal Sepsis in the Neonatal Intensive Care Unit: Vancomycin May Not Be Necessary as Empiric Therapy. Neonatology. 2011; 100: 180-185.*

8. *Rahbar M, Hajia M. Inducible clindamycin resistance in Staphylococcus aureus: a cross-sectional report. Pak J Biol Sci. 2007; 10:189-92.*

9. *Perez LR, Caierão J, Antunes AL, d'Azevedo PA. Use of the D test method to detect inducible clindamycin resistance in coagulase negative staphylococci (CoNS). Braz J Infect Dis. 2007; 11:186-8.*

10. *Performance Standards for Antimicrobial Susceptibility Testing: Sixteenth Informational Supplement M100-S16. Wayne, PA, USA: CLSI; 2006. Clinical Laboratory Standards Institute*

11. *Ferreira RB, Iorio NL, Malvar KL, Nunes AP, Fonseca LS, Bastos CC, Santos KR. Coagulase-negative staphylococci: comparison of phenotypic and genotypic oxacillin susceptibility tests and evaluation of the agar screening test by using different concentrations of oxacillin. J Clin Microbiol. 2003; 41:3609-14*

12. *Caierão J, Musskopf M, Superti S, Roesch E, Dias CG, d'Azevedo PA. Evaluation of phenotypic methods for methicillin resistance characterization in coagulase-negative staphylococci (CNS). J Med Microbiol. 2004; 53 :1195-9.*

13. *Shantala G B , Adithi S S, Rahul RK , Vasudeva Nagarathnamma T. Detection of inducible Clindamycin resistance in clinical isolates of Staphylococcus aureus by the Disc Diffusion Induction Test. J Clin Diagnos Res. 2011; 5:35-37*

14. *Krediet TG, Jones ME, Gerards LJ, Fleer A. Clinical outcome of cephalothin versus vancomycin therapy in the treatment of coagulase-negative staphylococcal septicemia in neonates: relation to methicillin resistance and mec A gene carriage of blood isolates. Pediatrics. 1999; 103(3):E29.*

15. *Pal N, Sharma B, Sharma R, Vyas L. Detection of inducible clindamycin resistance among Staphylococcal isolates from different clinical specimens in western India. J Postgrad Med. 2010; 56: 182-5.*

16. *Sun HL, Wang H, Chen MJ, Liu YM, Hu ZD, Liao K, Chu YZ, Lei JE, Zhang B, Yu YS, Hu BJ, Sun ZY, Zhang Z, He QY. [An antimicrobial resistance surveillance of gram-positive cocci isolated from 12 teaching hospitals in China in 2009 . Zhonghua Nei Ke Za Zhi. 2010; 49: 735-40 (Article in Chinese)*

17. *Angel MR, Balaji V, Prakash J, Brahmadathan KN, Mathews MS.Prevalence of inducible clindamycin resistance in gram positive organisms in a tertiary care centre. Indian J Med Microbiol.2008; 26 262-4;*

18. *aderi H, Emadi B, Owlia P. Phenotypic and genotypic study of macrolide, lincosamide and streptogramin B (MLSB) resistance in clinical isolates of Staphylococcus aureus in Tehran, Iran. Med Sci Monit. 2011; 17(2): 48-53.*

19. *Naderinasb M. Farshadzadeh S, Yousefi F, Sasam MS. Detection the inducible phenotypic methicillin resistanat Staphylococus auerus and coagulase-negative staphylocooi .Iran J Med Microbiol. 2007; 1: 25-31*

20. *Shoja S, Nahaei MR, Nashaei M. Detection of inducinle clindamycin resistance in Staphylococcus aureus and Staphylocoocus epidermidis by using D-test. Pharmaceutical Sciences. 2009; 15: 1- 8*

Corresponding Author
Abdolaziz Rastegar Lari,
Antimicrobial Resistance Research Center,
Tehran University of Medical Sciences,
Tehran,
Iran,
E-mail: lari@tums.ac.ir

Nonlinear methods of heart rate variability analysis in diabetes

Ana Laura Ricci Vitor[1], Naiara Maria de Souza[1], Roselene Modolo Regueiro Lorenconi[1], Carlos Marcelo Pastre[1], Luiz Carlos de Abreu[2], Vitor Engracia Valenti[3], Luiz Carlos Marques Vanderlei[1]

[1] Departamento de Fisioterapia, Faculdade de Ciências e Tecnologia da Universidade Estadual Paulista - UNESP, Presidente Prudente, SP, Brazil,

[2] Departamento de Morfologia e Fisiologia, Faculdade de Medicina do ABC, Santo André, SP, Brazil,

[3] Departamento de Fonoaudiologia, Faculdade de Filosofia e Ciências da Universidade Estadual Paulista - UNESP, Marília, SP, Brazil.

Abstract

Background: The autonomic dysfunction stands out among the complications associated to diabetes *mellitus* (DM) and may be evaluated through the heart rate variability (HRV), a noninvasive tool to investigate the autonomic nervous system that provides information of health impairments and may be analyzed by using linear and nonlinear methods. Several studies have shown that HRV measured in a linear form is altered in DM. Nevertheless, a few studies investigate the nonlinear behavior of HRV. Therefore, this study aims at gathering information regarding the autonomic changes in subjects with DM identified by nonlinear analysis of HRV.

Methods: For that, searches were performed on Medline, SciELO, Lilacs and Cochrane databases using the crossing between the key-words: diabetic autonomic neuropathy, autonomic nervous system, diabetes mellitus and heart rate variability. As inclusion criteria, articles published on a period from 2000 to 2010 with DM type I and type II population which assessed the autonomic nervous system by nonlinear indices HRV were considered.

Results: The electronic search resulted in a total of 1873 references with the exclusion of 1623 titles and abstracts and from the 250 abstracts remaining, 8 studies were selected to the final analysis that completed the inclusion criteria.

Conclusions: In general, the analysis showed that the nonlinear techniques of HRV allowed detecting autonomic changes in DM. The methods of nonlinear analysis are indicated as a possible tool to be used for early diagnosis and prognosis of autonomic dysfunction in DM.

Key words: autonomic nervous system, diabetic autonomic neuropathy, diabetes *mellitus*.

Introduction

Diabetes mellitus (DM) is a heterogeneous group of metabolic disorders which may be classified according to etiology in two main clinical classes: type 1 DM (DM1) and type 2 DM (DM2). They both present the common characteristic of hyperglycemia. This disease is associated to multiple complications that lead to dysfunction or failure in different organs (1-4).

Among the most common complications, it is highlighted the diabetic autonomic neuropathy (DAN) which is poorly recognized and understood despite its significant effects on several organs and systems (5-8). The most important form of DAN is cardiovascular autonomic neuropathy (CAN), it causes negative impact on the regulation of blood pressure, heart rate and heart rate variability (HRV) (9).

HRV is a clinical feature that can be observed by non-invasive tool to investigate the autonomic nervous system (ANS) it describes the oscillations of the intervals between consecutive heartbeats. It may be analyzed by linear and nonlinear methods and the changes in such patterns provide information on adaptations of abnormal autonomic modulation and health impairments (10, 11).

The linear analysis uses simple mathematics technics like statistics, geometrics and spectral methods that represents the autonomic nervous system and these components sympathetic and parasympathetic (10); while the HRV analysis through nonlinear methods are based on the chaos theory and have received attention because it is related to high irregular fluctuations of the complex series of the heart rate and it allows a better discrimination between normal and abnormal physio-

logy of human systens (12-14). Numerous studies have shown that HRV measured in a linear methods is altered in individuals with CAN (15-17). However, few studies investigated the nonlinear behavior of HRV in individuals with DM.

The lack of studies regarding to nonlinear indices and the importance of understanding conditions such as diabetes, which influence the proper functioning of the ANS, reinforce the importance of studies related to the issue. Thus, this study aimed at gathering information about the autonomic changes in DM subjects identified by means of nonlinear analysis of HRV in order to insert elements in the literature and contribute to the better comprehension of researchers and clinicians working with this population.

Methods

The structure of this methods were based on a assertion Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) that could be found on: www.prisma-statement.org.

Search strategy and selection

The revisions were made between September 2010 and October 2010. The Medline (via PubMed), Lilacs and Cochrane databases were searched using the following subject keywords: "diabetic autonomic neuropathy", "autonomic nervous system", "*diabetes mellitus*" and "heart rate variability". These words were defined by the Health Sciences Descriptors (DeCS) and their corresponding in English - Medical Subject Headings (MeSH).

The studies were selected by a reviewer and supervised by a senior reviewer. Based on the titles and abstracts, we excluded manuscripts not clearly related to the subject of the review. Thereafter, all the selected titles and abstracts were submitted to a final evaluation which considered the inclusion criteria and its reference lists independently checked to identify studies of possible relevance that were not found in the electronic search.

We excluded studies that presented no abstract or full text in English between 2000 to 2010 population with DM1 and DM2 subjects, those ones which studied a cause relationship, consequence and complication in relation to the reduction of HRV analyzed only by linear methods, as well as the ones addressed forms of drug and non-drug treatment for the reduction of HRV also by linear methods and experimental studies or literature reviews. As inclusion criteria we considered clinical trials that investigated the DM by using nonlinear HRV indices.

Results

The electronic search provided a total of 1873 references. Among these references, the first elimination resulted in the exclusion of 1623 titles and abstracts which were not clearly related to the subject of review. The titles of the remaining 250 abstracts were submitted to a final evaluation that took into account the inclusion criteria. The investigation of the reference lists confirmed the absence of relevant documents. Summaries of the eight studies analyzed were selected (Figure 1). Among the eight texts that made up the final selection, two are available in abstract form. Table 1 shows the levels of variability and the main results and conclusions of the studies included in this update.

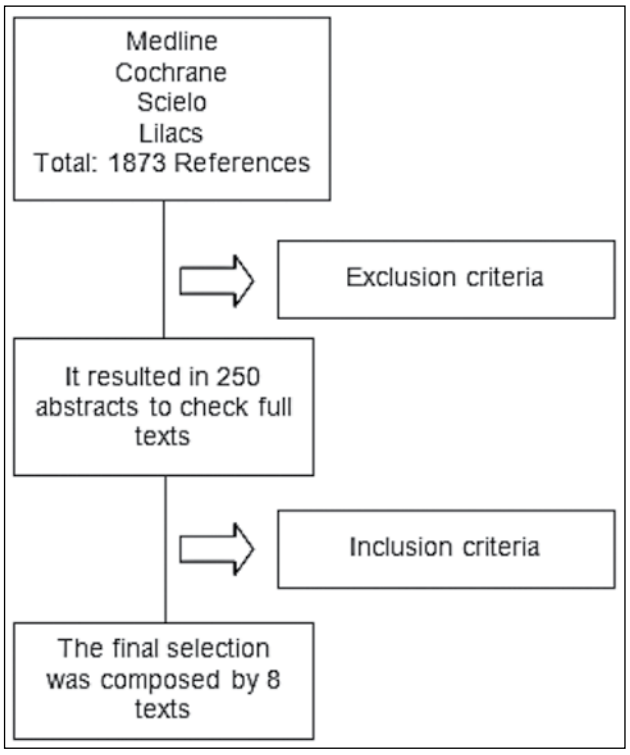


Figure 1. Chart that summarizes the search strategy and selection

Table 1. Studies using methods of nonlinear analysis of HRV in DM between 2000 and 2010

Authors and year	Rated index	Main conclusions
Li et al., 2003.	Lyapunov exponent[1]; ApEn[2]; Fractal dimension; Allan Factor; Complexity; Nonlinear energy operator[3]; Wavelet standard deviation.	They found that regardless of the presence of DAN, the nonlinear indices were different from healthy subjects with emphasis on the indexes[1, 2] and [3].
Curione et al., 2005.	Correlation dimension.	They found inversion of the circadian rhythm in DM2, which suggests that the chaotic component of the HRV have abnormal pattern during the day and may be potential indicator of cardiac autonomic dysfunction in this population.
Javorka et al., 2005.	MeanRR; SDNN *; RMSSD *; PNN50 *; LF (ms²) *; HF (ms²)*; Plot Poincaré *; SampEn.	They reported that several parameters based on nonlinear dynamics allowed distinguishing the difference of cardiac regulation in young type 1 diabetes subjects compared to healthy individuals.
Contreras et al., 2007.	LF *; HF *; SD1 for 1 to 10*.	They achieved significant reduction in rates of the frequency domain linear component and SD1 in the study group and this significant correlation with LF and HF regardless of the delay. In the control group they observed significant correlations between SD1 and HF for 1 and 2 delays, with LF and HF for 3 and 4 to 10 with LF.
Javorka et al., 2008.	MeanRR *; SDNN *; RMSSD *; LF *; HF *; EME (2-4) *; Compressão Entropy; Shannon Entropy ; Renyi Entropy 0,25 e 4*; Normal complexity index*; standard classification.	The magnitude and complexity of HRV are reduced in young patients with DM.
Javorka et al., 2008.	Det% *; L_{max}; TT *; L_{am} *; %Rec.	The measures derived from RQA revealed changes in the recurrence dynamics with reducing the complexity of mechanisms controlling heart rate in young people with diabetes. These parameters can be used together with other HRV parameters to better describe the breakdown in the regulation of HR in this population.
Trunkvalterova et al., 2008.	MeanRR; SDNN; RMSSD*; SampEn*; EME*.	MSE can detect abnormalities in cardiovascular control in type 1 diabetes young subjects.
Khandoker et al., 2009.	SDNN; RMSSD; LF; HF; LF/HF; SD1; SD2; SD1/SD2; original SampEn *; surrogate SampEn [=].	They found a significant reduction for CAN + SampEn and only for the visual analysis of the plot. SampEn and SD1/SD2 combined and are more sensitive to detect NAC than the Ewing test.

Footnotes: **: significantly different; DM1: type 1 diabetes, DM2: type 2 diabetes; CAN: cardiovascular autonomic neuropathy; DAN: diabetic autonomic neuropathy; HRV: heart rate variability; LF: low frequency; HF: high frequency; SDNN: Standard deviation of all normal RR intervals recorded in a time interval, expressed in ms; RMSSD: Root-mean square of differences between adjacent normal RR intervals in a time interval, expressed in ms; PNN50: Represents the percentage of adjacent RR intervals with a difference of duration greater than 50ms; SD1: standard deviation of the RR interval analyzed in short term in ms; SD2: standard deviation of the RR interval analyzed in short long in ms; ApEn: approximate entropy; SampEn: Sample entropy; EME: Multiscalte entropy analysis; RQA: Recurrence quantification analysis; L_{max}: Diagonal maximal length; L_{am}: Mean diagonal width; Rec: percentage of recurrence points; Det: Determinism; ms: milliseconds; TT: trapping time.*

Discussion

In general, the analysis of the selected texts for this review demonstrated that nonlinear methods for HRV analysis allowed detection of autonomic changes in DM and indicated this method to be used as a tool for early diagnosis and prognosis of autonomic dysfunction in these subjects.

It is well established in the literature that the conventional linear methods of HRV analysis can differentiate healthy from sick individuals, even in patients with DM. In addition, previous studies showed that HRV assessed by these methods is altered in individuals with CAN (15-17), the most important clinical form of DAN (9), a condition that is associated to significant impairments in quality of life of their bearers (5), the manifestations in the gastrointestinal and genitourinary (6) and the relationship with cardiovascular (7) and cerebrovascular events (8).

Early detection of CAN is vitally important to take preventive measures (9) and previous studies indicated that these changes are detectable by analysis of HRV even in subclinical stage (15, 16, 18). Despite the nonlinear methods are considered more effective to characterize the complex dynamics of the modulation of heart rate (19-22) than the linear methods, few researches investigated the nonlinear behavior of HRV in DM subjects.

Considering that the human body and its mechanisms of cardiovascular regulation interact in a deterministic and nonlinear way, the human body is better understood as a complex system and the use of nonlinear analysis of HRV provides greater sensitivity in detecting health compromises (12, 14). The nonlinear techniques allow describing features in qualitative analysis of HRV that provide additional information to quantitative assessments usually performed (9, 20, 22).

Among the selected studies, the following nonlinear indices were able to detect changes in autonomic DM: Lyapunov exponent, the complexity index, nonlinear energy operator, correlation dimension (23, 24), Poincaré plot (9, 20, 25), Sample entropy (SampEn) (9, 20, 22), Approximate entropy (ApEn) (23), multiscale entropy (EME) (21, 22), Renyi entropy (21), determinism (% Det), length of vertical lines - trapping time (TT) and laminarity (Lam) (18).

Methods commonly used for nonlinear analysis of HRV, as the Lyapunov exponent and correlation dimension were effective in detecting autonomic changes in DM, however, they require long periods of recording signals as a condition for their analysis. Thus, new methods have been continually developed (19) and among other characteristics, to be used for analysis in shorter periods of recording.

Among the new methods, the Poincaré plot, entropy and recurrence, just to mention some, have shown that the complexity of HRV is reduced in young patients with DM and seems more affected when analyzed in a linear fashion (9, 19, 21, 22, 25). Li et al. (23) showed significant difference, especially for the Lyapunov exponent, ApEn and the nonlinear energy operator, between diabetic and normal subjects regardless the presence or absence of CAN, indicate that autonomic dysfunction is not due to CAN but the presence of DM. Furthermore, the authors concluded that these methods indicate the state of the autonomic system and can be effectively used to detect CAN in the early stages. On the other hand, Khandoker et al. (9) compared DM2 subjects with and without CAN and discovered that autonomic dysfunction is more pronounced when CAN is present. The authors reported significant reduction of Poincaré plot and entropy in the CAN group and also reduced SDNN, RMSSD, SD1, SD2 indices in the CAN group despite the difference was not significant.

Khandoker et al. (9), also evaluated the sensitivity and specificity of linear indices of HRV, the Poincaré plot, Surrogate SampEn and SampEn compared to Ewing tests. Among the indexes evaluated, the SampEn had a sensitivity of 100% and specificity of 62.5%. However, when combined with SD1/SD2 indices obtained from the Poincaré plot it showed greater accuracy with 100% sensitivity and 88.24% of specificity. It should be noted that the association of two nonlinear indices demonstrated dysfunction of autonomic control with a greater sensitivity to identify the CAN than the Ewing tests. Besides that the graphical analysis of the Poincaré plot and SampEn have been increasingly used due to the facility to be obtained from short electrocardiogram recordings.

Using the correlation dimension, Curioni et al. (24) observed changes in the circadian rhythm of DM2 patients compared to healthy subjects, su-

ggesting that sick patients have abnormal patterns of HRV during the day and this can be a potential indicator of silent CAN .

Contreras et al. (25) reported changes in HRV in DM1 individuals compared to a control group, characterized by a reduction of the SD1 index of the Poincaré plot as well as in linear LF and HF indices obtained in the frequency domain. Their study group was about 54 years old (minimum 44 and maximum 66 years old) and the use of routine medications, enalapril, insulin and amiodarone were allowed. Noteworthy is the fact that among the analyzed studies this was the only one to mention the routine use of medication in this population. Also investigating the Poincaré plot, Javorka et al. (19) compared the data from DM1 subjects to a control group and observed a reduction of the Poincaré plot in all lengths and widths (10, 25, 50, 75 and 90º percent of the distribution of RR intervals), lower percentage points in the 3rd quadrant of the plot and reduced rates of linear time domain and frequency for the DM1 group.

The aforementioned authors also identified a negative correlation between the average RR interval and the percentage of points in quadrant II and IV of the Poincaré plot with the albumin-creatinine ratio and blood glucose level. Based on these results, the authors suggested that blood glucose levels and renal status of the patient (represented by the albumin-creatinine ratio) influence the autonomic function in DM1 patients (19).

Compared to the previous presented study, Contreras et al. (24) also identified changes in LF, HF and SD1 which indicate autonomic dysfunction. But in a younger DM1 population [average age 22.4 years ± 1)], which could indicate that despite the age influence HRV (26) in DM1 individuals age does not interfere.

Javorka et al. (21) identified autonomic changes in DM1 patients characterized by a statistical significant. Reduction of EME for 2, 3 and 4 scales, compression entropy, Renyi entropy with a weighting of 4. Moreover, lower values for the index of complexity for all standard and linear indices studied were also identified. The authors also reported that for the SampEn, scales up to 5 EME, with Renyi's entropy weighting of 0.25 and Shannon entropy, no significant results were obtained. In this study, the authors presented a great variety of information to demonstrate the clinical stability of patients such as metabolic control investigated through the quantification of $HbA1_c$ and plasma glucose, body composition and stability of blood pressure and heart rate.

Considering the selected studies, only Javorka et al. (20) made a correlation of an indicator of stability/instability with clinical indices of HRV in DM1 subjects. Trunkvalterova et al. (22) examined whether EME linear methods in the time domain (SDNN, RMSSD and average RR interval) would detect changes in young DM1 patients and as a result they identified statistical significant difference in the RMSSD and EME indexes. The authors reported that the EME allows better discrimination between healthy and young DM1 subjects compared to linear measurements in the time domain.

In the same line, Javorka et al. (21) concluded that HRV obtained through analysis of EME and compression entropy were able to detect diagnostic information of changes in heart rate in DM patients and suggest that the combination of these variables with linear measurements would provide a better diagnostic tool for the CAN.

In the same year, Javorka et al. (19) extended the evaluation of nonlinear dynamics in DM1 individuals by performing a quantitative analysis of the recurrence plot which showed a reduction of complexity in heart rate control with potential prognostic and diagnostic value. The results of this study showed a significant increase of% Det without significance for Lmax between the groups. For the analysis of vertical lines, differences were detected in TT which were also higher also for the study group, but no difference regarding to Lmax and Lam. According to the authors, one advantage of this method is that the structures of recurrence are recorded along the way, it does not require a pre-condition for filtering data.

The analysis of the literature on HRV in DM subjects has some gaps that need a broader approach to add information to clinical practice such as the following questions: does the presence of CAN effectively influence the outcome? Do the changes that culminate in clinical instability the changes in body composition and metabolic parameters changes aggravate the autonomic dysfunction? And how much is the use of routine medications, the time of illness and age affect the autonomic

behavior of these individuals, as well as the loss of complexity and simplification of the dynamics of heart rate influenced by the type of DM?

In summary, the information gathered in this review allowed to indicate able nonlinear methods for HRV analysis to detect autonomic changes in DM and could be preferred over the linear methods because allows a better discrimination between normal and abnormal physiology. The use of these methods independ on the cooperation of patients for its realization (9), provide additional information related to the autonomic behavior (21) and direct towards the improvement of the power of diagnosis and prognosis of autonomic dysfunction in this population (18, 21). Additionally, in a clinical routine assessment the magnitude and complexity represented by the nonlinear index can be easily quantified in small ECG recording and may be useful for monitoring drug and nonpharmacological treatment strategies in these individuals (20).

Taking into consideration the potential of HRV as a clinical tool to evaluate and identify health impairments and assuming that the nonlinear techniques allowed detection of autonomic changes in DM and is indicated to be used as a tool for early diagnosis and prognosis of autonomic dysfunction in DM suggests a wide path of research and clinical application of this method in DM patients and could be preferred over the linear methods because allows a better discrimination between normal and abnormal physiology.

References

1. *American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care. 2010; 33 (suppl 1): 62-69.*

2. *Oliveira AF, Valente JG, Leite IC, Schramm JM, Azevedo AS, Gadelha AM. Global burden of disease attributable to diabetes mellitus in Brazil. Cad Saúde Pública. 2009; 25(6): 1234-1244.*

3. *Oliveira AF, Valente JG, Leite IC. Fração da carga global do diabetes mellitus atribuível ao excesso de peso e à obesidade no Brasil. Rev Panam Salud Pública. 2010; 27(5): 338-344.*

4. *Sociedade Brasileira de Diabetes. Tratamento e acompanhamento do diabetes mellitus: Diretrizes da Sociedade Brasileira de Diabetes. 2007: 1-168.*

5. *Vinik AI, Erbas T. Recognizing and treating diabetic autonomic neuropathy. Cleve Clin J Med. 2001; 68(11): 928-930.*

6. *Vinik AI, Freeman R, Erbas T. Diabetic autonomic neuropathy. Semin Neurol. 2003; 23(04): 365-372.*

7. *Whang W, Bigger JT. Comparison of the prognostic value of RR-interval variability after acute myocardial infarction in patients with versus those without diabetes mellitus. Am J Cardiol. 2003; 92(3): 247-251.*

8. *Toyry JP, Niskanen LK, Lansimies EA, Partanen KP, Uusitupa MIJ. Autonomic neuropathy predicts the development of stroke in patients with non-insulin-dependent diabetes mellitus. Stroke. 1996; 27(8): 1316-1318.*

9. *Khandoker A, Jelinek H, Palaniswami M. Identifying diabetic patients with cardiac autonomic neuropathy by heart rate complexity analysis. Biomed Eng Online. 2009; 8(3).*

10. *Vanderlei LC, Pastre CM, Hoshi RA, Carvalho TD, Godoy MF. Noções básicas de variabilidade da frequência cardíaca e sua aplicabilidade clínica. Rev Bras Cir Cardiovasc. 2009; 24(2): 205-217.*

11. *Pumprla J, Howorka K, Groves D, Chester M, Nolan J. Functional assessment of heart rate variability: physiological basis and practical applications. Int J Cardiol. 2002; 84(1): 1-14.*

12. *Godoy MF. Teoria do caos aplicada à medicina. [Tese de Livre Docência]. São José do Rio Preto: Faculdade de Medicina (FAMERP); 2005. 179. Livre docente em Cardiologia. [citado em: março 2011]. Disponível em: http://www.mfgodoy.med.br/caos.pdf.*

13. *Voss A, Kurths J, Kleiner HJ, Witt A, Wessel N. Improved analysis of heart rate variability by methods of nonlinear dynamics. J Electrocardiol. 1995; 28 (suppl. 1): 81-88.*

14. *Ferreira MT, Messias M, Vanderlei LCM, Pastre CM. Caracterização do comportamento caótico da variabilidade da frequência cardíaca (VFC) em jovens saudáveis. Tend Mat Apl Comput. 2010; 11(2): 141-150.*

15. *Schönauer M, Thomas A, Morbach S, Niebauer J, Schonauer U, Thiele H. Cardiac autonomic diabetic neuropathy. Diab Vasc Dis Res. 2008; 5(4): 336-344.*

16. *Maser RE, Mitchell BD, Vinik AI, Freeman R. The association between cardiovascular autonomic neuropathy and mortality in individuals with diabetes. Diabetes Care. 2003; 26(6): 1895-1901.*

17. *Ewing DJ, Neilson JMM, Shapiro CM, Stewart JA, Reid W. Twenty four hour heart rate variability: effects of posture, sleep, and time of day in healthy controls and comparison with bedside tests of autonomic function in diabetic patients. Br Heart J. 1991; 65(5): 239-244.*

18. *Ewing DJ, Campbell IW, Clarke BF. Heart rate changes in diabetes mellitus. Lancet. 1981; 1(8213): 183-186.*

19. *Javorka M, Trunkvalterova Z, Tonhajzerova I, Lazarova Z, Javorkova J, Javorka K. Recurrences in heart rate dynamics are changed in patients with diabetes mellitus. Clin Physiol Funct Imaging. 2008; 28(5): 326-331.*

20. *Javorka M, Javorková J, Tonhajzerová I, Calkovska A, Javorka K. Heart rate variability in young patients with diabetes mellitus and healthy subjects explored by Poincaré and sequence plots. Clin Physiol Funct Imaging. 2005; 25(2): 119-127.*

21. *Javorka M, Trunkvalterova Z, Tonhajzerova I, Javorkova J, Javorka K, Baumert M. Short-term heart rate complexity is reduced in patients with type 1 diabetes mellitus. Clin Neurophysiol. 2008; 119(5): 1071-1081.*

22. *Trunkvalterova Z, Javorka M, Tonhajzerova I, Javorkova J, Lazarova Z, Javorka K, et al. Reduced short-term complexity of heart rate and blood pressure dynamics in patients with diabetes mellitus type 1: multiscale entropy analysis. Physiol Meas. 2008; 29(7): 817-828.*

23. *Li YQ, Gao F, Geng Q, Deng QK. Nonlinear dynamic analysis of heart rate variability in patients with diabetic autonomic neuropathy. Di Yi Jun Yi Da Xue Xue Bao. 2003; 23(2): 133-137.*

24. *Curione M, Cugini P, Cammarota C, Bernardini F, Cipriani D, De Rosa R, et al. Analysis of the chaotic component of the sinusal R-R intervals as a tool for detecting a silent cardiac dysautonomia in type 2 diabetes mellitus. Clin Ter. 2005; 156(4): 151-158.*

25. *Contreras P, Canetti R, Migliaro ER. Correlations between frequency-domain HRV indices and lagged Poincaré plot width in healthy and diabetic subjects. Physiol Meas. 2007; 28(1): 85-94.*

26. *Takahashi AC, Porta A, Melo RC, Quitério RJ, Silva E, Borghi-Silva A, et al. Aging reduces complexity of heart rate variability assessed by conditional entropy and symbolic analysis. Intern Emerg Med. No prelo 2011.*

Corresponding Author
Ana Laura Ricci Vitor,
Faculdade de Ciências e Tecnologia - FCT / UNESP,
Departamento de Fisioterapia,
Presidente Prudente,
Brazil,
E-mail: analaura.ricci@yahoo.com

Determine the effect of punch strokes on hearing levels of boxers

Ragip Pala

School of Physical Education and Sport, Firat University, Elazig, Turkey

Abstract

Although the injury risks of boxing is well known, this sport continuous to attract athletes and an increase of introduction to boxing is observed in the last decade. In terms of injury locations, head and face are reported as most common sports. Present study aimed to examine the hearing differences of elite amateur boxers as a result of punch strokes in boxing.

Subjects are interested in active boxing for 5-14 years (mean 6.67) and between the age of 18-32 (mean 21.71). Screened group consisted of 21 male boxers. Auditory brainstem responses, pure tone and high frequency audiogram tests were conducted for boxers and unscreened groups in the standard acoustically controlled rooms using Interacoustics Clinical Computer Audiometer.

Mean ± standard deviations are reported. Groups were compared by Student's *t* test $p<0.05$. Auditory brainstem responses and pure tone values were determined in range of I-V inter-pick latency (ms).There were no statistically significant differences in the hearing level of elite amateur boxers in contrast to non-boxers. It is seen to be important that amateur boxers wear protective materials as a helmet and mouth guard to minimize the risk of injury. The use of protective equipment must be encouraged for boxer's health.

Key words: Hearing, boxer, punch, boxing, sport

Introduction

A combat sport, also known as a fighting sport, is a competitive contact sport where two competitors fight under certain rules of engagement. Boxing is an example of combat sports and the one of the oldest sports. Two opponents make effort for success using their fists (1). Boxing may result in injuries to various parts of the body including injury associated with chronic, repetitive head blows (2). Permanent brain, eye and hearing damage of retired boxers exist as result of the repeated blows against their head (3).

Compulsory helmets and change in the scoring system is an important step to minimize the risk of boxing injury. In the past 30 years, significant improvements in ringside and medical equipment, safety, and regulations have resulted in a dramatic reduction in the fatality rate (4). Nevertheless, especially loss of hearing still occurs in post-traumatic events (5).

Superficial facial lacerations and head injuries are the most common injury reported in boxing (6). The extent of the injuries is correlated to the number of bouts fought. Due to the repeated and numerous blows against their head, hearing problems should not be ignored. In fact, a punch in boxing that turns the head can cause serious hearing problems (7) but the results are not conclusive. Since information on the incidence of hearing injuries in amateur boxing is limited. This study aimed to examine the hearing effects of punch strokes in boxing.

Methods

Participants: Screened group consisted of 21 male boxers of the Turkish national team. Boxers are involved in elite competitions such as World Championships, European Championships and Olympics for more than five years. Comparison group at the same age consisted of 21 healthy male, who had no hearing loss and head trauma. The stories and demographic characteristics (age, sports age and gender) were recorded from all participants. Subjects with former hearing problems or disorders that resulted in loss chronic neurological disease, subjects using an autotoxic agent, or with trauma and those with a history of hearing loss in their families were excluded from the study. All subjects were examined by an otolaryngologist and had a systemic examination.

Tests: The audiometric tests were carried out for all participants in the standard acoustically controlled rooms using Interacoustics Clinical Computer Audiometer Model AC-40 (Denmark). Measurements were made after rest period in a silent environment. To determine the hearing thresholds at 250, 500, 1000, 2000, 4000, (pure tone) 8000, 10000, 12000 and 16000 Hz (high frequency), the standard ascending/descending (after attenuation to inaudibility in 5-10 dB steps, the signal to be increased "until the tone is heard") method was applied to all subjects. Tests were performed in the frequencies at octave intervals from 250 to 16000 Hz and from 500 to 4000 Hz for air conduction and bone conduction, respectively. Hearing loss was defined as a decrease in the threshold sensitivity of 20 dB or greater at one or more test frequencies in relation to the baseline measurement. Auditory brainstem responses (BERA) test, wave amplitudes and interval ranges were evaluated to the all subjects. This study was performed at a University Medical Center. Informed consent was obtained from the subjects prior to the study. The design and procedures approved by Fırat University Ethical Committee.

Statistical analyses: The Statistical Package for the Social Sciences program was used for data analysis. Results were presented as mean ± standard deviation. Groups were compared by Student's *t* test $p<0.05$. BERA values were determined in I-V inter-pick latency durations.

Results

The screened group consisted of 21 boxers, who were active boxers for 5-14 years (mean 6.67) and were between the age of 18-32 (mean 21.71) (Table.1).

There were no statistically significant differences in I-V inter-pick latency durations in BERA test with the click stimulus of the unscreened and screened groups ($p<0.05$) (Table.2). BERA and high frequency averages were evaluated both the unscreened and screened groups. In standard audiometry, no statistically significant were found differences in boxer's hearing thresholds than unscreened group. In high-frequency hearing thresholds, an increase was found in 8000, 10000, 12000 and 16000 Hz hearing thresholds of boxers. However, increase in hearing thresholds was statistically significant only in 8000 and 12,000 test frequencies. Other test frequencies were not significant (Table. 3).

Discussion

Injuries are common in boxing. This is considered an occupational damage. In fact, ear injuries have represented only a relatively small percentage of all problems. In our study, there were no statistically significant differences in the hearing level of elite amateur boxers. Test results are in normal levels. Yet, it is important that amateur boxers wear protective materials as a helmet and mouth guard to minimize the risk of injury.

It is generally considered greater exposure to injury in many boxers in cochlea after blunt trauma. Although injuries of the ear are not threatening life, they may account for significant morbidity. They may cause severe pain, hearing loss, tinnitus, or vertigo. Ear trauma may occur secondary to a number of mechanisms, including blunt trauma (8).

In the literature found 107 injuries were reported from 427 fight participations, corresponding to an injury rate of 250.6 injuries per 1000 fight participations. The most frequently injured body region was the head/neck/face (89.8%), followed by the upper extremities (7.4%). Injury rates for amateur boxers have been reported at 9.1 injuries per 100 personal exposures and 14.0 injuries per 100 boxers respectively (9). The majority of these injuries were lacerations to the head and face. An increasing age and an increasing number of fights were both significant predictors of injury (10). There is only a small risk for serious injury, and that injuries occur in a hierarchy of upper extremity (441, 25%) and head/face (344, 19%) for amateur boxers (11).

Table 1. Descriptive statistics of boxers

	N	Minimum	Maximum	Mean	± SD
Age	21	18.00	32.00	21.7143	4.20883
Sport age	21	5.00	14.00	6.6667	2.76285
Gender	42	1.00	1.00	1.0000	.00000

Table 2. BERA values of control and boxers groups

Tests	Controls	Boxers
BERA test 30 nHL *	5.10 ± 0.64	4.86 ± 0.51
BERA test 40 nHL *	4.88 ± 0.63	4.94 ± 0.59
BERA test 50 nHL *	4.45 ± 0.55	4.50 ± 0.28

** Value of I-V inter-pick latency (ms). Data were given as mean ± standard deviation. Groups were compared by Student's t test (p<0.05).*

Table 3. Test frequency data of control and boxers groups

Test frequency (Hz)	Mean hearing threshold (dB HL)	
	Controls (21 subjects, 42 ears)	Boxers (21 subjects, 42 ears)
250	14,10 ± 6,34	15,93 ± 8,16
500	11,79 ± 5,04	13,69 ± 7,49
1000	10,48 ± 5,16	9,52 ± 4,79
2000	10,83 ± 5,51	12,02 ± 7,16
4000	11,55 ± 4,62	14,52 ± 10,75
8000	13,45 ± 5,89	19,88 ± 9,21*
10000	20,76 ± 5,77	21,67 ± 9,28
12000	19,00 ± 6,22	28,81 ± 11,14*
16000	24,57 ± 14,87	27,29 ± 14,99

** p<0.001 (Students't-test); Mean ± SD*

In a review of boxing data from the state of Nevada from September 2001 through March 2003, the overall incidence rate of injury was 17.1 per 100 boxer-matches, or 3.4 per 100 boxer-rounds. Facial laceration accounted for 51% of all injuries, followed by hand injury (17%), eye injury (14%), and nose injury (5%) (Fitzgerald 1996).

Brain injury in boxing, both acute and chronic, is the major risk for potential catastrophe. In spite of the perceived brutality associated with the sport, most injuries are minor, although serious injuries and deaths do occur, most commonly due to brain injury (12). Also brain injury from repetitive head blows has been reported in the boxer population (13). Besides permanent brain damage due to repeated and numerous blows to head, severe permanent damage to the hearing organ exists (2). Moreover, hearing disorders such as Tinnitus is a significant symptom that commonly occurs as a result of head or neck trauma can occur in athletes (14).

A study investigated the incidence, pattern, and severity of injuries resulting from participation in amateur boxing. The incidence of injuries in competition was 0.92 injuries per man-hour of play (or 0.7 injuries per boxer per year), while the incidence in training was 0.69 injuries per boxer, per year (15).

Another study related to hearing problems conducted a health management survey to identify the potential causes of boxing injuries. After a fight, many of the corresponding boxers complained from headache/heaviness in the head, tinnitus, difficulty in hearing and vertigo. Some experienced headache, ringing in the ears, and difficulty in hearing and vertigo in their daily lives (7). Our research has supported this temporary condition on amateur boxers. We think that the use of protective equipment must be encouraged for boxer's health.

A study supports the relevance of the neurophysiologic assessment of athletes engaged in violent sports which can cause brain impairment (16). There is increasing evidence that boxing can lead to chronic brain damage, ranging from mild subclinical dysfunction to the slowed motor performance, tremors, memory defects and slowness of thought associated with severe neurological impairment (17).

A review of the available records indicates that there have been a substantial number of fatalities in amateur boxers due to intracranial injuries sustained in the ring in comparison to the numbers of boxers at risk (18). Nonetheless, the rate of boxing-related head injuries, particularly concussions, remains unknown, due in large part to its variability in clinical presentation. Furthermore, the significance of repeat concussions sustained when boxing is being understood (4).

The safety of boxing is an issue that stimulates emotive responses on both sides of the debate, and calls to ban the sport continue. Nevertheless, on the basis of a systematic review, it was concluded that the current evidence, such as it exists, for chronic traumatic brain injury as a consequence of amateur boxing is not strong (19).

Conclusion

In conclusion, it is well known that injuries are common in boxing, occurring most often in head region. Many people have thought that the boxing is so dangerous that it should be abolished. In fact, compulsory wearing of helmets and other protective materials in amateur boxing competitions are important step to minimize the risk of injury.

Our results have been shown that there isn't any problem seriously in the hearing level of elite amateur boxers due to the use of protective equipments. Although there wasn't increase in hearing thresholds of elite amateur boxer's standard audiometry, we found a statistically significant increase in high-frequency audiometry at hearing thresholds 8000 and 12000 Hz. This situation is to show the less exposure to trauma of boxers due to the use of protective.

On the other hand amateur boxing is different from professional boxing, and has unique rules and equipment. There may be considerably greater exposure to injury in professional boxers in cochlea after blunt trauma. Further comparative studies are valuable to determine the optimal injury prevention strategies in professional versus amateur boxing. We recommend that future research should collect more knowledge on the formation of injury, as this is important for the development of effective injury prevention strategies.

Acknowledgments

I thank to Erol Keleş, MD, Faculty of Medicine, Fırat University and Yüksel Savucu PhD, School of Physical Education and Sport, Fırat University for their support and comments on this manuscript.

References

1. *Varlık S. Fundamentals of boxing. Öztek Pressing. Ankara. 1982: pp21-22.*
2. *Unterharnscheidt F. A neurologist's reflections on boxing. V. Conclude remarks. Rev Neurol 1995: 23(123): 1027-32.*
3. *Kaste M, Kuurne T, Vilkki, J, Katevuo K, Sainio K, Meurala H. Is chronic brain damage in boxing a hazard of the past? Lancet 1982: 27; 2(8309): 1186-8.*
4. *Jayarao M, Chin LS, Cantu RC. Boxing-related head injuries. Phys Sportsmed 2010: 38(3): 18-26.*
5. *Fitzgerald DC. Head trauma: hearing loss and dizziness. J Trauma 1996: 40: 488-96.*
6. *Bledsoe GH, Li G, Levy F. Injury risk in professional boxing. South Med J 2005: 98(10): 994-8.*
7. *Ohhashi G, Tani S, Murakami S, Kamio M, Abe T, Ohtuki J. Problems in health management of professional boxers in Japan. Br J Sports Med 2002: 36: 346-353.*
8. *Turbiak TW. Ear trauma. Emerg Med Clin North Am 1987: 5(2): 243-51.*
9. *Zazryn TR, Finch CF., McCrory P. A 16 year study of injuries to professional boxers in the state of Victoria, Australia. Br J Sports Med 2003: 37: 321-324.*
10. *Zazryn TR, McCrory PR, Cameron PA. Injury rates and risk factors in competitive professional boxing. Clin J Sport Med 2009: 19(1): 20-5.*
11. *Timm KE, Wallach JM, Stone JA, Ryan EJ. Fifteen years of amateur boxing injuries/illnesses at the United States Olympic training center. J Athl Train 1993: 28(4): 330-4.*
12. *Gambrell RC. Boxing: medical care in and out of the ring. Curr Sports Med Rep 2007: 6(5): 317-21.*
13. *Corsellis JAN. Boxing and the brain 1989: 298: 105-109.*
14. *Folmer RL, Griest SE. Chronic tinnitus resulting from head or neck injuries. Laryngoscope 2003: 113(5): 821-7.*
15. *Porter M, O'Brien M. Incidence and severity of injuries resulting from amateur boxing in Ireland. Clin J Sport Med 1996: 6(2): 97-101.*
16. *Rodriguez G, Vitali P, Nobili F. Long-term effects of boxing and judo-choking techniques on brain function. Ital J Neurol Sci 1998: 19(6): 367-72.*
17. *Richard J. Butler MSc. Neuropsychological investigation of amateur boxers. Br J Sp Med 1994: 28(3).*
18. *Ryan AJ. Intracranial injuries resulting from boxing. Clin Sports Med 1998: 17(1): 155-68.*
19. *Loosemore M, Knowles CH, Whyte GP. Amateur boxing and risk of chronic traumatic brain injury: systematic review of observational studies. BMJ 2007: 20; 335(7624): 809.*

Corresponding Author
Ragip Pala,
School of Physical Education and Sport,
Fırat University,
Elazig,
Turkey,
E-mail: ysavcucu@hotmail.com

Effects of the preoperative anxiety and depression on the postoperative pain in rhinoplasty and septoplasty patients

Altuntas EE[1], Kavakcı O[2], Kugu N[2], Muderris S[1]

[1] Department of Otorhinolaryngology, Faculty of Medicine, Cumhuriyet University, Sivas, Turkey,
[2] Department of Psychiatry, Faculty of Medicine, Cumhuriyet University, Sivas, Turkey.

Abstract

Objective: Anxiety and depressive disorders can be widespread among patients who are being treated in surgical clinics and they can affect operation outcomes. The aim of this study was to investigate the relationship between the level of their anxiety and depression in the preoperative period and the pain level in the postoperative period in rhinoplasty and septoplasty patients.

Material and methods: This study included 57 (51.8%) patients (rhinoplasty group) with external nasal deformity and 53 (48.2%) patients (septoplasty group) with septum deviation. These patients filled out the Hospital Anxiety and Depression Scale, sociodemographic data evaluation form before the surgery. Pain severity was rated by Visual Analogue Scale on the 1st postoperative day and before being discharged from the hospital by the patients.

Results: The mean depression score of all patients was 6.35±3.52 (range 1-15). The mean depression scores were 6.31±3.8 (range 1-15) in the rhinoplasty group and 6.37±3.2 (range 1-14) in the septoplasty group. There was no significant difference between the depression scores of two groups (t=0.091, p=0.927, P>0.05). The mean anxiety score of all patients was 6.5±3.38 (range 0-16). The mean anxiety scores were 6.73±3.34 (range 0-16) in the rhinoplasty group, and 6.24±3.44 (range 0-16) in the septoplasty group. There was no significant difference between the anxiety scores of two groups (t=0.75, p=0.049, P>0.05).

There was minimum positive correlation between the anxiety and depression level of the all subjects and 1st postoperative day Visual Analogue Scale score (r=0.05, p>0.05). There was a minimum positive correlation between the anxiety and depression level of the all subjects and before being discharged from the hospital Visual Analogue Scale score (r=0.06, p>0.05). But these correlations were not statistically significant.

Conclusion: The result of this study in this patient group showed that the presence of anxiety and depression preoperatively in septoplasty and rhinoplasty patients had not affected the pain level postoperatively.

Key words: Preoperative anxiety, preoperative depression, postoperative pain, rhinoplasty, septoplasty

Introduction

Nasal obstruction is one of the most common patient reports in otolaryngology and facial plastic surgery practices. Rhinoplasty is one of the most common cosmetic surgeries and the correction of septal deviation is one of the most common interventions performed by the otolaryngologist. The major indications for rhinoplasty are: cosmetic and cosmetic-functional. Currently septoplasty is used a technique that involves the remodeling of the bone and cartilaginous septum with a functional purpose while attempting to preserve the septal architectural elements [1].

Cosmetic surgeries are done to improve function and have a remarkable effect on physical and mental health [2, 3]. Nasal septal deviation causes impaired nasal breathing, and several pathologies such as developmental disorders, frequent infections, mental disorders olifactory and gustatory disorders may develop as a result of impairment in respiration, which is one of the most significant functions of the nose [4]. It is known that quality of life is impaired with the nasal obstruction.

Minimize post-operative pain after the surgery will increase satisfaction. Beforehand, measurements were performed using retrospective assessment of satisfaction or visual analogue scales.

The hypothesis of this study are ; (1) Rhinoplasty and septoplasty patients have higher pre-operative anxiety and depression levels (2) In these patients, preoperative anxiety and depression levels affect the post-operative pain levels.

Material and Methods

This prospective case-control study was performed at Cumhuriyet University Hospital between the dates May 2010-September 2011. This study included 57 (51.8%) patients (rhinoplasty group) with external nasal deformity and 53 (48.2%) patients (septoplasty group) with septum deviation. All patients were informed of the surgical procedure and examination process, written informed consent was obtained from each participants, and full medical history were obtained from all participants.

All subjects in the study underwent a detailed Ear Nose and Throat (ENT) examination by the same investigator (EA). The decision of surgery was given by the same physicians.

Basic criteria for selection of the patients are; (1) Chronic nasal obstuction should be the principal complaint of septum deviation, (2) subsisting of these complaints at least three months, (3) unimproved complaints in spite of at least four weeks medical therapy, (4) use of topical nasal steroids, topical or oral decongestant or oral antihistaminic and decongestant combination as medical treatment, (5) Consistency of the categorization of traumatic deformation to type 2, type 3 and type 4 category according to the severity of trauma that was represented in the study which had been performed by Higuera at al [5].

The exclusion criteria were impaired communicative or cognitive abilities, neurological disease, diabetes mellitus, hypertension, malignancy, renal failure, patients who develop complications and use of opioid medications. Furthermore, the patients who had sinonasal malignancies, taken radiation therapy to head and neck, septum surgery together with sinus surgery, been performed septoplasty, rhinoplasty, turbinoplasty and chronic sinusitis surgery before, acute nasal trauma patients, and the patients who had an anamnesis of nasal fracture within last three months and nasal valve collapse or a situation such as sarcoidosis, Wegener's granulomatosis, un-managealbe asthma and pregnancy were excluded from the study.

Sociodemographic data form was administered to all subjects. This form was prepared by researchers to collect information on variables such as participants' age, education, marital status, medical history and cigarette and alcohol use and occupational status.

In this study, Hospital Anxiety and Depression Scale was used as a short, reliable and meaningful evaluation criteria. HADS developed by Zigmond and Snaith [6] were administered to all subjects in the preoperative period in order to determine the levels of anxiety and depression and to measure the change in their severity. This scale was adapted to Turkish and reliability and validity findings were published by Aydemir et al [7]. The HADS is a 14-item scale with two sub-scales; one measuring depression, the other measuring anxiety. Each item is rated from 0 to 3. Scores are summed up separately. For the Turkish form of HADS, cut off score for anxiety scale was 10 and cut off for the depression scale was 7.

After collection of preoperative data, pain severity was rated by VAS on the 1st postoperative day (VAS 1) and before being discharged from the hospital (VAS 2) by the patients.

The patients' postoperative analgesic medication needs and the routes of analgesic application were monitored and noted down by the clinician. Analgesics were not applied routinely to the study participants; the route and frequency of analgesic application were determined according to the pain severity of the subjects. Contraindications to the specific agents were also noted. Some groups of analgesics (500 mg parasetomal tablet) were applied orally and intravenously while 1 gram Dipyrone ampoule (1 g/2 ml) was applied intramuscularly. Subjects were able to ask for changing the dosing regimen by rating their pain severity.

Statistical Package for Social Science (SPSS) 14.0 software program (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. Of the sociodemographic data, the categorical variables were expressed as numbers and percentages while the quantitative data were presented as mean ± standard deviation. Group comparisons were made using the Chi-square test. The correlation between all scores of the scale was evaluated using the Pearson correlation tests. A p value <0.05 was considered to be statistically significant.

Results

Overall 110 subjects were enrolled in this prospective case-control study which included 57 patients with external nasal deformity in rhinoplasty group [45 (78.9%) men, 12 (21.1%) women] and 53 patients with septum deviation in normal septoplasty group [39 (73.6%) men, 14 (26.4%) women]. Both groups were similar in term of gender ($x^2 = 0.43$, p=0.508, P>0.05).

The mean age of all patients was 24.60±6.69 years (range 15-52 years). The mean age was 23.4±7.29 (range 15-52 years) [25.83 ±6.93 years for women (range 16-40 years) and 22.76 ±7.33 years for men (range 15-52 years)] in the rhinoplasty group. In the septoplasty group, the mean age was 25.88±5.77 (range 15-40 years) [24.28±5.92 years for women (range 16-35 years) and 26.46 ±5.68 years for men (range 15-40 years)]. There was no significant difference between the two groups (t=1.96, p=0.052, P>0.05). While 69 of the subjects (62.7%) had high school education and above, 41 of them (37.3%) had lower education level. Seventy five subjects (68.2%) were unemployed, 35 of them (31.8%) were employed. While 97 (88.2%) of the subjects were not using alcohol, 13 of them (11.8%) reported rare alcohol use. Thirty-nine of the total number of participants (35.4%) reported cigarette use, 13 (11.8%) reported past history of smoking and 58 of them (52.7%) had never smoked. These data of both groups are summarized in Table 1. The VAS scores rated in the 1st postoperative day (VAS 1) and before being discharged from the hospital (VAS 2) are summarized in Table 2.

There was minimum positive correlation between the anxiety and depression level of the all subjects and VAS1 score (r=0.05, p>0.05). There was minimum positive correlation between the anxiety and depression level of the all subjects and VAS2 score (r=0.06, p>0.05). But these correlations were not statistically significant.

The mean depression score was 6.35 ±3.52 (range 1-15). The mean depression score was 6.31±3.8 (range 1-15) [4.67±2.77 for women (range 2-10) and 6.76 ±3.94 men (range 1-15)] in the rhinoplasty group. In the septoplasty group, the mean depression score was 6.37±3.2 (range 1-14) [5.0±2.48 for women (range 2-11) and 6.87 ±3.34 for men (range 1-14)]. There was no significant difference between the two groups depression scores (t=0.091, p=0.927, P>0.05).

The mean anxiety score was 6.5 ±3.38 (range 0-16). The mean anxiety score was 6.73±3.34 (range 0-16) [7.25±2.3 for women (range 4-10) and 6.6 ±3.58 for men (range 0-16)] in the rhinoplasty group. In the septoplasty group, the mean anxiety score was 6.24±3.44 (range 0-16) [7.36±3.75 for women (range 3-15) and 5.84 ±3.28 for men (range 0-16)]. There was no significant difference between the two groups anxiety scores (t=0.75, p=0.049, P>0.05).

According to HADS cut-off score, depression was detected in 22 (38.6%) of the patients in the rhinoplasty group and 24 (45.3%) of the patients in the septoplasty group. There was no difference between the two groups (x^2=0.51, p=0.477, P>0.05). According to HADS cut-off score, anxiety was detected in 14 (24.6%) of the patients in the rhinoplasty group and 9 (17.0%) of the patients in the septoplasty group. There was no difference be-

Table 1. Characteristics of the sample

Alcohol use		**n (%)**
Rhinoplasty group	Yes (Rarely)	6 (10.5%)
	No	51 (89.5%)
Septoplasty group	Yes (Rarely)	7 (13.2%)
	No	46 (86.8%)
Cigarette use		**n (%)**
Rhinoplasty group	Active smoker	22 (38.6%)
	Quit smoking	4 (7%)
	Nonsmoker	31 (54.4%)
Septoplasty group	Active smoker	17 (32.1%)
	Quit smoking	9 (17%)
	Nonsmoker	27 (50.9%)
Educational level		**n (%)**
Rhinoplasty group	Lower than high school education	16 (28.1%)
	High school and higher education	41 (71.9%)
Septoplasty group	Lower than high school education	25 (47.2%)
	High school and higher education	28 (52.8%)
Occupation		**n (%)**
Rhinoplasty group	Unemployed	40 (70.2%)
	Employed	17 (29.8%)
Septoplasty group	Unemployed	35 (66.0%)
	Employed	18 (34.0%)

Table 2. Postoperative VAS scores

Group	Score	VAS 1 (n/%)	VAS 2 (n/%)
Rhinoplasty group	0–3 Score	11 (19.3%)	50 (87.7%)
Septoplasty group		5 (9.4%)	35 (66.0%)
Rhinoplasty group	4–6 Score	41 (71.9%)	7 (12.3%)
Septoplasty group		21 (39.6%)	18 (34.0%)
Rhinoplasty group	7–9 Score	5 (8.8%)	0 (0%)
Septoplasty group		27 (50.9%)	0 (0%)

tween the two groups (x^2=0.95, p=0.329, P>0.05). The depression and anxiety levels of subjects according to the gender are presented in Table 3.

Data for route of analgesic application are summarized in Table 4. There was no significant difference between the two groups route of analgesic application (t=1.31, p=0.193, P>0.05).

Discussion

This study was to investigate the relationship between the level of their anxiety and depression in the preoperative period and the perceptions of pain level in the postoperative period in rhinoplasty and septoplasty patients with the HADS and VAS. It is remarkable that the literature usually has a tendency of publishing the studies comparing the preoperative and postoperative psychological status in septoplasty and rhinoplasty patients.

Psychological factors such as anxiety and/or depression have been reported to be important predictors of the postoperative pain status. Studies carried out on this topic have indicated that postoperative pain could be minimized when patients with high level of anxiety were identified and treated appropriately in the preoperative period [8]. Wallace [9] and Brander [10] have shown that there were associations between preoperative anxiety and the increase in the postoperative pain and duration of wound recovery. Many studies have been reported that interventions directed to preoperative anxiety improved postoperative behavior and recovery [11, 12]. Besides medical treatment, different methods such as pychoeducation [13], music [14], hypnosis [15] and relaxation [16] have tried in order to reduce the pain level after the surgery. The results of these studies have implications for future studies for the use of new techniques to reduce the anxiety level before surgery.

Based on the history and demographic data of rhinoplasty and septoplasty patients, the average patient is defined as a single, 24-year-old young woman with reasonable economic status and a university degree that is jobless, has had no previous aesthetic surgery and has undergone surgery for aesthetic reasons [17, 18]. Most of the rhinoplasty and septoplasty patients in this study were in the same age group as those for whom Schulman et al.[17] and Zahiroddin et al.[18] studies. Unlike the studies of Schulman [17] and Zahiroddin [18] most of our cases were males of marriageable age who are dependent on their families due to unemployment. Various studies have reported different rates of depression and anxiety in these operations such as; de Lima Ramos et al.[19] investigate the quality of life, self-esteem, and depression in patients with nasal deviation, using quality-of-life questionnaires that have been tested for reliability, validity, and sensitivity, to determine the real psychological impact of this facial feature on the

Table 3. Depression and anxiety scores of subjects

Group	Gender	Depression		Anxiety	
		n (%)	n (%)	n (%)	n (%)
		Yes	No	Yes	No
Rhinoplasty group	Male	20 (44.4%)	25 (55.6%)	11 (24.4%)	34 (75.6%)
	Female	2 (16.7%)	10 (83.3%)	3 (25.0%)	9 (75.0%)
Septoplasty group	Male	21 (53.8%)	18 (46.2%)	5 (12.8%)	34 (87.2%)
	Female	3 (21.4%)	11 (78.6%)	4 (28.6%)	10 (71.4%)

Table 4. Route of analgesic application

Route of analgesic application	Rhinoplasty group n (%)	Septoplasty group n (%)
Intravenous	23 (% 40.4)	21(%39.6)
Oral	18(% 31.6)	22(%41.5)
Intravenous+oral	16 (% 28.1)	10 (%18.9)
Total	57 (%100.0)	53 (%100.0)

patient's life. Patients with nasal deviation (n = 32) were assigned to the study group, and patients without nasal deviation (n = 28) were assigned to the control group in this study and quality-of-life was assessed using the Medical Outcomes Study 36-Item Short Form Health Survey questionnaire; the Rosenberg Self-Esteem/Federal University of São Paulo, Escola Paulista de Medicina Scale; and the 20-items Self-Report Questionnaire.

Depression was detected in 11 patients (34.4 %) in the study group and in two patients in the control group, with a significant difference between groups. In the present study, nasal deviation was found a risk factor for depression and had a negative impact on quality of life. Patients with nasal deviation reported higher depression scores on the 20-items Self-Report Questionnaire than did controls. These important results revealed the psychological and emotional state of the patients, and indicate that further and broader studies on depression are necessary. Zahiroddin et al. [18] studied the relationship between mental health and self-concept with rhinoplasty requests in referral cases of rhinoplasty to the oral and maxillofacial surgery and ear, nose and throat wards of Taleghani Hospital in Tehran and the matched controls during 2003–2004. The comparison of sub-groups mental health of rhinoplasty patients (i.e. depression, anxiety, somatic complaints, and social maladjustment) in which 6% of controls and 8% of rhinoplasty patients had a high cut-off point on the depression score. Twelve per cent of controls and 15% of rhinoplasty patients had high cut-off points on their anxiety score and they said that results shows there is no relationship between mental healths to undergo rhinoplasty. ,

In this study, average rates of depression and anxiety remained below the cut-off point of HAD in the evaluated group. The results of this study did not confirm our first hypothesis that depression and anxiety were higher in this group, only 48 patients(43.64%) were over cut-off score for depression and 23 patients (%2.09) were above the cut-off score for anxiety. Similar findings were reported at different surgical procedure in literature [20, 21]. Anxiety and depression scales of our patients were found to be higher when compared to other findings over the patients who have been performed septoplasty and/or rhinoplasty in various studies [18, 19]. This difference between anxiety and depression scores may be due to the different social and cultural structures.

Along with findings that anxiety and depression scales of our patients were higher, nevertheless anxiety and depression with pain perception was primarly evaluated and any relation was detected between them. The results that we obtained from this study showed us both all the patients did not have anxiety and depression before surgery and there was no difference between two groups. Henceforth, the results of our study did not confirm our second hypotesis either. The reason of this may be the elective and minor surgery or expectation of becoming more beautiful than before after this cosmetic surgery.

Navarro-García et al.[22] investigated the preoperative levels of anxiety and depression in patients awaiting heart surgery and to identify the risk factors associated with the development of these mood disorders and evaluated the relationship between preoperative anxiety and depression and postoperative morbidity and pain. According to their findings preoperative anxiety increased the postoperative pain in these patients.

Ene et al. [20] evaluate the relationship between preoperative factors that have been shown to predict postoperative pain and the self-reports of pain intensity in a population of 155 men undergoing radical prostatectomy, and also to investigate if previous pain score could predict the subsequent pain score. Possible or probable preoperative anxiety was reported by 25% of these patients

and there was no significant correlation between preoperative anxiety (HAD-A) and postoperative pain. The incidence of preoperative depression was lower 12%, but depression was found to correlate with postoperative pain in this study. These results show that it would be meaningful to identify radical prostatectomy patients at high risk for severe postoperative pain; depressive patients who might benefit from a more aggressive therapy instituted in the very early postoperative period.

In studies of Navarro-Garcia [22] et al. and Ene et al.[20] the relationship was represented between the post-operative pain and pre-operative anxiety and depression. In both studies, hospitalization duration, the stress comprised by the current disease over patient, and the severity of the pain after these surgeries were higher than the septoplasty and rhinoplasty patients. This difference may be due to the different types of surgery. The number of the studies in literature that investigating the effects of septoplasty and rhinoplasty operations over physiological and psychological situations of patients have being significantly increased in last years. Most of these studies emphasized comparing the preoperative and postoperative psychological situations. In our study, the association between the preoperative anxiety and depression level and postoperative pain level was evaluated using HADS in rhinoplasty and septoplasty patients.

No significant difference was detected in both groups. The reason of this may be; low intensity of pain in post operative period, gender, social, cultural or educational differences or shorter hospitalization time after septoplasty and rhinoplasty surgery due to these operations are elective and short applications, so they cause lower anxiety and depression and do not have significant effect on the pain after surgery.

Conclusion

The level of pain shortly after surgery is one of the factors determine the contentedness. However, preoperative anxiety and depression are not established as determine the level of postoperative pain in this study group. In this study, anxiety and depression levels were evaluated with HADS, these are not diagnosed clinically and this scale may not be sensitive enough. In future studies, as this patient group, scanning appliances facilitate more detailed assesments can be used for larger samples. Also, the effects of preoperative anxiety and depression on postoperative pain for other surgical applications of ENT can be evaluated.

As a result according to our findings, existence of preoperative anxiety and depression in rhinoplasty and septoplasty patients which require short hospitalization in elective conditions did not found to have a relationship with postoperative pain.

Acknowledgement

We would like to express our gratitude to Ziynet Cınar for his contribution to statistical analyses and interpretation of this study.

References

1. *Sessions RB, Troost T. The nasal septo. In: Cummings CHW, Fredrikson JM, Harker, LA, editors. Otolaryngology-Head neck sed. St. Luis: Mosby ed; 1992; 786-806.*

2. *Faria FS, Guthrie E, Bradbury E, Brain AN. Psychosocial outcome and patient satisfaction following breast reduction surgery. Br J Plast Surg. 1999; 52(6): 448–452*

3. *Klassen A, Jenkinson C, Fitzpatrick R, Goodacre T. Patients' health related quality of life before and after aesthetic surgery. Br J Plast Surg. 1996; 49(7): 433–438*

4. *Stewart MG, Smith TL, Weaver EM, Witsell DL, Yueh B, Hannley MT, Johnson JT. Outcomes after nasal septoplasty: results from the Nasal Obstruction Septoplasty Effectiveness (NOSE) study. Otolaryngol Head Neck Surg. 2004; 130(3): 283-90. PubMed PMID: 15054368.*

5. *Higuera S, Lee EI, Cole P, Hollier LH Jr, Stal S. Nasal trauma and the deviated nose. Plast Reconstr Surg. 2007; 120(7 Suppl 2):64S-75S. Review. PubMed PMID: 18090730.*

6. *Zigmond AS, Snaith PR. The hospital anxiety and depression scale. Acta Psychiatr scand. 1983; 67: 361-70*

7. *Aydemir Ö, Güvenir T, Küey L, Kültür S. Validity and Reliability of Turkish Version of Hospital Anxiety and Depression Scale Turkish Journal of Psychiatry. 1997; 8(4): 280-287.*

8. *Imasogie N, Chung F. Risk factors for prolonged stay after ambulatory surgery: economic considerations. Curr Opin Anaesthesiol. 2002; 15(2): 245–9.*

9. *Wallace LM. Trait anxiety as a predictor of adjustment to and recovery from surgery. Br. J Clin Psycho.l 1987; 26: 73–4.*

10. *Brander VA, Stulberg SD, Adams AD, Harden RN, Bruehl S, Stanos SP, Houle T Predicting total knee replacement pain: a prospective, observational study. Clin Orthop. 2003; 416: 27–36*

11. *Johnston M, Vogele C. Benefits of psychological preparation for surgery: a meta-analysis. Ann Behav Med .1993; 15: 245–56.*

12. *Caumo W, Levandovski R, Hidalgo MP. Preoperative anxiolytic effect of melatonin and clonidine on postoperative pain and morphine consumption in patients undergoing abdominal hysterectomy: a double-blind, randomized, placebo-controlled study. J Pain. 2009; 10(1): 100–8.*

13. *Kastanias P, Denny K, Robinson S, Sabo K, Snaith K.What do adult surgical patients really want to know about pain and pain management? Pain Manag Nurs. 2009; 10(1): 22–31.*

14. *Ebneshahidi A, Mohseni M. The effect of patient-selected music on early postoperative pain, anxiety, and hemodynamic profile in cesarean section surgery. J Altern Complement Med. 2008; 14(7): 827–31.*

15. *Mauer MH, Burnett KF, Ouellette EA, Ironson GH, Dandes HM. Medical hypnosis and orthopedic hand surgery: pain perception, postoperative recovery, and therapeutic comfort. Int J Clin Exp Hypn. 1999; 47(2): 144–61.*

16. *Roykulcharoen V, Good M. Systematic relaxation to relieve postoperative pain. J Adv Nurs. 2004; 48(2): 140–8.*

17. *Shulman O, Westreich M and Shulman J. Motivation for rhinoplasty: changes in 5970 cases, in three groups, 1964 to 1997. Aesthetic Plast Surg. 1998; (22), 420–424.*

18. *Zahiroddin AR, Shafiee-Kandjani AR, Khalighi-Sigaroodi E. Do mental health and self-concept associate with rhinoplasty requests? J Plast Reconstr Aesthet Surg. 2008; 61(9): 1100-3. Epub 2007 Sep 21. PubMed PMID: 17889635.*

19. *de Lima Ramos S, Hochman B, Gomes HC, Abla LE, Veiga DF, Juliano Y, Dini GM, Ferreira LM. Effect of nasal deviation on quality of life. Plast Reconstr Surg. 2011; 128(1): 132-6. PubMed PMID: 21399564.*

20. *Ene KW, Nordberg G, Sjöström B, Bergh I. Prediction of postoperative pain after radical prostatectomy. BMC Nurs. 2008; 7: 14. PubMed PMID: 19068111; PubMed Central PMCID: PMC2635357.*

21. *Singh R, Ripley D, Pentland B, Todd I, Hunter J, Hutton L, Philip A. Depression and anxiety symptoms after lower limb amputation: the rise and fall. Clin Rehabil. 2009; 23 (3): 281–6.*

22. *Navarro-García MA, Marín-Fernández B, de Carlos-Alegre V, Martínez-Oroz A, Martorell-Gurucharri A, Ordoñez-Ortigosa E, Prieto-Guembe P, Sorbet-Amóstegui MR, Induráin-Fernández S, Elizondo-Sotro A, Irigoyen-Aristorena MI, García-Aizpún Y. Preoperative mood disorders in patients undergoing cardiac surgery: risk factors and postoperative morbidity in the intensive care unit. Rev Esp Cardiol. 2011; 64(11): 1005-10. PubMed PMID: 21924811.(Abst.)*

Corresponding Author
Emine Elif Altuntas,
Department of Otorhinolaryngology,
Faculty of Medicine,
Cumhuriyet University,
Sivas,
Turkey,
E-mail: ealtunta@yahoo.com

The asthma patients and their adherence in habitual exercise behavior: a transtheoretical model perspective

Sen-Ji Chen[1], Shih-Ying Deng[2], Frank, F. C. Pan[3]

[1] CEO, Bao-Chien Hospital Group, Taiwan, Republic of China,
[2] National Taitung Hospital, Taiwan, Republic of China,
[3] Healthcare Business Administration, Tajen University, Taiwan, Republic of China.

Abstract

This research adopted the transtheoretical model to examine current status of the exercise behavior change of the asthma patients, and the effects of regular exercise on these patients' behavior changes in exercise. 198 samples were taken from a medical center in Taiwan. Test results shown that proper intervention significantly helped building habitual exercise. Although the survey indicated that asthma patients in Taiwan were unlikely to be sedentary, changing behavior into regular exercise remain invalid for some asthma patients. Since the regular exercise greatly helped reducing deterioration of lung function, this study suggested the healthcare team to maintain a non-stop and comprehensive network to reinforce the exercise will of the asthma patients.

Key words: Asthma, lung function, physical exercise, transtheoretical model

Introduction

Asthma is a chronic respiratory tract inflammation caused by mast cells, eosinophils and other inflammatory cells, the inflammation response to a wide and broad level of an airstream blockade in the patient's respiratory tract, and accordingly makes the respiratory tract excessively sensitive to a wide variety of triggers. In the etiology, asthma could be categorized into endogenous, exogenous, and mixed (1) by its sources of cause. In clinic practice, endogenous asthma that caused by innate factors is common in adult patients, the exogenous and mixed factors are generally found for the children. Asthma is a particular serious health problem to the aged people of which can easily result in mortality. Asthma patients are likely to suffer with a highly sensitive respiratory tract, of which would be badly affected by an allergen, named as asthma attack. Causes of asthma are plenty and the routes incurring asthma are complex. The Environmental Protection Administration (EPA) as well as public health professionals had confirmed that either allergic components from various sources or environmental changes can independently induce asthma (2). This may partly explain why asthma is widely prevailed as a serious health problem in Taiwan where the weather is characterized with humid and warm climate.

Dysprea, chest distress and cough are typical reflections for asthma attacks. This will affect maliciously a patient's life quality, and in many cases lead to a sudden death without timely care. The Department of Health (DOH) of Taiwan estimated that there are over 100 million people suffering from asthma in the world (3), of which around fifteen hundreds died from asthma with a mortality rate at seven per hundred thousandths in Taiwan (3). Exercise-Induced Asthma (EIA), an asthma illness induced by physical movement has been recognized recently as one of the causes of asthma other than environmental allergen (4). EIA is dreadful. Therefore, many of the asthma patients reluctant to take physical exercises despite that most physicians suggest taking proper exercise to help substantiate cardiopulmonary functions (5, 6). In clinical practice, physicians advised asthma patients certain forms of physical exercises other than medical treatments to escort an acceptable life quality. This research attempts to provide further evidence of how the regular exercise can help escorting life quality by comparing two groups of patients who are having and having not habitual exercises. Since the main concern on the asthma patients in this research centers around the behavior changes from reluctant to accept proper

physical exercise, the transtheoretical model (7) is appropriate as the base of the current study.

The transtheoretical model of behavior change

The trans-theoretical model (TTM) integrated key constructs from other major behavior change theories to explore how people modify a problem behavior or acquire a positive behavior (7, 8, 9). The TTM was first applied in the studies of how misbehaviors or addictive behaviors could be corrected. The Stages of Change is the central to the TTM, along with a series of independent variables, the Processes of Change, and a series of outcome measures, including the Decisional Balance and the Temptation scales. It was then widely applied in various studies on diet abnormalities, obesity, high-fat diet, exercise, health screening, and many others. The five stages of behavior change in TTM are precontemplation, contemplation, preparation, action, and maintenance stages. Content of each stage is illustrated in short in the following.

Stage 1, the precontemplation: The object is not ready to make any change in the coming six months of the period. Reasons behind are many, objects not in the project may simply because no intention or not aware of such a need, or even had experienced failure before.

Stage 2, the contemplation: The objects start to realize their behavior problems, and intend to change behavior in the next six months. In this stage, the objects are not ready to participate and act to lead an actual behavior change. Objects may recognize the advantages a behavior change will produce, yet perceived difficulties associated with the change may concurrently against an actual execution.

Stage 3, the preparation: Objects of study in this stage will start to change their behaviors presently in the future (e.g.: one month) and try to take some fragmentary actions in the past, such as: to participate in the correlate course, to buy some books or participate in guidance classes of sports.

Stage 4, the action: Objects of study in this stage are able to achieve: "three to five times a week, thirty minutes for each time, the exercise intensity can reach the moderate-intensity" amount of regular exercise, but the duration of the time is not reaching to six months.

Stage 5, the maintenance: Objects of study in this stage are maintaining to do the regular exercise, staying more than six months, and they do many efforts to prevent the relapse of the behavior not to do exercise.

Methods of changing

To sum up, ten methods are included in the transtheoretical model, either tangible or intangible, in the experiential aspect and the behavior level respectively (10). There are five methods in the former aspect, namely as methods of Consciousness Raising, Dramatic Relief, Environmental Re-Evaluation, Self Re-Evaluation, and Social Liberation. Another five methods included in the latter aspect are Counter conditioning, Helping Relationships, Reinforcement Management, Self Liberation, and Stimulus Controls. Each stage of progress has its own focus. The experiential aspect of the precontemplation, contemplation, and preparation status are the core in the early stage, and the action and the maintenance are the focus methods of the behavior level in the terminal stages (11). Although each stage has its special focus methods, this does not exclude the importance that other methods may have. To integrate the changing stages of a person and the methods the promoter may apply, carefully evaluated and identified methods should be taken at a right time when a need emerges (11). To implement, the public health educators should initiate efforts from particular focus, then evaluate the peculiarity of the behavior changes of the objects, and accordingly make an appropriate adjustment for the ultimate goal.

Materials and methods

Research framework

Previous discussion could be summarized as the framework of this research, illustrated as in figure 1.

Study design

This study uses a questionnaire survey to collect information, adopts a longitudinal cohort study. The objects received a pretest in the beginning of the study, and the data were filed. After a six-month of a period, the objects receive a post test. We then compare these two sets of data to examine the progress.

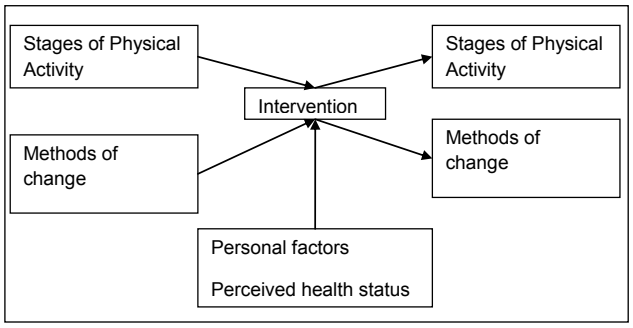


Figure 1. Intervention design

Measurement

We use a structured questionnaire to collect data on personal background, movement stages, and changes of physical activity. The movement stage is measured by a scale developed by Marcus and Forsyth (2009) with four questions (12). This is to classify the respondent's current movement status. A "Three-day physical activity record" is used as an instrument to measure the daily exercise activity (13), of which had been successfully applied in a wide range of population in Taiwan.

Results

Descriptive statistics

The research successfully collected 98 valid responses, of which 166 are men (84.7%) and 32 women (15.3%). Ages are between 39 and 83 with an average at 68.1 years old. Most participants are married (170 cases. 86.7%). The majority educational level is primary education (62 cases. 31.6%). As to the status of movement change, the majority is in the maintenance phase (72; 36.4%), followed by the pre-contemplation (45, 22.7%), the preparation phase (36, 18.2%), action stage (23, 11.6%), and the contemplation stage (22, 11.1%), as shown in table 1.

On the types of exercise, 80 (40.8%) participants took two sports, 68 (34.7%) chosen only one type of exercise, and 50 (11.2%) participate three or more types of physical movement. Walking is the most common (146 cases, 51.4%) and gymnastic is the second (72 cases. 25.4%).

Table 1. Movement stage classification

Item \ Category	N=198	%
Pre-contemplation	45	22.7
Contemplation	22	11.1
Preparation	36	18.2
Action	23	11.6
Maintenance	72	36.4

There were 101 patients out of 198 cases completed the entire six-month project. The progress of behavior change of these 101 cases is shown as in Table 2.

Changes in different stages

The one-way ANOVA was used to test the differences of changes in the process, as shown in table 3. Self liberation prevails as the most frequent used method in the change process, next by the "Counter conditioning". The "Consciousness raising" received the least frequency in the contemplation stage. Duke-Kramer comparison method was also used in this research to determine the average differences between two stages, as shown in table 3.

Behavioral process is the main category in every stage $[F(4, 93) = 12.08, p \leq 0.05)]$, among which the Self liberation is the major process in the Precontemplation stage (mean=2.66; SD= 0.94); the Counter-restriction (3.63, 1.24) and the Self liberation (3.63, 0.88) for Contemplation; the Counter-restriction for Preparation (3.65, 0.63); the Self liberation for both Action (3.88, 0.43) and Maintenance (3.75, 0.80).

Regular exercise in different stages

Exercise behaviors could be classified into regular (Action and Maintenance stages) and irregular (Precontemplation, Contemplation and Preparation) exercise groups based on the frequency of participating physical exercises. A two-sample t test analysis shows that the irregular group experienced much fewer changes to maintain exercise behavior in both experiential and behavior changes, as shown in table 4.

Table 2. Descriptive statistics on change process

Processes of change	Means	S. D.	Rank
Experiential change	2.26	0.59	
Consciousness-raising	1.73	0.72	10
Dramatic relief	2.35	0.88	5
Environmental re-evaluation	2.07	0.78	9
Self re-evaluation	2.83	0.65	3
Social liberation	2.32	0.94	6
Behavior change	2.72	0.61	
Counter conditioning	3.43	0.94	1
Helping relationships	2.31	0.93	7
Reinforcement mgmt.	2.37	0.60	4
Self liberation	3.41	0.80	2
Stimulus control	2.09	0.86	8

Discussion and conclusion

Current research indicated that most asthma patients are in the maintenance phase of exercise. This is inconsistent with previously studies who had advocated that the asthma patients are likely to share a comparatively sedentary lifestyle (12). Dispute of this kind may stem from different interpretation on the term of a regular exercise, of which we defined it as a 20-minute non-stop force movement each time and three or more times a week rather than a typical 3-3-3 rule (three times a week, and 30 minutes exercise each time with heartbeats at 130/m). As a result, non-conventional physical exercises such as housekeeping works and walking, etc. were included as an exercise. This research suggests that patients in Taiwan, who suffer with a chronic obstructive pulmonary problem, prefer to take the walk as a supportive exercise rather than other types of bodily movements. In fact, few of them maintain a sedentary lifestyle.

The current research indicated that counter conditioning, self-liberation, and self re-evaluation are the leading items received most popular responses for behavioral changes. This means respondents are confident with their own recognition and capability against the others. This explained partially why the problematic asthma patients who failed to adhere with the physician's order of exercise engagement generally respond to such an order by doing nothing changes. Asthma patients who are reluctant to become a regular exercise participant are extremely dangerous by exposing themselves to a risk of sudden death. Since the patients in the later stages of change (action and maintenance stages) will take a much lengthier process than those of the other stages (10, 12), healthcare professionals who supervise the patients in these stages can be more challenging than others.

Table 3. One-way ANOVA and Tukey-Kramer comparison of change (N=98)

Process of change	PC	CO	PR	AX	MN	F
Cognitive Processes	1.81(0.54)	2.85(0.92)	2.27(0.46)	2.36(0.45)	2.46(0.54)	6.87**
Consciousness raising	1.31(0.14)	2.13(0.84)	1.83(0.15)	1.25(0.34)	1.91(0.10)	3.49*
Dramatic relief	2.03(0.93)	3.25(1.41)	2.11(0.66)	2.56(0.83)	2.57(0.85)	2.74
Environmental reevaluation	1.59(0.56)	2.38(0.88)	2.12(0.66)	2.25(1.17)	2.27(0.81)	3.67*
Self reevaluation	2.32(0.72)	3.13(0.88)	2.79(0.45)	3.44(0.55)	3.07(0.51)	8.36***
Social liberation	1.75(0.81)	3.38(0.88)	2.51(0.92)	2.31(1.28)	2.49(0.38)	3.94**
Behavioral Processes	2.12(0.60)	3.83(0.88)	2.89(0.49)	2.98(0.52)	2.94(0.42)	12.08***
Counter conditioning	2.52(0.76)	3.63(0.83)	3.65(0.63)	3.75(0.61)	3.75(0.51)	17.19***
Helping relationship	1.97(0.52)	2.25(0.35)	2.50(0.54)	2.81(0.85)	2.49(0.57)	4.63**
Reinforcement management	1.74(0.85)	2.63(0.73)	2.49(1.02)	2.31(0.63)	2.53(0.86)	3.58*
Self liberation	2.66(0.94)	3.36(1.24)	3.54(0.80)	3.88(0.43)	3.75(0.80)	7.40***
Stimulus control	1.69(0.67)	2.00(1.14)	2.29(0.73)	2.17(0.96)	2.22(0.93)	1.86

PC, Precontemplation; CO, Contemplation; PR, Preparation; AX, Action; MN, Maintenance

*Figures in bracket are standard deviations; *p ≤ 0.05, ** p ≤ 0.01, *** p ≤ 0.001*

Table 4. t-test analysis for different groups of regularity

Processes	Irregular (n=48)	Regular (n=50)	t
	Mean(SD)	Mean(SD)	
Cognitive process	2.05(0.58)	2.45(0.53)	3.54**
Consciousness raising	1.59(0.62)	1.86(0.78)	1.82
Dramatic relief	2.11(0.86)	2.57(0.84)	2.65**
Environmental - reevaluation	1.85(0.11)	2.27(0.11)	2.73**
Self-reevaluation	2.56(0.66)	3.10(0.52)	4.50**
Social liberation	2.15(0.96)	2.48(0.91)	1.74
Behavioral process	2.49(0.27)	2.95(0.44)	4.00**
Counter conditioning	3.06(0.90)	3.74(0.52)	4.51**
Helping relationship	2.21(0.58)	2.52(0.60)	2.58**
Reinforcement management	2.10(0.98)	2.51(0.84)	2.21*
Self-liberation	3.80(0.98)	3.76(0.78)	3.79**
Stimulus control	1.97(0.77)	2.21(0.93)	.44

*$p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$

Based on the results from the survey, we proposed several recommendations for healthcare professionals to reinforce the patients' behavioral changes. Firstly, the healthcare team shall take every opportunity to communicate the message of exercise benefits with the patients as often as possible. Second, the hospital organizes and networks patient groups, and activates patient-to-patient interactions to form and deliver social support to the group members. Third, utilize the technology-based communication instruments to remind regularly the physician's orders. Turning the asthma patients' inactive lifestyle into a habitual exercise help slowing the deterioration of the patient's lung function and significantly reduce the risk of sudden death.

Acknowledgment

Earlier version of this study was presented in the International Borneo Business Conference in Sarawak, Malaysia in 2010. We thanks for the financial support from the Bao-chien Hospital and Taitung Hospital.

References

1. *Huang KC. Talking about pediatric asthma. Health World. 1991; 64:35-49.*
2. *Environmental Protection Administration (EPA). Manual of Asthma Care. Booklet from Environmental Protection Administration. Taipei: Executive Yuan, R.O.C. 1996 (In Chinese).*
3. *Department of Health (DOH). Asthma Treatment Guidelines, Concise Edition. Taipei: Department of Health, R.O.C. 2009 (In Chinese).*
4. *Rubenfeld MF, Georas N. The treatment of acute severe asthma in the adult: an overview. Formulary. 2003; 38(9): 538-544.*
5. *Szentagothai K, Gyene I, Szocska M, Osvath P. Physical exercise program for children with bronchial asthma. Pediatr. Pulmonol. 1987;3:166-172.*
6. *Jain SC, Rai L, Valecha A, Jha UK, Bhatangar SOD, Ram K. Effect of yoga training on exercise tolerance in adolescent with childhood asthma. J. Asthma. 1991; 28(6): 437- 442.*
7. *Prochaska JO, DiClemente CC. Stages and processes of self-change of smoking: Toward an integrative model of change. J. Consult Clin Psychol. 1983;51(3):390-395.*
8. *Prochaska JO, DiClemente CC, Norcross JC. In search of how people change: Applications to addictive behavior. Am. Psychol. 1992; 47: 1102-1114.*
9. *Prochaska JO, Velicer WF. The transtheoretical model of health behavior change. Am J. Health Promot. 1997; 12: 38-48.*

10. *Velicer WF, Prochaska JO, Fava JL, Norman GJ, Redding CA. Smoking cessation and stress management: applications of the transtheoretical model of behavior change. Homeostasis. 1998; 38: 216-233.*

11. *Marcus BH, King TK, Clark MM, Pinto BM, Bock BC (). Theories and techniques for promoting physical activity behaviors. Sports Med. 1997; 22(5): 321-31.*

12. *Marcus BH, Forsyth LH. Motivating People to Be Physically Active (2nd). Champaign, Illinois, USA: Human Kinetics, 2009; p. 168.*

13. *Bouchard C. Bouchard three-day physical activity record. Med. Sci. Sports Exerc. 1997; 29(6): S19-S24.*

Corresponding Author
Frank, F. C. Pan,
Healthcare Business Administration,
Tajen University,
Taiwan,
Republic of China,
E-mail: Taiwan.pan@msa.hinet.net

Health & nutrition behaviors of cancer survivors in Malaysia

Yong HY[1], Zalilah MS[1], Nurfaizah S[1], Yong HW[2], Mirnalini K[1], Zailina H[2]

[1] Department of Nutrition and Dietetics, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, 43400 UPM Serdang, Selangor Darul Ehsan, Malaysia,

[2] Department of Community Health, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, 43400 UPM Serdang, Selangor Darul Ehsan, Malaysia.

Abstract

In Malaysia, the incidence of cancer is on the rise but with effective treatment and care, many cancer patients have better survivorship. This study describes the health and nutrition of cancer survivors in Malaysia. Respondents were 457 women diagnosed with breast, colorectal, cervix, ovarian and stomach cancers. All cancer patients were interviewed using a pre-tested questionnaire and physically measured by trained enumerators. Most were diagnosed with Stage I (47.5%) and Stage II (42.7%) cancers and underwent surgery (96.9%), chemotherapy (83.8%) and radiotherapy (78.7%). More than half of respondents were overweight (34.4%) and obese (17.7%) while 41.8% had normal body weight. About 66% of the women had at risk waist circumference (≥ 80cm). For all food groups except meat/fish/poultry/legumes, the mean number of servings was less than the recommended servings. More than two thirds of the women had moderate (39.4%) and high (37.4%) levels of physical activity. Nearly half (49.7%) of respondents reported the use of CAM as complementary to conventional treatment. In conclusion, efforts to promote the adoption and maintenance of healthy lifestyle behaviors among these cancer survivors are warranted. Subgroups such as cancer survivors who are overweight or obese, at higher risk of abdominal fatness and ate fewer than recommended servings of fruits and vegetable may require more attention as they are at greater risk of cancer recurrence, developing secondary cancers and other diet-related chronic diseases.

Key words: physical activity, body mass index, dietary intake, CAM, cancer survivors

Introduction

In 2008, there were 12.7 million new cancer cases worldwide with more than half (56%) occurred in developing countries and 44% in developed countries (IARC, 2008). In Peninsular Malaysia, a total of 21,773 cancer cases were diagnosed in Peninsular Malaysia with more cases in women (54.2%) than men (45.8%) (NCR, 2006). The most common cancer diagnosed were breast (16.5%), colorectal (13.2%), lung (9.4%), cervical (4.9%) and nasopharynx (4.5%). While breast cancer was the most common cancer diagnosed among women, colorectal cancer was most prevalent among men. It is projected that the number of people diagnosed with cancer in the world will double by the year 2030 with higher rates occurring in both middle and low-income countries (WHO, 2009). With increasing world population and exposure to cancer, preventive efforts could be a challenge to health professionals and policy makers. As more people with cancer survive longer due to advances in medical technology, there is a growing interest in the role of lifestyle in long term quality of life.

Studies have found that cancer survivors have a strong interest in making positive changes in lifestyle and health-related behaviors, including diet, physical activity, and smoking (Demark-Wahnefried et al., 2000; Blanchard et al., 2003). The Women's Healthy Eating and Living Study (WHEL) (Thomson et al., 2002) showed that 60% of breast cancer survivors reported increasing fruit and vegetable servings and 80% reported decreasing fat intake since diagnosis. Patterson et al. (2003) reported that two thirds of breast, colorectal, and prostate cancer patients made changes in diet, dietary supplement use and physical activity even after 2 years post-diagnosis. Similarly, Irwin et al.

(2004) reported that 52% of breast cancer survivors increased their physical activity from moderate to vigorous intensity activities in the first to the third year post-diagnosis, respectively.

Adoption and maintenance of healthy lifestyle by cancer survivors has the potential to reduce risk of cancer recurrence (Doyle et al., 2006; Ganz, 2001). However, post-diagnosis behavioral changes are often not maintained (Irwin et al., 2004; Demark-Wahnefried et al., 2006). Cancer survivors tend to return to their pre-diagnosis lifestyle after few years of cancer diagnosis. Despite being highly motivated to make changes in dietary intake, physical activity and dietary supplement use, cancer survivors might find the adoption and maintenance of healthy lifestyle to be challenging. An important first step in promoting a healthy lifestyle to improve the overall quality of life of cancer survivors is to determine the degree to which cancer survivors adhere to health and nutrition recommendations. As such information is lacking in Malaysia, this paper aimed to describe health and nutrition of cancer survivors in Malaysia.

Methods

Subjects

This was a cross-sectional survey conducted in eight general hospitals and four breast cancer support groups in seven states of Peninsular Malaysia. A total of 457 women with cancers of the breast, colorectal, cervix, ovarian and stomach voluntarily participated in this study. Pregnant and lactating cancer patients as well as those with cancer recurrence at the time of data collection were excluded from this study. The study protocol was approved by the Medical Research Ethics Committee of Faculty of Medicine and Health Sciences, Universiti Putra Malaysia and the Medical Research Ethics Committee of Ministry of Health Malaysia. Prior to data collection, permission to conduct the study was obtained from the respective hospitals and breast cancer support groups. A study information sheet was given to the respondents and informed consent was obtained from all the respondents prior to data collection.

Measurements

All cancer patients were interviewed by trained interviewers either at outpatient clinics, support groups or home setting. All respondents received a monetary incentive RM15 (USD 5) upon completion of all measurements.

Anthropometric measurements

Current weight and height were measured using TANITA digital weighing scale (TANITA Corporation of America, Inc, United States) and SECA body meter (SECA, British Indicators Ltd, United Kingdom), respectively. Weight and height measurements of respondents were transformed into Body Mass Index (BMI) and classified according to the World Health Organization (WHO, 1998) cut off points. Waist circumference was measured using a SECA microtoise tape (SECA, British Indicators Ltd, United Kingdom). Waist circumference ≥80cm is considered as increased risk of metabolic complication while waist circumference ≥88cm denotes a substantially increased risk of metabolic complication in women (World Health Organization, 1998).

Dietary intake

One day 24-hours diet recall was undertaken to assess the intake of energy and macronutrients. The respondents were required to recall all food and beverages consumed for the past 24-hours. The recall form consisted of time of eating or drinking, types of food and beverages, food ingredients and quantity of foods and beverages consumed by the respondents. Household measurements (plates, bowls, cups and spoons) were used to assist respondents to recall the portion size of food and beverages consumed. Dietary data were then analyzed using Nutritionist Pro software (First Data Bank, 2005). Total energy intake, percentage of energy from macronutrients and the number of servings for grains, meats and legumes, fruits, vegetables and dairy products were calculated. Number of servings for all food groups was then categorized according to the Malaysian Dietary Guidelines (NCCFN, 2010).

Physical activity

Current physical activity level was measured using Global Physical Activity Questionnaire

(GPAQ) (WHO, 2001). Women were requested to recall the number of days in the last 7 days they did vigorous intensity activity or/both moderate intensity activity at 3 major settings (activity at work/ domestic, travel to and from places, recreational activities), as well as the number of hours and minutes per day they did the activities, respectively. The respective total hours for physical activity were calculated and multiplied with metabolic equivalent (MET) hours per week and the values were then categorized into low, moderate and high.

Complementary and Alternative medicine (CAM) practices

CAM practices of cancer patients were identified using items adapted from Molassiotis et al. (2005) and Howell et al. (2006). The women were required to report any type of CAM used as either complementary (use it together with conventional medicine) or alternative (exclusively depends on CAM therapy). If women were not past or current users of CAM, they were requested to provide reasons for not using CAM. For those who were past and current CAM users, information were obtained on types of CAM use, perceived benefits and concerns of CAM use.

Data Analysis

All data were analyzed using the SPSS version 15 (Chicago, IL, USA). The demographic, socioeconomic and health data of cancer survivors are presented descriptively as mean, standard deviation, frequency and range.

Result

Table 1 presents the socio-demographic characteristics and cancer history of women (N=457). More than half (58.6%) of the women were Malays followed by Chinese (30.6%) and Indian (10.8%). A majority (81.8%) of the women was married. The mean years of schooling was 8.91 ± 3.76 years and about 68.7% of women were unemployed. Majority (86.2%) of women were breast cancer survivors. The mean age of cancer diagnosis was 48.57 ± 9.32 years with mean age of breast cancer diagnosis was at 48.43 ± 9.15 and other cancers at 48.98 ± 10.08 years. The mean duration of survival among cancer survivors in this study was 4.91 ± 4.13years with higher mean years of survival for other cancers (5.13 ± 4.82 years) compared to breast cancer (4.70 ± 3.44years). A majority of the survivors (89.2% breast cancer; 95.2%other cancers) were diagnosed at early stages (Stage I and Stage II) and had undergone surgery (96.9%), received radiotherapy (78.7%) and chemotherapy (83.8%) treatments.More than half of women were overweight (34.4%) and obese (17.7%) while 41.8% had normal body weight (Table 2). More than half of the women (66.1%) had at risk waist circumference, with 25.2% of the women had waist circumference ≥80 cm and 40.9% had ≥88 cm, respectively.

The mean percentage of energy from carbohydrate, protein and fat were 56.12 ± 10.39%, 16.39 ± 4.68% and 27.72 ± 8.62%, respectively. A majority of the women consumed <8 servings of grains and cereal products (78.6%), <3 servings of vegetables (96.1%), <2 servings of fruits (81.8%) and <1 serving of milk and dairy products (84.7%). More than half (55.4%) of respondents had ≥2 servings of meat/ fish/ poultry/ legumes. On average, the respondents spent 100.94 ± 110.72 minutes daily for moderate to vigorous physical activity. The most time spent was on activities at workplace (72.48 ± 96.95 minutes/day), followed by recreational activities (15.43 ± 30.36 minutes/day) and travel related activities (13.04 ± 22.66 minutes/day), respectively. The mean time spent for sedentary activity by the respondents was 213.25 ± 141.93 minutes daily. More than half of the respondents had moderate (39.4%) and high (37.4%) level of physical activity. About 49.7% of cancer patients reported use of CAM as complementary rather than alternative therapy. Of the 5 categories of CAM, biologically based therapies were the most commonly used CAM with vitamins (46.7%), other dietary supplements (31.7%) and herbs and herbal products (14.3%) being commonly used by cancer survivors. For spiritual activities, the common ones practiced were prayers and meditation. Many CAM users perceived that CAM increased their body's ability to perform daily activities (79.7%), improved their physical and emotional well being (63.0%) and reduced side effects of conventional treatment (33.0%). Generally, most CAM users (81.9%) did not have any concern about CAM use (Table 3).

Table 1. Socio-demographic characteristics and cancer history of women (N=457)

Variable	n (%)	Mean ± SD
Age (years)		52.96 ± 9.51
Ethnicity		
Malay	268 (58.6)	
Chinese	140 (30.6)	
Indian	49 (10.8)	
Marital status		
Married	374 (81.8)	
Divorced/ widowed	59 (12.9)	
Years of education (years)		8.91 ± 3.76
Employment status		
Employed	143 (31.3)	
Unemployed	314 (68.7)	
Monthly personal income (RM)*		632.45 ± 1269.50
Monthly household income (RM)*		2120.27 ± 2490.60
Types of cancer		
Breast cancer	394 (86.2)	
Other cancers[b]	63 (13.8)	
Age at cancer diagnosis (years)		48.62 ± 9.32
Breast cancer		48.43 ± 9.15
Other cancers[b]		48.98 ± 10.08
Years of survival (years)		4.91 ± 4.13
Breast cancer		4.70 ± 3.44
Other cancers[b]		5.13 ± 4.82
Stage of breast cancer		
Stage I	167 (42.3)	
Stage II	185 (46.9)	
Stage III	42 (10.8)	
Stage of other cancers[b]		
Stage I	50 (79.4)	
Stage II	10 (15.8)	
Stage III	3 (4.8)	
Current treatment/ treatment received		
Lumpectomy[a]	71 (15.5)	
Mastectomy[a]	310 (67.8)	
Other types of surgery[b]	62 (13.6)	
Radiotherapy	350 (78.7)	
Chemotherapy	380 (83.8)	
Tamoxifena	156 (34.1)	
Reloxifen	3 (0.7)	

[a] *Breast cancer patients*
[b] *Colostomy, polypectomy, hysterectomy, total hysterectomy unilateral, bilateral, gastrectomy*
** Currency exchange rate RM 1 = 0.3330 USD*

The main concerns were on dietary supplements in respect to the content (53.7), safety (41.5%) as well as the effectiveness (46.3%) and potential adverse effects (26.8%). More than half of the non-CAM users (54.3%) were concerned with the potential adverse effects of CAM (Table 3). About 34% of non-CAM users were fully satisfied with conventional treatment they received. Other rea-

sons included non-CAM users did not believe in CAM (23.5%), discouragement from their physicians (10.9%) and unable to pay for CAM treatment (10.4%).

Discussion

A higher BMI (Chlebowski et al., 2002; Kroenke et al., 2005), excessive weight gain (Caan et al., 2005; Caan et al., 2006; Caan et al., 2008)

Table 2. Nutritional status and physical activtiy of respondents (N= 457)

Variables	n (%)	Mean ± SD
Anthropometric measurements Body Mass Index (kg/m^2)[a]		25.80 ± 5.20
Underweight (< 18.5)	28 (6.1)	
Normal (18.5-24.9)	191 (41.8)	
Overweight (25.0-29.9)	157 (34.4)	
Obese (> 30)	81 (17.7)	
Waist circumference (cm)a		84.78 ± 11.72
< 80	155 (33.9)	
≥ 80[b]	115 (25.2)	
≥ 88[c]	187 (40.9)	
Dietary intake		
Calories (kcal/day)		1342 ± 410.48
Percentage of energy from carbohydrate (%)		56.12 ± 10.39
Percentage of energy from protein (%)		16.39 ± 4.68
Percentage of energy from fat (%)		27.72 ± 8.62
Number of serving for food groups (servings/day)		
Grain/cereal/tuber (8-12)		6.17 ± 2.12
< 8	359 (78.6)	
≥ 8*	98 (21.4)	
Vegetable (3)		1.18 ± 0.86
< 3	439 (96.1)	
≥ 3*	18 (3.9)	
Fruit (2)		0.70 ± 0.99
< 2	374 (81.8)	
≥ 2*	83 (18.2)	
Meat/fish/poultry/legumes (2-3)		2.08 ± 1.19
< 2	204 (44.6)	
≥ 2*	253 (55.4)	
Milk/dairy product (1-2)		0.33 ± 0.57
< 1	387 (84.7)	
≥ 1*	70 (15.3)	
Physical activity		
Total physical activity (minutes/day)		100.94 ± 110.72
Activity at work (minutes/day)		72.48 ± 96.95
Travel to and from places (minutes/day)		13.04 ± 22.66
Recreational activities (minutes/day)		15.43 ± 30.36
Sedentary activity (minutes/day)		213.25 ± 141.93
Level of activity		
Low	106 (23.2)	
Moderate	180 (39.4)	
High	171 (37.4)	

a World Health Organization (1998)
b Increased risk of metabolic complications
c Substantial risk of metabolic complications
** Recommended servings based on Malaysian Dietary Guidelines (2010)*

and excess abdominal fat (Abrahamson et al., 2006) may put cancer survivors at higher risk of developing cardiovascular diseases, diabetes and cancer recurrence as well as adverse prognostic. The present study showed that more than half of cancer survivors were overweight (34.4%) and obese (17.7%), and had at risk waist circumference (66.1%). Courneya et al. (2008) reported that about 52% of Canadian cancer survivors were overweight or obese regardless of the types of

Table 3. Use of complementary and alternative medicine (CAM) (N=457)

CAM usage	n (%)
CAM users	227 (49.7)
Types of CAM use	
Biologically based therapies	
Vitamins[a]	106 (46.7)
Other dietary supplements[c]	72 (31.7)
Herbs and herbal product[s]d	39 (14.3)
Minerals[b]	23 (10.1)
Healing water	16 (7.0)
Mind-body therapies	
Spiritual activities	84 (37.0)
Yoga	2 (0.9)
Energy therapies	
Qi gong	8 (3.5)
Tai chi	4 (1.8)
Manipulative and body-based therapies	
Reflexology	3 (1.3)
Message	2 (0.9)
Alternative medical systems	
Hemotherapy	3 (1.3)
Perceived benefits of CAM use	
To increase body's ability to perform daily activities	181 (79.7)
To improve physical and emotional well-being	143 (63.0)
To counteract side effects of conventional treatment	75 (33.0)
To enhance immune function	48 (21.1)
To prevent cancer recurrence	8 (3.5)
Concerns about CAM use	
No	186 (81.9)
Yes	41 (18.1)
Types of concern	
Content of dietary supplements	22 (53.7)
Effectiveness of dietary supplements	19 (46.3)
Safety of dietary supplements	17 (41.5)
Potential adverse effects of dietary supplements	11 (26.8)
Non CAM users	230 (50.3)
Reason for not using CAM	
Potential side effects of CAM therapy	125 (54.3)
High satisfaction with conventional treatment	78 (33.9)
Did not believe in CAM therapy	54 (23.5)
Discouraged by physicians	25 (10.9)
Unable to pay for CAM therapy	24 (10.4)

[a] *Multivitamins, vitamin C, vitamin B-complex, vitamin E, vitamin A, vitamin B1, vitamin D*
[b] *Calcium, Ferum*
[c] *Sea cucumber (gamat), spirulina, honey, EPO, fish oil, omega-3, habatussaudah, fiber*
[d] *Chinese herbs, hearbal products (e.g. Herbal life and CNI), dukong anak (Phyllanthus niruri), misai kuching (Orthosiphon stamineus), mas cotek (Ficus deltoidea), ginseng, pegaga (Hydrocotyle asiatica), kacip Fatimah (Labisia Pumila)*

cancer and gender. Similarly, Demark-Wahnefried et al. (2005) showed that an approximately 70% of breast and prostate cancer survivors were overweight or obese. As the present study did not measure the weight at various time points (e.g., weight pre-diagnosis and weight at diagnosis), it could not assess the exact time point for cancer survivors becoming overweight or obese.

Weight gain is a common occurrence for women after breast cancer diagnosis. Most previous studies showed that breast cancer survivors gained 1-2kg during the first year after breast cancer diagnosis (Freedman et al., 2004; Irwin et al., 2005; Halbert et al., 2008; Gu et al., 2009; Heideman et al., 2009). In the present study, about 86% of respondents were breast cancer survivors. A significant weight gain (3.47 ± 7.53 kg) was observed among these breast cancer survivors (n=368) with almost half of them (47%) gained at least 5% of weight from a year preceding breast cancer diagnosis to on average 4 years post- diagnosis (data no shown). The amount of weight change among breast cancer survivors in this study is similar to those (1.7 – 4.6kg) observed in Western populations (Pierce et al., 2002; Irwin et al., 2005; Caan et al., 2006), but different from those reported in the Chinese (median weight gain is 1.0kg after 36 months post-diagnosis) (Gu et al., 2009) and Korean breast cancer survivors (loss of 0.4kg at 2 years after breast cancer treatments) (Han et al., 2009). However, the comparison between the present study's findings with these studies should be done with caution due to the different time points of weight change being examined. The time period measured in the present, LACE and WHEL study studies was from a year preceding breast cancer to study entry or on average 4- 5 years post-diagnosis. The SBCSS study examined weight change pattern from diagnosis to 6, 18 and 36 months post- diagnosis while the Korean study assessed weight change between weight during treatment and weight after adjuvant treatment.

Most studies (Salminen et al., 2000; Maunsell et al., 2002; Thomson et al., 2002; Patternson et al., 2003) found that increased fruit and vegetable consumption is one of the most frequently observed dietary changes among cancer survivors, although these studies did not quantify the dietary change. However, the present study showed that the number of servings for all food groups, except for meat/fish/poultry/legumes was less than the recommended servings. The Health, Eating, Activity and Lifestyle (HEAL) study of women with breast cancer in the United States also found that 75.8% of women consumed fewer than five servings of fruits and vegetables, with a daily average intake of 1.6 ± 1.2 serving and 2.0 ± 1.3 serving , respectively (Wayne et al., 2004). A high fruits and vegetables intake has been shown to lower the risk of cancer recurrence, as well as mortality (Pierce et al., 2007; Thomson et al., 2011). Although there are no studies to date that confirm which compounds in fruits and vegetables are most protective against cancer, cancer patients and survivors are encouraged to consume five or more servings of a variety of coloured fruits and vegetables daily for health benefits.

The daily intake of fruits and vegetables among women in the present study is similar to the findings of the Malaysian Adult Nutrition Survey (2006) and Malaysia NCD Surveillance I 2005–2006, which reported that about 75.5% of Malaysian women and 73% of Malaysian adults did not meet the dietary guideline for fruit and vegetable intakes (3 to 5 servings per day) (MOH, 2006). A high proportion of the world's population, including Malaysians, do not eat an adequate amount of fruits and vegetables (< 5 servings/day). As Malaysia has a variety of local and imported fruits and vegetables that are available thought the year, it is surprising that a high proportion of women in this study consumed inadequate amounts. Price may be a possible reason for the low fruit and vegetable intake as previous studies found that low-income consumers reported price of fruits and vegetables is an important barrier to consumption (Reickes et al., 1994; Havas et al., 1998). In this study, the mean monthly household income was RM 2120.27 (USD 676) with about 72% of cancer survivors were in the low-income group of less than RM 2300 (USD 765) in Malaysia (Economic Planning Unit, 2010).

Studies have shown inconsistent findings in the level of post-diagnosis physical activity. Several studies showed that cancer survivors are physically active (Bellizzi et al., 2005) compared to non-cancer control (Emaus et al., 2009). However, Abdul-Samad et al. (2008) reported that majority (74.6%) of breast cancer survivors had low physical activity and only 25.4% had moderate and high physical

activity. The comparison of physical activity levels across studies should be interpreted with caution due to differences in physical activity assessment and classification. In addition, stage of cancer diagnosis, treatment modalities and time since diagnosis, could also explain the differences in cancer survivors' capacity or ability to undertake physical activity.

CAM use tends to be prevalent among cancer survivors. A survey in 14 European countries found that 35.9% cancer patients used some forms of CAM and the prevalence ranged from 15% to 73% among countries (Molassiotis et al., 2005). Similarly, a high proportion of cancer survivors in Singapore (56%) (Shih et al., 2005), Malaysia (50%) (Mirnalini and Lim, 2006), Japan (44.6%) (Hyodo et al., 2005) and Iran (35%) (Montazeri et al., 2006) reported using CAM. The prevalence rates of CAM use seem to vary across studies, depending on the definition of CAM used. Biological based therapies (e.g., dietary supplements) and mind-body therapies (e.g., spiritual activities) were the most commonly used CAM therapies in the present study. Other studies have reported common use of herbal remedies, dietary supplements, homeopathy, spiritual therapies and massage among cancer survivors (Richardson et al., 2000; Cassileth et al., 2001; Swisher et al., 2002).

The study has several limitations. Bias might occur as respondents were requested to self-report dietary intake and physical activity. As dietary intake was assessed by 24-hour diet recall, under reporting could occur due to poor memory and social desirability bias (i.e under report foods that are high energy dense). It is also believed that women in the present study could have misreported (i.e. over-reporting) their physical activity level for several reasons. Jakicic et al. (1998) found that 40-60% of overweight women over-reported their physical activity levels. Since slightly more than half (52.1%) of the women in the present study were overweight and obese, there is a possibility that moderate and vigorous physical activities were over-reported. It is also possible that women could have misinterpreted moderate and vigorous intensity activities, which resulted in overestimation of their physical activity level (Harrison et al., 2009). In addition an interview-administered physical activity questionnaire is prone to social desirability bias (Motl et al., 2005). As the questionnaire requires disclosure in front of an interviewer, this might increase the likelihood of over-reporting physical activity of higher intensity. Despite these limitations, this study has provided important information on weight status and lifestyle behaviors of cancer survivors that are lacking in Malaysia.

Conclusion

Most of the cancer survivors in this study were overweight or obese, had low fruit and vegetable intake, and had at risk waist circumference. These results highlight specific intervention aimed at reducing health risks among cancer survivors. Consumption of fruits and vegetables is an important determinant of survival and prevention of cancer recurrence. Thus, it is important to develop strategies to increase fruit and vegetable for cancer patients or survivors. The high prevalence of CAM use among cancer survivors heightens the need for further research on the safety, efficacy, and health benefits of these therapies, as well as provide health professionals and the general public particularly cancer patients with guidelines on safe use of CAM.

Acknowledgements

This research was supported by the Fundamental Research Grant Scheme (FRGS) from the Ministry of Higher Education. Acknowledgement is accorded to Directors, Heads of departments and staff of hospitals for their cooperation and assistance.

References

1. *Abdul-Samad, A.A., Al-Kamil, E.A. & Al-Sodani, A.H. (2009). Breast Cancer and Selected Lifestyle Variables: A Case-Control Study. Bahrain Medical Bulletin. 31(4).*
2. *Bellizi, K.M., Rowland, J.H., Jeffery, D.D. & McNeel, T. (2005). Health Behaviors of Cancers Survivors: Examining Opportunities for Cancer Control Intervention. Journal of Clinical Oncology. 23,8884-8893.*
3. *Blanchard, C.M., Denniston, M.M. & Baker, F. (2003). Do adults change their lifestyle behaviors after a cancer diagnosis? Am J Health Behav. 27:246-56.*
4. *Boon, H., Stewart, M., Kennard, M.A. & et al. (2000). Use of complementary/ alternative medicine by breast cancer survivors in Ontario: prevalence and perceptions. Journal of Clinical Oncology. 18,2515-2521.*

5. *Burstein, H.J., Gelber, S., Guadagnoli, E. & Weeks, J.C. (1999). Use of alternative medicine by women with early-stage breast cancer. New England Journal of Medicine. 340,1733-1739.*
6. *Cassileth, B.R., Schraub, S., Robinson, E., Vickers, A. (2001). Alternative medicine use worldwide. Cancer. 91,1390–1393.*
7. *Courneya, K.S., Katzmarzyk, P.T. & Bacon, E. (2008). Physical Activity and Obesity in Canadian Cancer Survivors: Population-based Estimates From the 2005 Canadian Community Health Survey. Cancer. 112,2475–82.*
8. *Danaei, G., Vander Hoorn, S., Lopez, A.D., Murray, C.J. & Ezzati, M. (2005). Causes of cancer in the world: comparative risk assessment of nine behavioural and environmental risk factors. The Lancet. 366(9499),1784-1793.*
9. *Demark-Wahnefried, W., Peterson, B., McBride, C., Lipkus, I. & Clipp, E. (2000). Current health behaviors and readiness to pursue life-style changes among men and women diagnoses with early stage prostate and breast carcinomas. Cancer. 88:674-84.*
10. *Demark-Wahnefried, W., Aziz, N.M., Rowland, J.H. & Pinto, B.M. (2005). Riding the crest of the teachable moment: promoting longterm health after the diagnosis of cancer. Journal of Clinical Oncology. 23,5814–5830.*
11. *Emaus, A., Veierod, M.B., Tretli, S., Finstad, S.E., Selmer, R., Furberg, A.S., Bernstein, L., Schlichting, E. & Thune, I. (2009). Metabolic profile, physical activity, and mortality in breast cancer patients. Breast Cancer Res Treat. [On-line] Available from http://www.springerlink.com [Access on 18th November 2009].*
12. *Ferlay, J., Bray, F., Pisani, P. & Parkin, D.M. (2004). GLOBOCAN 2002. Cancer Incidence, Mortality and Prevalence Worldwide. IARC Cancer Base No. 5 Version 2.0. Lyon, France: IARCPress.*
13. *Havas., S., Treiman., K., Langenberg., P., Ballesteros., M., Anliker., J., Damron., D. & Feldman R. (1998). Factors associated with fruit and vegetable consumption among women participating in WIC. J Am Diet Assoc .98:1141-1148.*
14. *Harris, P., Ilora, G., Finlay, G., Cook, A., Thomas, K.J. & Hood, K. (2003). Complementary and alternative medicine use by patients with cancer in Wales: a cross sectional survey. Complementary Therapies in Medicine. 11,249–253.*
15. *Irwin, M.L., McTiernan, A., Baumgartner, R.N., Baumgartner, K.B., Bernstein, L., Gilliland, F.D. & Ballard-Barbash, R. (2005). Changes in Body Fat and Weight after a Breast Cancer Diagnosis: Influence of Demographic, Prognostic, and Lifestyle Factors. Journal of Clinical Oncology. 23,774-782.*
16. *Mathers, C. & Loncar, D. (2006). Projections of global mortality and burden of disease from 2002 to 2030. PLoS Medicine. 3,442.*
17. *Mirnalini, K. & Lim, C.L. (2006). Dietary supplementation and alternative medicine use among Malaysian Cancer Survivors. Asia Pacific Journal of Clinical Nutrition. 15(Suppl),S19.*
18. *Mirnalini, K., Zalilah, M.S., Safiah, M.Y., Tahir, A., Siti Haslinda, M.D., Siti Rohana, D., Khairul Zarina, M.Y., Mohd Hasyami, S. & Normah, H. (2008). Energy and Nutrient intakes: findings from the Malaysian Adult Nutrition Survey (MANS). Malaysian Journal of Nutrition 14(1),1-24.*
19. *Ministry of Health (MOH). (2006). Malaysia NCD Surveillance-I 2005/2006: NCD Risk Factors in Malaysia. Ministry of Health Malaysia, Putrajaya. Malaysia.*
20. *Ministry of Health (MOH). (2006). Food Consumption Statistic of Malaysia 2003 for Adult Population Aged 18 to 59 Years. Ministry of Health Malaysia, Putrajaya. Malaysia.*
21. *Molassiotis, A., Fernadez-Ortega, P., Pud, D., Ozden, G., Scott, J.A., Panteli, V., Margulies Browall, A.M., Magri, M., Selvekerova, S., Madsen, E., Milovics, L., Bruyns, I., Gudmundsdottir, G., Hummerston, S., Ahmad, A.M.A., Platin, N., Kearney, N. & Patiraki, E. (2005). Use of complementary and alternative medicine in cancer patients: A European survey. Annals of Oncology. 16,655–663.*
22. *Montazeri, A., Sajadian, A., Ebrahimi, M. & Akbari, M.E. (2006). Depression and the use of complementary medicine among breast cancer patients. Support Care Cancer. 13(5),339-342.*
23. *National Coordinating Committee on Food and Nutrition (2005). Recommended Nutrient Intakes for Malaysia (RNI). A Report of the Technical Working Group on Nutritional Guidelines. Ministry of Health Malaysia. Putrajaya.*
24. *National Coordinating Committee on Food and Nutrition (2010). Malaysian Dietary Guidelines. Ministry of Health Malaysia (MDG). Putrajaya.*
25. *Ng, L.W. & Kandiah, M. (2000). Lifestyle changes in women with breast cancer. Thesis (Bac Sc). Universiti Putra Malaysia.*
26. *Ono, T., Guthold, R. & Strong, K. (2005). WHO Global Comparable Estimates.*
27. *Patternson, R., Neuhouser, M.L., Hedderson, M.M., Schwartz, S.M., Standish, L.J. & Bowen, D.J. (2003). Changes in diet, physical activity, and supplement use among adults diagnosed with cancer. Journal of the American Dietetic Association. 103,323-328.*
28. *Pierce, J.P., Stefanick, M.L., Flatt, S.W., Natarajan, L., Sternfeld, B., Madlensky, L., Al-Delaimy, W.K., Thomson, C.A., Kealey, S., Hajek, R., Parker, B.A.,*

Newman, V.A., Caan, B. & Rock, C.L. (2007). Greater survival after breast cancer in physically active women with high vegetable-fruit intake regardless of obesity. Journal of Clinical Oncology. 25:2345-2351.

29. *Reicks., M., Randall., J.L. & Haynes., B.J. (1994). Factors affecting consumption of fruits and vegetables by low-income families. J Am Diet Assoc. 94:1309-1311.*
30. *Richardson, M.A., Sanders, T., Palmer, J.L. & et al. (2000). Complementary/ alternative medicine use in a comprehensive cancer center and the implications for oncology. Journal of Clinical Oncology. 18,2505-2514.*
31. *Shen, J., Andersen, R., Albert, P.S. & et al. (2002). Use of complementary/alternative therapies by women with advanced-stage breast cancer. Biomed Central Complementary and Alternative Medicine. 2,2-8.*
32. *Shih, V., Chiang, J.Y.L. & Chan, A. (2005).Complementary and alternative medicine (CAM) usage in Singaporean adult cancer patients. European Journal of Oncology Nursing. 9(2),124-30.*
33. *Skeie, G., Hjartaker, A., Braaten, T. & Lund, E. (2009). Dietary change among breast and colorectal cancer survivors and cancer-free women in the Norwegian Women and Cancer cohort study. Cancer Causes & Control. 20,1955–1966.*
34. *Swisher, E.M., Cohn, D.E., Goff, B.A. & et al. (2002). Use of complementary and alternative medicine among women with gynecologic cancers. Gynecologic Oncology. 84,363–367.*
35. *Tien-Pen, H. & Mohd Sadullah, A.F. (2003). A comparison study on motorcycle traffic development in some Asian countries – case of Taiwan, Malaysia and Vietnam. The Eastern Asia Society for Transportation Studies (EASTS) International Cooperative Research Activity.*
36. *Toles, M. & Demark-Wahnefried, W. (2008). Nutrition and the Cancer Survivor: Evidence to Guide Oncology Nursing Practice. Seminar of Oncology Nurse. 24(3),171–179.*
37. *Wayne, S.J., Lopez, S.T., Butler, L.M., Baumgartner, K.B., Baumgartner, R.N. & Ballard-Barbash, R. (2004). Changes in Dietary Intake after Diagnosis of Breast Cancer. Journal of the American Dietetic Association. 104,1561-1568.*
38. *World Heath Organization (WHO). (2004). Global Strategy on Diet, Physical Activity and Health. Fifty-seventy World Health Assembly. Resolution WHA57.17: Geneva.*
39. *World Health Organization (WHO). (2008). World Health Statistics 2008.Geneva: World Health Organization. France.*
40. *World Health Organization. (2009). Cancer. [Online]. Available from http://www.who.int. [cited on 18th November 2009].*

Corresponding Author
Zalilah Mohd Shariff,
Department of Nutrition and Dietetics,
Faculty of Medicine and Health Sciences,
Universiti Putra Malaysia,
Selangor,
Malaysia,
E-mail: zalilah@medic.upm.edu.my

Impact of nursing care initiatives on the knowledge level and perception of caregiving difficulties of family members providing home care to stroke patients

Hulya Temize[1], Sebahat Gozum[2]

[1] Ankara Mevki Dispensary Anittepe, Ankara, Turkey,

[2] Akdeniz University Faculty of Healthcare Sciences Department of Public Health Nursing Antalya, Turkey.

Abstract

Objectives: Taking into account the difficulties of at-home care that caregivers of stroke patients face regularly, we conducted a prospective study usings pre-test and post-test control groups to evaluate the impact of training on the quality of proper care giving and related stress control capacity, as well as the impact of telephone follow-ups on the perception of care giving burden and the level of care giving knowledge.

Methods: The data space of study was constituted by patients who were diagnosed with stroke at the Neurology Clinic of the Military Hospital at Ankara, resided in the city center of Ankara and had been discharged to their homes after completion of treatment, having only at-home care from their relatives and their care givers. A total of 80 patients seen between the January 2008 and March 2009 and their caregivers constituted the sample space of the survey.

After the pre-interview with the family caregivers that formed the study group, the Caregiving Difficulty Determining Scale and Caregiving Knowledge Level Scale were applied as pre-tests. Face-to-face personal training lasting 45 to 60 minutes was conducted with every individual and a training manual was then given to families as a caregiving guide. After discharge, an investigator called the families once a week, answered the questions they had, and provided them a phone number for easy access. The investigator continued to call the patient and caregivers once a week for three months following the discharge. Four weeks after the discharge, an investigator visited the patients and caregivers at their homes, discussed the caregiving issues that caused the most stress, and answered their questions within the framework of the training that was provided. The Caregiving Difficulty Determining Scale and the Caregiving Knowledge Level Scale questionnaires were administered as post-tests during home visits to family members.

Results: The knowledge pre-test scores of the study group caregivers were 58.12 ±14.30 while the post-test scores increased to 91.1 ±8.1. Pre-test scores (54.4±14.1) and post-test scores (55.4±13.8) of the control group were found to differ by only by 1 point. We determined that training and consultancy services provided to the study group caregivers affected their knowledge level. In the study group, the caregivers' pre-test mean scores for the burden of care-giving were 48.5±13.4, the post-test mean scores 42.67±10.4, while the respective numbers for the were 52.2±12.9 and 57.2±7.7 respectively. This finding shows that training, telephone counseling and home visits provided to caregivers of stroke patients are very effective in significantly reducing the load of caregivers.

The results of the study reveal that providing professional training and counseling to family members of stroke patients regarding home care fundamentals before discharge will have a positive impact on caregiving and reduce the difficulties faced by caregivers.

Key words: Stroke; Family Education; Patient Discharge; Telephone Communication; Nursing Care; Home-care Services.

Introduction and aim

Stroke is the third most important cause of death following heart disease and cancer globally. One person suffers a stroke every minute on average and one person dies due to stroke every three minutes in the United States of America. Stroke is

the most common cause of physical function loss in adults in Europe and makes up 3-4% of the total healthcare costs [1]. The World Health Organization data reveal that 15 million persons suffer minor strokes every year [2]. The incidence of hypertension is expected to increase 60% by 2025 and affect 1.56 billion people which could lead to an increased number of stroke sufferers [3].

The WHO indicates that stroke, with increased socioeconomic importance, is the main reason for long-term disability. It causes major emotional and socioeconomic problems for the patients, their families and healthcare institutions. The lifelong cost of a patient is 59.800 USD-30.000 USD. Stroke and coronary heart disease together are expected to be the most important causes of loss of healthy living in 2020. Stroke is the third most common cause of death in the world and the most common cause of disability. It also makes up a large part of hospital presentations and healthcare costs in developed countries [4]. Disability following stroke both decreases the patient's quality of life and also leads to societal and socioeconomic problems by affecting the patient's family [5]. Despite the huge cost of stroke regarding public health, this load becomes even larger both financially and emotionally when the effect of the disorder on the relevant family members is also considered.

Studies have revealed that primary caregivers suffer many difficulties such as emotional stress, physical disease, decreased social activities and problems with family relations and work life [6,7]. Nurses are healthcare staff that provide professional care to both healthy and sick individuals at all stages of life. Providing care is one of the oldest and traditional roles of the occupation that the nurses independently provide and it continues to be important among the current occupational roles. Public health nurses can, with the right approach, help caregivers provide care successfully [8]. Public health nurse will encounter patients with stroke and their caregivers frequently during home visits. The nurse should train the family members to increase their ability to care so that they can provide the necessary care and not suffer from the exhaustion syndrome because of their role [9].

The family member to provide care for a stroke patient should be informed about home care before the patient is discharged and should be directed to a healthcare specialist who can provide the required support when necessary. The training for stroke patients should start at the hospital and continue at home. The discharge training should include information on drugs and treatment, recognizing complications, preventing complications, avoiding risk factors, follow-up frequency, self-care, wound care, preventing pressure ulcers, catheter care, special feeding, diarrhea and constipation, the importance of sleep and sleep-related problems, active and passive motion exercises, improving health, decreasing or totally stopping alcohol use and smoking, anticoagulant drug use, bladder-intestine status, cognitive status, devices and orhoses, falls, and safety and psychosocial conditions[5,10]. The training can be provided by telephone in addition to home visits for consultancy and support in urban areas.

Material-Method

The study was started on 12.02.2007 after consent was obtained from the ethic committee and the subjects who were participating voluntarily in the study. The Neurology Clinic of the hospital in Ankara had 37 beds and worked with a 95% bed occupancy rate. The study universe consisted of patients who had received a diagnosis of stroke (CVO) during 2008 and 2009 and had been treated at the Ankara province center to be sent home afterwards, and who were cared for by their family members but did not receive any institutional care, in addition to these patients' caregivers. Randomization was performed by placing the patients and their caregivers into the study group for one week and the control group the next week consecutively from the date the data collection began. Each group consisted of 40 caregivers. The retrospective evaluation revealed a study power of 0.99 and a power of 1.7 when the 40-person sample in each group was compared regarding caring burden perception with the t-test for independent groups during retrospective evaluation.

The questions that defined the patient and the caregiver were created by the investigator. The question form consisted of 11 questions on the caregiver's age, marital status, education, employment status, occupation, income status, relationship to the patient, the person providing support

during the caring process, and whether the caregiver had a chronic disease and the patient any disease besides a stroke[11]. The Barthel Index[12] was used during discharge to determine factors that affected the caring burden and the patient's level of dependence. The Norton Decubitus Risk Definition Scale[13] was used to determine decubitus risks and to inform the family regarding individuals that had a high risk. The lowest scale score was 0 while the highest was 15. A low score indicated a high decubitus risk.

The knowledge questions were created by the investigator following a literature survey [14-21] and were reviewed by two nurses and a measurement evaluation specialist. They consisted of 20 multiple choice questions with a single correct answer and were prepared taking into account the problems the caring family member could face while providing care for the stroke patient. Studies that use the Barthel index have defined the limit as 60 and scores above this value indicate independent functioning. The scale scores are interpreted as follows:[10]

0-20	Fully Dependent
21-61	Markedly Dependent
62-90	Moderately Dependent
91-99	Mildly Dependent
100	Fully Independent

The Barthel index (BI) consists of 10 items on daily living activities and mobility. It evaluates feeding, wheelchair use, self-care, bathing, walking, going up and down the stairs, getting dressed and bladder and bowel continence.

The Zarit Caregiver Burden Scale (ZCBS) was used to evaluate the difficulties in providing care as perceived by the family caregivers . The Caregiver Burden Scale developed by Zarit, Reever and Bach-Peterson in 1980 has been adapted into Turkish by Inci in 2006. This scale can be completed by the caregivers themselves or by questioning by the investigator and consists of 22 statements that define the impact of providing care on the caregiver's life. The scale has a Likert-type evaluation that changes from 0 to 4 as "never, rarely, frequently and almost always". The minimum scale score is 0 and the maximum 88. The items in the scale are directed towards the social and emotional areas and a high scale score indicates a high level of problems experienced. The internal consistency (alpha) of the test has been determined as 0.91, the test-retest reliability as 0.86 and the inter-investigator consistency as 0.63. The internal consistency coefficient of the Turkish form is 95 while the test-retest consistency coefficient is 90. The Cronbach alpha coefficient of the Caring Burden Scale was 0.88 in this study.

The study preliminary tests were administered to the caregivers of the patients admitted to the Neurology Clinic for the first time with a CVO diagnosis at the time of the study. Preliminary tests were the Descriptive Features Form, the Barthel Index and Norton Decubitus Risk Definition Scale, the Caring Burden Scale (BVYÖ) and the Caring Knowledge Level Form (BVBDF). The data were collected at the Neurology Clinic with face-to-face interviews of the patient's caregiver. One-to-one discharge training was provided to the patient caregiver in the study group and a training booklet provided. Following the discharge, the final tests (Caring Burden Scale and Caring Knowledge Scale Form) of the study were collected following the home visit, telephone training and consultancy services. An appointment was made with the caregivers before the home visit and interviews were carried out and another reminder was provided by telephone before the interview. Preliminary data were also collected from the control group before discharge but no intervention was made. The control group was monitored with the routine follow-up of the clinic and a training booklet was provided after the final tests were administered. In the period after the final tests were administered to the study group (3 months later), the final tests of the control group (Caring Burden Scale and Caring Knowledge Level Form) were administered during a home visit and study data were collected.

Discussion

The results (study group mean score 58.1, control group mean score 54.4, $p>0.05$) for the knowledge level of the caregivers in the study regarding providing care to the stroke patient were moderate in the study and control groups, considering that the full score was 100. Evaluation of the least well-known and best known subjects regarding caring by the caregivers (Table 1) revea-

led that the best known subjects were the signs of depression, the early signs of stroke, knowledge of the drugs used, techniques of communicating with the patient who is unable to talk and eating and swallowing problems. Preventing bleeding, what to pay attention to while the patient has an epileptic seizure and has a nasogastric catheter placed, the importance of rehabilitation, bed bath and preventing the recurrence of stroke were subjects not known by approximately half of the caregivers. Living at home following a stroke is full of difficulties. The caregivers have various roles, needs and difficulties during this period. Nursing interventions are therefore important. Institutional care is expensive and separates the individual requiring the care from social life, necessitating more widespread caring services that enable care within the close environment together with home care. However, the inadequate knowledge of the caregivers on caring causes a shortened life expectancy for persons cared for at home. Studies have shown that caregivers are faced with some problems and being a caregiver is a stressful role [17-22]. Feldman et al.[22] have determined that 36% of caregivers are inadequate in providing care. The Özde et al.[23] study has shown that the caregiver age, gender, city of residence and the hospital of the same city have a significant effect on the caregiver stress scale and that the caregiver burden plays an important role on the stroke prognosis. An experimental study by Hackl et al.[24] on the caregivers of stroke patients has shown that 65.6% of caregivers are female. This fact leads to an increase in the burden and responsibilities of the family. The mean age of the caregivers was 53.32±9.81 and 54.7±11.62 in the study and control groups respectively. Nagura et al.[25] reported a mean age of 62 for caregivers in their study. We can see that the caregivers are middle-aged when we take into account the life expectancy in Turkey and other countries. This may lead to negative consequences regarding the caregiver's health and the stroke patient's care. The caregiver will both have to take care of his/her own health problems due to advancing age and carry the burden of the stroke patient's care and health problems. The caregivers

Table 1. Distribution of the Correct Responses of Caregivers within the Scope of the Study Regarding the Caring Knowledge Level

Matters related to caring knowledge level	Correct answer		Wrong answer	
	Number	%	Number	%
15- Signs of depression	32	40	48	60
1– Early signs of stroke	34	42.5	46	57.5
3– Information on drugs used	35	43.7	45	56.2
11- Communication methods	36	45	44	55
20- Eating and swallowing problems	39	48.7	41	51.3
18- What to do to prevent bleeding	41	51.3	39	48.7
14- What to do during an epileptic seizure	42	52.5	38	47.5
4– What to do when a nasogastric catheter is present	43	53.7	37	46.3
5– The importance of rehabilitation	44	55	36	45
19- What to do in the bed bath	45	56.3	35	43.7
16- What to do to prevent recurrence of stroke	46	57.5	34	42.5
10- Finding a solution to visual field loss	52	65	28	35
13- Creating a positive body image	54	67.5	26	32.5
9– Urinary catheter care	58	72.5	22	27.5
7– Skin care	61	76.3	19	23.7
8– Keeping diabetes under control	62	77.5	18	22.5
12- Regaining the ability to decide	63	78.7	17	21.3
17- Knowing the complications	66	82.5	14	17.5
2– Communicating with the person who can't speak	74	92.5	6	7.5
6– Oral care	78	97.5	2	2.5

Table 2. The Subject that Attracted the most Attention and Required the Most Training during the Home Visits and Telephone Conversations with the Study Group Caregivers

Subject Attracting Questions*	Number	Percentage (%)
Coping with stress	3	7.5
Recognizing comp. signs	2	5.0
Institution info	4	10.0
Catheter care	5	12.5
Preventing pressure ulcers	8	20.0
Curing itching	5	12.5
Constipation	6	15.0
Diarrhea	5	12.5
Feeding problems	2	5.0

**The matter most important for each caregiver was determined and the percentages were calculated using n=40.*

were university graduates in 42.5% of the cases in the study. This made it easier to train them regarding providing care. A chronic disease was present in 65% of the caregivers. This will also make caring more difficult. Our patients made up a group who were dependent for daily activities and had a risk of decubitus ulcer development. The dependency level can be thought to affect the perception of the care burden. Interviews with the study group revealed that 8 caregivers had used consultancy services for pressure ulcers (Table 2) indicating that the caregivers were aware of the pressure ulcer risks. A study on stroke patients with a home care need by Nagura et al.[25] showed that the most commonly developing problems were infection and decubitus ulcers. These ulcers, caused by the dependency on a bed and the physical limitation in the patient can only be decreased by good care and training the caregivers. The nursing intervention was effective in this study and no patient in the study group developed decubitus lesions.

Gündüz et al.[26] have recommended adding the Short Form-36 to the evaluation of the partners of the stroke patient at outpatient departments so that partners who need training and support can be determined, as being the partner of a stroke patient will have a negative effect on the quality of life. Using this form will be beneficial when evaluating the home caregivers of stroke patients. Yildirim et al.[27] have emphasized the need for a holistic approach that also includes the evaluation of the psychiatric state of caregivers by healthcare professionals during the process in patients who have a mild to moderate level of dependency with chronic neurological disease. It is reported that home-carers suffer from limitation of their freedom, stress and depression and their mental health is negatively affected [25]. We found that both study and control group caregivers had serious problems when we evaluated the perception of the caring burden with data from the preliminary tests.

Evaluation of the study group caregivers' caring burden mean scores before and after the nursing intervention (Table 3) showed that the preliminary test mean score was 48.50±13.35, and the final test mean score 42.67±10.41. The control group caregivers' preliminary mean score was 52.20±12.93, and the final test mean score 57.15±7.72. The caring burden of the study group showed a statistical decrease in the final test but the perceived burden was still high. Grant et al.[28] also found significant changes in favor of the study group in other parameters measured but the exhaustion level, which may be accepted as an indicator of the caring burden severity, was similar in the study and control groups. These results indicate that various interventions are necessary to decrease the caring burden. The caring burden of the control group increased over time. Providing information, consultancy and telephone follow-up for the study group during the intervention period enabled caregivers to obtain information on matters they felt anxious about and they felt more comfortable when they knew there was a nurse that followed and evaluated them. The caring burden increased over the duration of the intervention period (3 months) in the control group. This difference between the study and control groups shows that the intervention was effective. The nursing intervention in this study decreased the caring difficulties of the family member caregivers. The results of this study support the results of the other studies listed below. Providing care and consultancy services is one of the independent occupational roles of nurses. The Lidell[29] study states that social and professional support is effective in decreasing the care burden. Hackl et al.[24] have reported that caregivers of stroke patients need psychosocial help and that training providing the solutions to these problems

is important. Evans[30] has reported that families suffer difficulties with problem solving, communication and coping with emotional situations following a stroke. Interventional studies aimed at supporting the family caregivers of stroke patients in recent years have reported that discharge training, home visits, telephone consultancy and web-based training by nurses have a positive effect on the caregivers, prevent unnecessary presentations at the hospital and increase the independence level of the patients.16-18, 32-34

The treatment and care of stroke patients continue at home after their discharge and the responsibility is transferred to the caring family. The patient and the family face various physical, psychosocial and financial problems during this process. Analyses of these problems reveal that most can be solved by monitoring at home. Repeated hospitalizations will decrease when home care services are supported by the institutions and the net result will be a positive contribution to the family and national budget.

Analysis of the within-group preliminary test-final test caring knowledge level and caring burden of the study group and control group caregivers showed that the knowledge preliminary test of the study group had increased from 58.12 to 91.12 after the intervention and the difference was statistically significant. This change demonstrates that training on caring for the stroke patient increases the knowledge level. Grant et al.[28] have found in their experimental study that the social problem solving skills, ability to cope and mental and social functions of stroke patients who had discharge training and a home visit and were followed-up by telephone were better than in the control group. Pierce et al.[33] have evaluated the effect on patient care of providing web-based training to the family members of stroke patients for a year in their study. The presentation at the emergency service and readmission to the hospital rates were lower in the study group caregiver's patients and it was emphasized that providing information to caregivers decreases unnecessary use of healthcare resources. The results of this study support the conclusion of previous studies that providing training/consultancy to the family members caring for a stroke victim will make a positive contribution to the results.

Conclusions

This study has been conducted as an experimental study with a prospective, preliminary test and final test control group to determine the effect of training, telephone consultancy and home visits to stroke patient caregivers on the knowledge of caregivers and their perception of the care burden. The caregiver training was as individual discharge training after which a training booklet was provided. The training was repeated with a home visit a month later. The telephone consultancy service continued for 3 months and 12 calls were made. The caregivers were provided a telephone number they could use at all times. The second home visit was at the end of the 3rd month when the final tests were administered.

The study group caregiver preliminary test mean score for caring burden was 48.50±13.35 and the final test mean score was 42.67±10.41 while the respective scores for the control group were 52.20±12.93 and 57.15±7.72. These valu-

Table 3. Comparison of the Prelimininary Test - Final Test Caring Knowledge and Caring Burden Mean Scores of the Study Group and Control Group Caregivers

Caring knowledge level	Study Group	Control Group	Significance*
Preliminary test	58.1 ± 14.3	54.4±14.1	*t* =1.180 p>0.05
Final test	91.1 ± 8.1	55.4 ± 13.8	t=14.089 **p< 0.001**
Significance**	t=17.129 **p<0.001**	t=2.082 **p<0.05**	
Caring burden perception			
Preliminary test	48.5±13.4	52.2±12.9	*t* =1.259 p>0.05
Final test	42.7±10.4	57.2±7.7	t=7.06 **p< 0.001**
Significance**	t=5.014 **p< 0.001**	t=4.146 **p< 0.001**	

**t test for dependent groups*
***t test for independent groups*

es reveal that the burden of caregivers is at high levels, especially before the training. The caring burden perception of the caregivers in the study group decreased following the training home visit and telephone consultancy services. The control group did not receive any intervention and their caring burden was seemed to increase at the end of 3 months. We found that training, telephone consultancy and home visit to the caregivers of stroke patients provided a significant decrease in their caring burden.

The intervention provided to the study group increased their caring knowledge level significantly (Study group knowledge preliminary test score 58.12 ±14.30, knowledge final test score 91.12±8.12; control group knowledge preliminary test score 54.37 ±14.10, knowledge final test score 55.37±13.83). Stroke patient caregivers therefore need to receive training on caring. This will increase the quality of care and facilitate caring. These trainings must be routine during discharge from the hospital. Once discharged from the hospital, the patient and the caregiver should not be left to their own resources. Home visits must be made and there should be continuous communication between the stroke center and the patient's home. We suggest that investigators who plan to undertake an interventional study on the subject evaluate the care-related results such as the dependence level of the patients for daily living activities, decubitus development status and the usage reason and frequency of healthcare services of the stroke patients besides the status of the caregivers.

References

1. *Tran BQ, Buckley KM, Prandoni CM. Use of Telehealth Technology in Support of Homebound Caregivers of Stroke Patients. Caring 2002; 21(3): 16–21.*
2. *Woo J, Hui E, Chan WM. Telerehabilitation – A New Model for Community-Based Stroke Rehabilitation. J Telemed Telecare 2004; 10(4): 199–205.*
3. *Kantz B, Wandel J, Fladger A, Folcarelli P, Burger S, Clifford JC. Developing Patient and Family Education Services: Innovations for The Changing Healthcare Environment. J Nurs Adm 1998; 28(2): 11–18.*
4. *Kumral E, [Epidemiology of Cerebrovascular Diseases] Turkiye Klinikleri J Neurol 2004;2(1):15-21.*
5. *Anderson C,Rubenach S, Mhurchu C, Clark M, Spencer C, Bappsc W. A."Home or Hospital for Stroke Rehabilitation? Results of A Randomized Controlled Trial I: Health Outcomes At 6 Month " Stroke 2000; 31(5): 1024-1031.*
6. *Toseland RW, Smith G, Mccallion P. Family Caregivers of The Frail Elderly Handbook of Social Work Practice with Vulnerable and Resilient Populations. Gitterman, A. Ed. Columbia University Press, 2001; 11-18.*
7. *Kasuya RT, Polgar B, Takeuchi R. Caregiver Burden and Burnout. Postgrad Med 2000; 108(7):119-123.*
8. *Wyller TB, Bonita R. Prevalence of Stroke and Stroke-Related Disability / Response. Stroke 1998; 29(4): 866–868.*
9. *Almborg AH, Ulander K, Thulin A, Berg S. Understanding The Needs of Families Discharge Planning of Stroke Patients: The Relatives' Perceptions of Participation. JCN 2009;18:857–858.*
10. *Barthel M, Mahoney K. Agency For Health Care Policy And Research Publication. After Stroke Recovery Patient Guidelines Booklet; Government Printing Office Washington Dc. 2002; 23–27*
11. *Küçükgüçlü Ö,Esen A,Yener G [Validity and Reliability Analysis of the Turkish Society for Caregiver Burden Inventory] J Neurol Sci. 2009; 26(1)18: 60-73.*
12. *Kucukdeveci AA, Yavuzer G, Tennant A, Suldur N, Sonel B, Arasil T. Adaptation of The Modified Barthel Index for use in Physical Medicine and Rehabilitation in Turkey. Scand J Rehabil Med 2000;32:87-92.*
13. *Norton D. Calculating the risk: reflections on the Norton scale. Decubitus 1989; 2: 24.*
14. *Grant JS, Elliott TR, Giger JN, Bartolucci AA. Social problem-solving telephone partnerships with family caregivers of persons with stroke. Int J Rehabil Res. 2001; 24: 181-9.*
15. *Torres-Arreola LP, Doubova SV, Hernandez SF, Torres-Valdez LE, Constantino-Casas NP, Garcia-Contreras F, Torres-Castro S. Effectiveness of two rehabilitation strategies provided by nurses for stroke patients in Mexico. J Clin Nurs. 2009;18:2993-3002.*
16. *Bakas T, Farran CJ, Austin JK, Given BA, Johnson EA, Williams LS. Stroke caregiver outcomes from the Telephone Assessment and Skill-Building Kit (TASK). Top Stroke Rehabil. 2009;16:105-21.*
17. *Bakas T, Austin J, Okonkwo KF, Lewis R, Chadwick L. Needs, concerns, strategies, and advice of stroke caregivers the first 6 months after discharge, J Neuroscience Nurs 2002; 34: 242–252.*

18. *Durna Z., Krespi Y., Memiş S. et al. ''Hasta ve Yakınları İçin İnme El Kitabı (Stroke Manual for Patients and Relatives), İstanbul Üniversitesi Yayın No:4379, İstanbul 2003.*

19. *Glandon G, Elliott T, Giger J.N,W,M "Caregiving Problems And Feelings Experienced By Family Caregivers of Stroke Survivors the First Month after Discharge", Int J Rehabil Res. 2004; 27(2): 105-111.*

20. *Grant J.S, O'connell B, Baker L, Prosser A,"The Educational Needs of Caregivers of Stroke Survivors in Acute and Community Settings", J Neuroscience Nurs 2003; 35(1) 21-28.*

21. *Pierce L, Finn M, Gordon,Steiner V, Families Dealing With Stroke Desire Information About Self-Care Needs, Rehabilitation Nursing, 2004; 29(2)14.*

22. *Feldman FH, Waliser MN, Gould DA, Levine C. When the caregivers needs care: the plight of vulnerable caregivers. A J Pub Health 2002; 92:409.*

23. *Ozde A, İnce B, Somay G, Çakmak S, Uludüz D, Bulkan M et al. [The Caregiver Burden and Stroke Prognosis] J Neurological Sciences 2009, 26:(2)19; 139-152.*

24. *Hackl M, Holzner B, Gunther V, Saltuari L. Care of stroke patients by relatives social support and coping strategies. Dtsch Med 1997; 122: 669–75.*

25. *Nagura E, Igata A, Fujita H, Inove T, Kano K, Matsura T, Tokuda H, Hosokawa T. Characteristics of Bedridden Elderly People Living at Home and In a Hospital. Nippon Ronen Igakkai Zasshi 1997; 34: 589–95.*

26. *Gündüz B, Erhan B [Quality of Life of Stroke Patients' Spouses Living in the Community in Turkey: Controlled Study with Short Form-36 Questionnaire] J Neurol Sci Turk 2008; 25(4): 226-34.*

27. *Yıldırım SA, Özer S, Yılmaz Ö, Düger T, Kılınç M [Depression, Anxiety and Health Related Quality of Life in the Caregivers of the Persons with Chronic Neurological Illness] J Med Sci 2009;29(6):1535-42.*

28. *Grant JS, Elliott TR, Weaver M, Bartolucci AA, Giger JN. Telephone intervention with family caregivers of stroke survivors after rehabilitation. Stroke. 2002; 33: 2060-5.*

29. *Lidell E. Family support - a burden to patient and caregiver. E J Cardiovascular Nurs 2002; 1: 149-152.*

30. *Evans R. The Family's Role In Stroke Rehabilitation. J Phys Med Rehabil 1992; 3: 135–139.*

31. *Shyu YI, Chen MC, Chen ST, Wang HP, Shao JH. A family caregiver-oriented discharge planning program for older stroke patients and their family caregivers. J Clin Nurs. 2008; 17: 2497-508.*

32. *Madeline M, Lorentz BA, Telenursing and home. Home Healthcare 2008; 26(4): 237–243.*

33. *Pierce LL, Steiner VL, Khuder SA, Govoni AL, Horn LJ. The effect of a Web-based stroke intervention on carers' well-being and survivors' use of healthcare services. Disabil Rehabil. 2009; 31: 1676-84.*

Corresponding Author
Hulya Temize,
Ankara Mevki Dispensary Anittepe,
Ankara,
Turkey,
E-mail: temizerh@yahoo.com

Comparison of complications and marital satisfaction in women taking contraceptive ampoules of cyclofem and ld contraceptive pills

Esmaelzadeh Sedigheh[1], Gholamitabar Tabari Maryam[2], Bijani Ali[3], Poorebrahim Mehdi[4]

[1] Department of Gynecology & obstetrics,Babol University of Medical Science, Babol, Iran,
[2] Department of Midwifery, Islamic Azad University Of Sari, Sari, Iran,
[3] Non-communicable Pediatric Disease Research Center, Amircola Hospital, Babol University of Medical Science, Babol, Iran,
[4] Mazandaran Red crescent University, Iran.

Abstract

Introduction: There are several methods of contraception, No single method is sufficient and satisfactory in all cases._In this study we investigated the comparison of side effect and marital satisfaction between the women taking Cyclofem contraceptive ampoule and LD combined pill.

Material and Methods: This study was performed on 300 married women use cyclofem and LD combined pill for family planning.150 people in each group. Data collection tools included two types of questionnaires; one for studying the complications and the other for examining the marital satisfaction(Enrich Couple Questionnaire).

Result: The two groups using contraception methods were different in terms of occupation and education; (respectively P=0.002 and p=0.04). 48 % of Cyclofem users reported Amenoreha, which was higher than LD users (3/3%)with significant difference (P=0.000). In Contraceptive LD users, Days of menstrual bleeding was lower than Cyclofem users. (1/3% vs. 22%) and the difference was significant (P=0.000). Mood changes and Decreased libido in LD users were more than Cyclofem users and the difference was significant (P=0.000) & (p=0.01). respectively.Breast pain and tenderness in LD users was less than Cyclofem users (6/7% vs. 14%) and the difference was statistically significant (p=0.03).

Conclusion: the side effects caused by Cyclofem and LD are not fatal and irreversible. By proper counseling and teaching women using these methods, health staff can help more use and continuance of these methods; especially regarding the possible side effects.

Key word: Cyclofem,contraceptive,side effect

Introduction

Family planning includes methods taking which helps couples give birth to desirable children and arrange the interval between the pregnancies(1). There are several methods of contraception, which varies from relatively simple forms to surgical procedures. No single method is sufficient and satisfactory in all cases. (2) There are many types of contraception methods among which hormonal method includes oral contraceptives (combined pill) (3). LD pills combined of 30µg ethinyl estradiol and 15µg levonorgestrel is a standard combination (4). Although the combined contraceptive pills are an option for many women in the world, daily prescription of them is considered a defect. Recently, the results of major studies have shown that women, both new and old users, complain from daily consumption and prefer to benefit monthly options (5). Cyclofem ampoule with 1-month intervals is a very effective contraception method that contains 25 mg medroxyprogesterone acetate and 5mg estradiol cypionate (6). An important difference between oral contraceptive pills and this medicine is that it contains natural estrogen. At present it is revealed that natural estrogen has highly favorable effects on lipid metabolism and cardiac activity, which acts as tissue blood flow increase and the anti-sclerosis effect (7) and has advantages including long effect, ease of prescription and non-interference with intercourse (8). Despite these advantages and its potential benefits, it is observed that contraception applicants are not inclined to use it, and prefer to use LD pills. Although the advantages of contraceptive pills are widely known, their effectiveness in contraception depends on the proper use and its continuity as well

as the consumer-related conditions. Given that our population is young, considering pregnancies in lower ages is one of the important points. The need for proper implementation of family planning, especially in young and adolescent women is quite tangible. In addition, since fertility reaches a peak during the second decade of life (9), and fertility in the age of 25 comprise the largest percentage, it is very important to select appropriate contraception method in women under 25 in order to avoid major medical, social and economic problems. On the other hand, any contraception method has advantages and disadvantages as well as absolute and relative contraindications. The appropriate method is a method which has more advantages than disadvantages (10).None of the contraceptive methods is fault-free and all come with some complications. Below items could be mentioned for complications of hormonal methods: menstrual disorders, amenorrhea, irregular uterine bleeding, weight gain, headache, decreased libido, nervousness, fatigue, mood changes, etc. (12,13,14,15). The studies have shown that such complications are occurred with different rates in different communities.(16,17,18) Thus, the complaints of side effects occurrence for the clients could be reduced by careful consideration of side effects, and their satisfaction would be promoted. Consumers of such hormonal methods face physical, psychological and mental disorders due to unwanted complications, which sometimes affect marital satisfaction; marital satisfaction is a condition in which married couples are happy and satisfied with each other.(19) Many variables are effective on how couples communicate with each other during their common life including income, employment, children, illness and sexual satisfaction.(20) Changes in physical and psychological status of these individuals may lead to unfavorable reactions and behaviors by avoiding their housekeeping obligations as well as routine duties and functions. Although marital satisfaction and factors affecting it has been focus of attention by Iranian researchers, there are no studies on this particular issue on these people. Therefore, considering the shortages and the importance of this topic, the researchers decided to study the comparison of complications and marital satisfaction between the women taking Cyclofem contraceptive ampoule and DMPA.

Materials and Methods

This study is comparative and was conducted by convenience sampling. Population under study was women using contraceptive methods of Cyclofem and DMPA provided from health centers in Babol. Precondition for entering the study was at least two 3-month periods; i.e. 6-month use of Depo Medroxyprogesterone ampoule and at least 3 one-month periods; i.e. 3 months use of Cyclofem ampoule due to adjustment of side effects of the hormonal methods after first few months of use. Furthermore, the samples should not use any other hormonal method while using this method. Sample size was determined as 150 people in each group. Data collection tools included two types of questionnaires; one for studying the complications and the other for examining the marital satisfaction. Questionnaires related to complications were prepared considering the previous studies and the existing scientific resources in two parts: (1) profile consisting of 6 questions and (2) a part related to the complications of ampoules including 15 questions. Enrich Couple Questionnaire translated by Mohammad Hussein Asoodeh et al including 4 subscales and 35 questions about satisfaction, communication and conflict resolution was used to examine the marital satisfaction. This questionnaire as a valid research instrument has been used in many researches and clinical works. Data so collected were analyzed by statistical software SPSS/v19 applying descriptive statistics, chi-square test, t-test and Pearson Correlation.

Results

All respondents have been in age range of 18 to 51.Average total age of respondents was 32/07± 7/671 and there was no significant difference between the two groups using Cyclofem and LD pills from in terms of age and number of children. However, the two groups using contraception methods were different in terms of occupation and education; (respectively $P = 0.002$ and $p = 0.04$).

According to Table, 37/3% of LD pill users reported without their menstrual disorders with no change, that was more than Cyclofem users (16/7%) and was significantly different ($p = 0.000$). Regarding Amenoreha, 48 % of Cyclofem users reported

Amenoreha, which was higher than users of LD pills (3/3%) with significant difference (P = 0.000). In LD users, Days of menstrual bleeding was reduced more than users of Cyclofem. (1/3% vs. 22%) and the difference was significant (P = 0.000). Spotting in LD users was lower than users of Cyclofem ampoule (24/1% vs. 39/2%) and the difference was significant (P = 0.000). Four percent of LD users reported the increase of menstrual bleeding days more than users Cyclofem ampoule (0%) and was a significant difference (p = 0.03). 14% of LD users reported more regular menstrual cycle that was more than users of Cyclofem ampoule (0%) and was significantly different (P = 0.000). Regarding increased menstrual bleeding and more irregular menstrual cycle, both groups were similar and not significantly different.

Regarding mood changes, LD users were more sensitive than users of Cyclofem ampoule (41/5% vs. 16/7%) and the difference was significant (P = 0.000). Also early fatigue in LD users was lower than users of Cyclofem ampoule (2 % vs. 10/7 %) and the difference was significant (P = 0.002). However, both groups were similar and were not significantly different in terms of early crying, decreased power and increased anger.Decreased libido LD users was 22%, which was higher than users of Cyclofem (11/3%) and was significantly different (p = 0.01). Users of Cyclofem ampoule reported a higher decrease in vaginal discharge than LD users (2/7% vs. 8/7%), that was significantly different (p = 0.02). Regarding weight change, both groups were identical and were not significantly different (p > 0.0 5). LD users reported lower levels of abdominal bloating than users of Cyclofem ampoule (4/7% vs. 24%) and the difference was significant (p = 0.000).

Breast pain and tenderness in LD users was less than Cyclofem users (6/7% vs. 14%) and the difference was statistically significant (p = 0.03). Back pain in LD users was less than users of Cyclofem ampoule (10/7% vs. 23/3) (p = 0.004). Also Sprained foot in LD users was less than users of Cyclofem ampoule (10/7% vs. 36/7%) and the difference is significant (P = 0.000). In terms of other complications, both groups are identical and are not significantly different (p > 0.05). Regarding the use of Cyclofem ampoule, 62% for a year, 22/7% for two years, and 15/3% have used this ampoule for three and more years. Regarding the use of LD pills, 40/9 % for a year, 12/1% for two years and 47% percent used it for three and more years. The comparison between the duration of use of Cyclofem ampoule and LD pills showed that there is a significant difference between the duration of use and the type of contraception method (p = 0.000). It means that the continuation rate of using LD pills was longer than that of Cyclofem ampoule.

The relationship between continuation of use and age of users in the two groups of women using Cyclofem ampoule and LD pills showed that there is no significant relationship between the continuation of using contraception methods in women using Cyclofem ampoule and their age (Rho=0.23, P=0.09). However, there is a significant relationship between the continuation of using contraception methods in women using LD pills and their age (Rho = 0.39, P = 0.000).

Pearson correlation test showed that there was no significant relationship between marital satisfaction and age, education, number of children and occupation. Marital satisfaction scores in women using Cyclofem ampoule were minimum 100 and maximum 136. Marital satisfaction scores in women using LD pills were minimum 102 and maximum 142. Average marital satisfaction in women using LD was significantly greater 116/13 ± 8/658 than the average marital satisfaction in women taking contraceptive method of Cyclofem 114/53±7/16 (P = 0.01).

Discussion

In this study, the complications of menstrual disorders in women using menstrual Cyclofem was significantly more than women using LD, but decrease of bleeding days and spotting, and increase of bleeding days and more regular menstrual cycle in LD users was significantly greater than Cyclofem users.The most common menstrual disorder in women taking LD pills was spotting, while it was menstrual stoppage in women using Cyclofem. In the study of Yazdanpanah, the most common menstrual disorder in women taking Cyclofem was prolonged bleeding which is inconsistent with this study. In the study of Mir Mohammad Ali (19), the most common complication of menstrual disorder in women taking LD pills

Table 1. Relative frequency of some side effects in users of contraceptive Cyclofem ampoule and LD pills

Side effect	Depomedroi %N	Cyclofem %N	P value	Side effect	Cyclofem %N	Depomedroxi %N	p value
Amenoreha	(74)3/50%	72))48%	P=o.77	Painful coit	(8)3/5%	(9)6%	P=0.80
decreasing days of bleeding	(2)3/1%	(2)3/1%	P=0.99	lokoreh	(13)7/8%	(6)4%	P=0.09
breakthrough bleeding	(29)3/19%	(31)7/20%	P=0.77	Decrease libido	(17)3/11%	(21)14%	P=0.48
Increase days of bleeding	(8)3/5%	0	P=0.004	Increase libido	(12)8%	(8)3/5%	P=0.35
Increase bleeding	(2)3/1%	0	P=0.15	Weight Without change	(74)3/49%	(77)3/51%	P=0.72
Regular menstruation	(1)0.3%	0	P=o.31	Increase weight	(51)34%	(50)3/33%	P=0.90
Irregular menstruation	(10)7/6%	(9)6%	P=0.81	Decrease weight	(21)14%	(20)3/13%	P=0.86
Mood Without change	(71)3/47%	(74)3/49%	P=0.72	Hirsutism	(20)3/13%	(17)3/11%	P=0.59
sensitivity	(23)3/15%	(25)7/16%	p=0.75	vomiting	(11)3/7%	(11)3/7%	P=1
Easy for crying	(2)3/1%	(3)2%	P=0.65	headache	(29)3/19%	(31)7/20%	P=0.77
nervousness level	(25)7/16%	(28)7/18%	P=0.65	Breast tendency	(21)14%	(20)3/13%	P=0.86
Early exhaustion	(24)16%	(16)7/10%	P=o.17	backache	(35)3/23%	(43)7/28%	P=0.29
Decrease power	(5)3/3%	(4)7/2%	P=0.73	vertigo	(16)7/10%	(18)12%	P=0.71
Sprained foot	(55)7/36%	(51)34%	P=0.62	Face rush	(12)8%	(14)3/9%	P=0.68
Hair sheding	(22)7/14%	(29)3/19%	P=0.28	Abdominal bloat	(36)24%	(35)3/23%	P=0.89

was reduced bleeding days, while in the study of Sidali (20) the most common complication was bleeding between two cycles and spotting was at the next order, the amount of which is less than the present study and is inconsistent with this study.

The incidence of amenorrhea in Cyclofem users was 48%, while Kamalifard (21) reported its amount 22% and Yazdanpanah (22) reported it 14/7%.In this study, breast tenderness in Cyclofem users was significantly higher than that of the LD users, which is consistent with the study of Sidali (20), but it's amount in this study was much more than the study of Sidali.

In this study, the incidence of headache and nausea in Cyclofem users was higher than LD users, while in the study of Sidali (20) the incidence of headache in LD users was higher than Cyclofem users, which was inconsistent with this study.

In this study, one-year continuation rate of Cyclofem and LD pills in users was respectively 62% and 40/9%. While in his study, Kamalifard (21) reported one-year continuation rate of Cyclofem 27%. Yazdanpanah (22) also reported one-year continuation rate of Cyclofem 21/2% in his study. In the study conducted in Kenya (23) one-year continuation of Cyclofem was reported 56% (article of Kamali). In a similar study conducted in Muslim countries like Indonesia and Tunisia, one-year continuation rate of Cyclofem was respectively 66/5% and 28/2% (24). The one-year continuation of LD was reported 28/5% in the study of Moradan (25). The difference in continuation rates in various studies can be due to cultural, economic and social differences of the studied population as well as the quality of consultation before the injection methods.

Generally based on the results of this study and similar studies, the side effects caused by Cyclofem ampoule and LD are not significantly different, and these complications are not fatal and irreversible. By proper counseling and teaching women using these methods, health staff can help more use and continuance of these methods; especially regarding the possible side effects.

Refrences

1. *Ghasem zadeh S.Evaluation the Acknowledge of married women 10-49 years about family planning.1995,4(8). [Persian]*
2. *Vilson R.Gynecology & obstetrics Disorder.Lorni A, Aditor. Tehran, shahrab, 1th ed.2010. [Persian]*
3. *Speroff L, Fritz MA. Clinical gynecologic endocrinology and infertility, Lippincott Williams & Wilkins, 2005: p:833-911.*

4. *Endricat J, Hite R, Bannemerschult R,Gerlinger C, Schmidt W Multicenter,Comparative Study of Cycle control .(2001) .efficacy and tolerability of two low-dose oral contraceptives containing20 7g ethinylestradiol /1007g levonorgestrel and 20 7g ethinylestradiol / 500 7g norethistrone.Contraception; 64(1) , 3-10*

5. *Ragnheidure I . Bjarnadottir ,Tuppurainen M, Stephen R. Killick.(2002). Comparison of cycle control with a combined contraceptive vaginal ring and oral levonorgestrel/ ethinylestradiol.Am J Obstet Gynecol, 186, 389-94.*

6. *Stubblefield Ph, Carr-Ellis S , Kapp N. (2007).[Family planning In: Berek J, Berek & Novak's Gynecology], (Translated by:Ghazijahani B,et al), 14th ed, Tehran, Golban publisher, 266(persian)*

7. *Concept foundation [Home page] 2000-2003-Available at:[Onlin] www.Conceptfoundation.org/ index. Htm[4/4/2009].*

8. *Sang G.W ,Shao Q.X ,Ge R.S ,Ge J.L,Chen J.K,Song S,et al .(1995). A Multicentered phase III comparative clinical trial of Mesigyna ,Cyclofem ,and Injectable NO.1 given monthly by intramuscular injection to Chinesewomen. Contraception. 51, 167-183.*

9. *Shojaee. Tehrani H,Ebadi fard A.Population & family planning & Reproductiv Health.1th ed, Tehran,Iranian Students Book Agency,2000,p:3-30. [Persian]*

10. *Rayan KJ,Berkodtiz R,Barpiri R.L.The principle of Gynecology disease. Ghzi jahani B, Editor, Tehran, Nashr, 2008. [Persian]*

11. *Polaneczky M., Guarancaccia M., Alon J., Wiely J., Early experience with the contraceptive use of depot medroxy progestrone.Family planning perspective, Vol(28), N(4), 1996, pp: 174-178.*

12. *Hagh Peykar's, Poindexter,A.N., Batemar, L.R., Dimtmores, J. R., Experience of injectable contraceptive user in an urban setting. Obestet Gynecol, Vol(88), N(2) 1996, PP: 227-232.*

13. *Fraser, I.S., Dennerstein, GJ,Depo-provera use in an Australian metropolitan practice: The Medical Journal of Australia. N(160), 1994,PP:553-558.*

14. *Nelson, A.L,Counseling lssues and management of side effects for woman using depot medroxy progesterone acetate. The Journal of Reproductive Medicine, Vol(41)N(5), Supp, 1996, PP: 391-400.*

15. *Kaunitz AM. Injectable Depot Medroxyprogestron Acetate Contracaption: an update for U.S clinicians.Int J. Fertil 1998; Vol.43, No.2, PP.73-83.*

16. *Davidson A.R, Kalmuss D, Cushman L.F, Romero D, Heartwell S et al. Injecable contraceptive discontinuation and sabsequent unitended pregnancy among low income women. American Journal of Public Health 1997; Vol.87, No.9, PP.1532-34.*

17. *Mirahmadizadeh A, Nakhai Amroodi N, Tabatabai SH, Shafieian R. [Marital satisfaction and related factors in Shiraz]. Iranian Journal of Psychiatry and Clinical Psychology 2003; 8(4): 56-63[Persian].*

18. *The reasons of marital satisfaction,Culture and research .Avalable in www.fpm.ir/archive/no-169/farsi:2006.*

19. *Mirmohammadali M,Mirmolaei T,Babaei Gh,Borghei N.The comparative study of side effect DMPA with OCP(LD) in reproductive women referring to health center in Kalaleh.J Nursing and Midwifery Faculty of Tehran(Hayat).2002,8(2),p:21-31.[Persian]*

20. *Sidali A,Ahmadi M,Jannesari SH,Alavi H.Comrarison The Common Side Effects in Monthly Contraceptive Low Dose and Injection Cyclofem in Selected Cities of Khoozestan Depended on Medical Sciences University of Gondishapor Ahwaz. J Nursing and Midwifery Faculty of Tabriz.2011,21:13-21. [Persian]*

21. *Kamalifard M, Mohammadalizadeh S, Sadeghi H, Hasanzadeh R. Comparison of Continuation Rates and Reasons for Discontinuation of Cyclofem and Depo-Provera in Health Houses of East Azarbaijan, Iran. Nursing and midwirey jurnal of Tabrize medical science. 2011. 18, P:22-30. [Persian]*

22. *Yazdanpanah M, Eslami M,Andalib P, Motlaq M,Jadidi N,Nakhaee N.Acceptability and side effects of Cyclofem© once-a-month injectable contraceptive in Kerman, Iran. Iranian Journal of Reproductive Medicine.2010; Vol.8. No.4. pp: 191-196. [Persian]*

23. *Rominjo joseph K, Sekkadde C,Karanja J,Rivera R, Nasutiou M, Nutley T. (2005).Comparative acceptability of combined and progestine only injectable contraceptives in Kenya. Contraception,72, P138-145.*

24. *Garza-Flores J. Cyclofem©/Cyclo-ProveraTM: Emerging countries' perspective. Int J Gyn Obst 1998; 62 (Suppl. 1): S31-S36.*

Corresponding Author
Gholamitabar Tabari M,
Sari,
Mazandaran,
Iran,
E-mail: Maryam_tabari@yahoo.com

Nasal carriage of staphylococcus aureus in patients admitted to a pediatric department: a point prevalence study

Mustafa Gulgun[1], Muge Oguzkaya-Artan[2], Zeynep Baykan[3], Cem Artan[4]

[1] Kayseri Millitary Hospital, Department of Pediatrics, Kayseri, Turkey,
[2] Erciyes University, Halil Bayraktar Health Services Vocational College, Kayseri, Turkey,
[3] Erciyes University, Medical School, Department of Medical Education, Kayseri, Turkey,
[4] Kayseri Training and Research Hospital Department of Medical Microbiology, in Chest Diseases Clinic Turkey.

Abstract

Background: This study was planned to evaluate the prevalence and risk factors of nasal *Staphylococcus aureus* carriage this point prevalence study was conducted at Pediatric Clinic of Kayseri Military Hospital, Turkey.

Methods: Nasal swabs were collected and a questionnaire including demographics, medical history and potential risk factors was completed after admission to the pediatric department between April 15 and June 15. Totally 507 children were investigated in the study period. Isolates of *S. aureus* were identified by standard methods. The susceptibilities of the isolates to 8 antibiotics (oxacillin, erythromycin, clindamycin, trimethoprim-sulfamethoxazole (SXT), chloramphenicol, vancomycin, ripfampycin, gentamycin, tetracycline, mupirocin) were determined by the disk diffusion method.

Results: Of the 507 children enrolled, 96 (18.9%) were colonized with *S. aureus.* Six (6.2%) of the 96 *S. aureus* isolates were meticillin resistant (MRSA) and none of them had any identified risk factors. A high erythromycin resistance rate (20.8) was observed among the strains. Resistance to 2 or more antibiotics was noted in 11 (11.4%) isolates.

Conclusion: This data document that rate of meticillin-resistant *S. aureus* carriage remains low, and erythromycin resistant and multi resistant strains are notable among children without traditional risk factors.

Key Words: Staphylococus aureus, carriage, point prevalence.

Introduction

Staphylococcus aureus is an important infectious agent causing a variety of infections ranging from mild to serious. Over the last 20 years the incidence of both community-acquired and hospital-acquired *S. aureus* infections have increased, while antibiotic treatment is increasingly hampered by the spread of *S. aureus* strains, which are resistant to multiple antibiotics including methicillin and, more recently, vancomycin (1-3). Therefore, prevention of staphylococcal infections is now more important than ever. Carriage of *S. aureus* in the nose appears to play a key role in the epidemiology and pathogenesis of infection. Epidemiological data is useful in monitoring changes in disease trends in children and planning healthcare programmes for them. Unfortunately, most of the published data were from special groups or medical records. Therefore to estimate the prevalence of *S. aureus* nasal carriage and antibiotic resistance of the isolates, we cultured children attending to the pediatric clinic.

Materials And Methods

Study design: This was a point prevalence study conducted at Pediatric Clinic of Military Hospital in Kayseri, Turkey. The hospital is a secondary-care hospital located in one of the biggest cities with a total population of approximately one million located in the middle Anatolia region of Turkey, which is an important commercial and industrial centre.

A nasal swab sample was collected and a questionnaire was completed after admission to the pediatric clinic. Totally 507 children were investigated in the study period. A detailed, structured questionnaire concerning demographics (age, attending to day care centre/school, education and occupation of the mother and the father, household number, having a pet, smoking in the house), medical history (hospitalization in the previous one year, surgery in the previous one year, emer-

gency department visit or antibiotic usage in the past 6 months, chronic disease, reason for this visit to hospital), and some potential risk factors (participation in contact sports, household contact to a healthcare worker, history of hospitalization of a family member in the previous one year, history of recurrent skin infections) for nasal *S. aureus* carriage were completed by parents of the children. For specimen collection oral permission was obtained from the parents.

According to 2003 Turkey Demographic and Health Survey, average household population size was 4.1 that in our study family size was categorized as ≤4 and >5. Primary education in Turkey is 8 years that the level of education is divided in to two groups. The poverty level for Turkey in 2006 was 1 000 NTL (New Turkish Lira) that the socioeconomic level was defined according to this level.

Specimen collection: A culture of the anterior nares was obtained from each subject. The questionnaire included the name, age, sex, respiratory infection during the last 30 days, number of household, passive smoking, attending to kindergartens-day care centers, period of time attending the day-care centers (months), time at the day care centre, mother's education, father's education, sibling under age of 5, number of people sharing the same room with the child, household income. Information about household members working in the health care facilities was also recorded.

Laboratory methods: Specimens for culture were obtained with a cotton swab, placed in the transport medium and then transported to and processed in our microbiologic laboratory within 4 hours. Isolates of *S. aureus* were identified by standard methods. Oxacillin susceptibility was assessed by the disc diffusion method according to the Clinical Laboratory Standards Institution (CLSI), 2006 (4).

The susceptibilities of the isolates to 8 antibiotics (oxacillin, erythromycin, clindamycin, trimethoprim-sulfamethoxazole (SXT), chloramphenicol, vancomycin, ripfampycin, gentamycin, tetracycline, mupirocin) were determined by the disk diffusion method according to CLSI, 2006 (4). To detect inducible clindamycin resistance, double disk diffusion test (D test) was performed by placing the clindamycin and erythromycin disks 15 mm apart. The test serves as an in vitro marker for the possible mutation to constitutive resistance to clindamycin in vivo. The D test was considered positive if blunting of the zone of inhibition around clindamycin occurred opposite the erythromycin disk (5,6).

Statistical analysis

Statistical Package for the Social Sciences (SPSS) for Windows (Version 13.0;SPSS, Chicago, IL, USA) software was used for the statistical analysis of the data. Descriptive data were expressed as simple frequencies and percentages. Univariate analyses of categorical variables were done with the chi-square test and Fisher's exact test when appropriate. The level of significance was set at 0.05 using the two-tailed method.

Results

In this study 507 children between 0 and 17 years of age were evaluated. The mean age was 60.1±43.7 months. Two hundred and seventy seven (54.6%) of the children were boys and 230 (45.4%) were girls. The most common reason for admission to the hospital was upper respiratory tract infections. Table 1 shows the demographic factors of the study population. Of the 507 patients enrolled, 96 (18.9%) patient were colonized with *S. aureus.* Six (6.2%) of the 96 *S. aureus* isolates were MRSA. Overall, 6 (1.2%) of 507 patients were colonized with MRSA.

Age, sex, attending to kindergarten-day care centre-school, participation in contact sports, antibiotic usage in the past 6 months associated with the rate of nasal *S. aureus* carriage (Table 2).

The analysis of other variables, such as maternal and paternal education, family size, family income, smoker in household, pet in house, underlying existing chronic diseases, history of hospitalization of a family member in the previous one year, history of recurrent skin infections were not found to be significantly different between nasal carriers and others.

Methicillin-resistant *S. aureus* was isolated in 6 (6.2%) children. All of these 6 children were boy. Four were between 13-60 months and two were older than 60 months of age. Four were attending to kindergarten-day care centre-school. None of them had a chronic disease. They do not have any household contact to a health care worker.

One of them was hospitalized in the previous one year, five of them had an emergency department visit in the past 6 months, all of them declared that they used antibiotic in the past 6 months. None of them had a surgery in the previous one year. The antibiotic sensitivity patterns of the isolates were shown in Table 3.A high erythromycin resistance rate (20.8) was observed among the strains. All tested strains were sensitive to vancomycin. Resistance to 2 or more antibiotics was noted in 11 (11.4%) isolates. There were 11 stains which were D+. Six strains were methicillin-resistant *S. aureus*. Resistance to 2 or more antibiotics rather than methicillin was noted in four of the strains. One of the strains was resistant to erythromycin, SXT, and rifampicin; one was resistant to clin-

Table 1. Demographic characteristics of the study population: number and percentage of children

Characteristics	Number	%
Age (n=501)		
≤12 months	126	25.1
13-60 months	169	33.7
> 60 months	206	41.2
Sex (n=507)		
Boy	277	54.6
Girl	230	45.4
Attending to kindergarten-day care centre-school (n=496)		
Yes	235	47.4
No	261	52.6
Maternal Education (n=505)		
Less than primary education (<8 years)	186	36.8
Primary education and more (≥ 8 years)	319	63.2
Paternal Education (n=493)		
Less than primary education (<8 years)	22	4.5
Primary education and more (≥ 8 years)	471	95.5
Occupation of the mother (n=497)		
Unemployed (housewife)	437	87.9
Employed	60	12.1
Family size (n=507)		
≤4	418	82.4
5 and over	89	17.6
Family income (n=492)		
≤1000 NTL	91	18.5
>1000 NTL	401	81.5

Table 2. Relationship between nasal S. aureus carriage and demographic features and clinical history

Risk factors	Nasal S. aureus carrier No. (%)	OR	(95 %CI)	p
> 60 months	52 (25.2)	2.092	1.326-3.299	0.002
Boy	62 (22.4)	1.662	1.049-2.636	0.031
Attending to kindergarten- day care centre- school	56 (23.8)	1.836	1.163-2.898	0.011
Household contact to a healthcare worker	4 (13.3)	0.635	0.216-1.866	0.483
Participation in contact sports	21 (33.9)	2.506	1.400-4.486	0.003
Hospitalization in the previous one year	10 (18.5)	0.958	0.463-1.981	1.000
Surgery in the previous one year	7 (18.4)	0.981	0.418-2.304	1.000
Emergency department visit in the past 6 months	53 (19.0)	0.946	0.577-1.550	0.899
Antibiotic usage in the past 6 months	76 (21.3)	1.815	1.013-3.253	0.047

Table 3. Antibiotic sensitivity pattern of 96 isolates of S. aureus isolated from nasal carriers

Antibiotics	R No. (%)	S No. (%)
Oxacillin	6 (6.3)	90 (93.7)
Clindamycin	8 (8.3)	88 (91.7)
Erythromycin	20 (20.8)	76 (79.2)
Gentamicin	2 (2.1)	94 (97.9)
Vancomycin	-	96 (100.0)
SXT	5 (5.2)	91 (94.8)
Rifampicin	2 (2.1)	94 (97.9)
Mupirocin	3 (3.1)	93 (96.9)
Fusidic acid (n=51)	1 (2.0)	50 (98.0)
Tetracycline	11 (11.5)	85 (88.5)

S= susceptible; R=resistant

damycin, erythromycin, gentamicin, SXT, rifampicin and tetracycline; one was only resistant to tetracycline; one was only resistant to gentamicin; one was resistant to clindamycin, erythromycin, SXT, fusidic acid and tetracycline; one was resistant to clindamycin, erythromycin, mupirocin and tetracycline.

Discussion

S. aureus is one of the commonly seen human pathogens causing a wide range of infection and so strategies for prevention are important (7,8). Nasal carriage of *S. aureus* has been demonstrated to be a significant risk factor for nosocomial and community-acquired infection in a variety of populations (1). This study demonstrated the carriage of *S. aureus* in unselected children who lacked predisposing factors for *S. aureus* acquisition and who attended pediatric clinic. Nasal carriage rates for *S. aureus* have been reported to vary from 18% (9) to 50% (10) in different populations. There are studies evaluated the prevalence of nasal carriage of *S. aureus* and MRSA in children. From Turkey: Harputluoglu et al. (11) were evaluated 87 deaf children with the mean age of 10±2.35, and 56 healthy children with the mean age of 11±3.13. *S. aureus* was isolated from 18 (20.7%) deaf children, and 35.7% in control group. The oxacillin susceptibility in deaf children was 100% and in control group 85%. Ciftci et al. (3) from Afyonkarahisar, Turkey, evaluated 1134 children between 4 and 6years of age, and found 28.4% *S. aureus* carriage and 0.3 % MRSA. Soysal et al. (12) found 17.3% carriage rate among 1 000 children attending a pediatric outpatient clinic. And carriage rate of MRSA found 0.1% in this study. From the world; Creech et al.(6) were collected 500 children presenting for health maintenance visits. There were 182 children (36.4%) colonized with *S. aureus*, and 46 (9.2%) colonized with MRSA. Hussain et al. (13) from University of Chicago Children's Hospital evaluated 500 children from January to August 1999. The target population was 500 healthy children <=16 years of age who attended this facility to receive well child care. One hundred twenty-two (24.4%) children were colonized with *S. aureus*, and three (2.5%) of the 122 were MRSA. From Taiwan Lo et al. (14) found that nine (13.2 %) of the 68 children had MRSA, and 17 (25%) had *S. aureus* carriage. Nasal swabs were collected from 500 children at well-child visits at either university hospital pediatric clinic or a private pediatric office by Nakamura et al. (15) In this study 249 from the university clinic and 251 from the private practice, 159 patients were <12 months of age, 124 were between 13 and 36 months of age and 211 were >36 months of age. One hundred forty-five patients (29% of 500) were colonized with *S. aureus*, and four patients (0.8% of 500) had MRSA. Our study was conducted at pediatric clinic of Kayseri Military Hospital, Turkey. The age of the children was between 0 and 17 years. The mean age was 60.1±43.7 months. Ninety-six patients (18.9%) were colonized with *S. aureus.* Six (6.2%) of the 96 *S. aureus* isolates were MRSA. Overall, 6 (1.2%) of 507 patients were colonized with MRSA. These rates are similar to other studies which are conducted on the same age groups. For Creech et al. (6) this may because of age groups, especially 5-14 years group have a ratio of 23%. The report of the Lo et al. (14) is a point prevalence study, and they found a single predominant community-acquired MRSA colonization. The lowest ratio of MRSA is from Turkey. Ciftci et al. (3) were evaluated 1134 children and found 0.3% MRSA in 28.4% *S. aureus* colonized children, and also Ciftci et al. (3) reported that the education levels of the mother and father were found to be associated with the rate of nasal carriage. In our study just like Lo et al. (14) and Hussein et al. (13) there were no identified risk factors.

In our isolates, the susceptibility to various antibiotics was shown in table 3. Resistance to two or more antibiotics was 11.4%. Susceptibility to clindamycin and erythromycin was 91.7 and 79.2%, respectively. The inducible resistance to clindamycin was 11.4% in erythromycin resistant *S. aureus* strains in our study. A study from Delialioglu and colleagues (16), they were found 14.7%, Lim et al. (17) found 14.6% inducible resistance. A case report from Siberry et al (18) said that a surgical site infection caused by clindamycin-susceptible, erythromycin-resistant methicillin-resistant *S. aureus* did not respond to treatment with clindamycin. Inducible clindamycin resistance in staphylococci can not be detected when erythromycin and clindamycin discs are placed in nonadjacent positions. By applying proper disc placement, on a routine basis to detect inducible clindamycin resistance, clindamycin used effectively on staphylococcal infections.

This data showed that rate of meticillin-resistant *S. aureus* carriage remains low, and erythromycin resistant and multi-resistant strains are notable among children without traditional risk factors.

References

1. *Kluytmans, J., Van Belkum, A., Verbrugh, H. Nasal carriage of Staphylococcus aureus: Epidemiology, underlying mechanisms, and associated risks. Clin Microbiol Rev 1997;10:505-520.*

2. *Wertheim, H.F.L., Melles, D.C., Vos, M.C., et al. The role of nasal carriage in Staphylococcus aureus infections. Lancet Infect Dis 2005; 5:751-762.*

3. *Ciftci, I.H., Koken, R., Bukulmez, A., Ozdemir M, Safak B, Cetinkaya Z. Nasal carriage of Staphylococcus aureus in 4-6 age groups in healthy children in Afyonkarahisar, Turkey. Acta Paediatrica 2007; 96: 1043-1046.*

4. *Clinical Laboratory Standards Institute. Performance standards for antimicrobial susceptibility testing: Sixteenth Informational Supplement. M100-S15. Wayne, PA, USA, 2006.*

5. *Fiebelkom, K.R., Crawford, S.A., McElmee,l M.L., et al. Practical disk diffusion method for detection of inducible clindamycin resistance in Staphylococcus aureus and coagulase-negative staphylococci. J Clin Microbiol 2003; 41: 4740-4744.*

6. *Creech, C.B., Kernodle, D.S., Alsentzer, A., et al. Increasing rates of nasal carriage of methicillin-resistant Staphylococcus aureus in healthy children. Pediatr Infect Dis J 2005; 24: 617-621.*

7. *Kuehnert, M.J., Kruszon-Moran, D., Hill, H.A., et al. Prevalence of Staphylococcus aureus nasal colonization in the United States, 2001-2002. J Infect Dis 2006; 193: 172-79.*

8. *Salgado, C.D., Farr, B.M., Calfee, D.P. Community-acquired methicillin-resistant Staphylococcus aureus: A meta-analysis of prevalence and risk factors. Clin Infect Dis 2003; 36 :131-136.*

9. *Shands, K.N., Schmid, G.P., Dan, B.B., et al. Toxic-shock sendrome in menstruating women: associated with tampon use and S. aureus and clinical features in 52 cases. N Engl J Med 1980; 303:1436-1442.*

10. *Chesney, P.J., Bergdoll, M.S., Davis, J.P., Vergeront, J.M. The disease spectrum, epidemiology, and the etiology of toxic shock sendrome. Ann Rev Microbiol 1984; 38:315-138.*

11. *Harputluoglu, U., Egeli, E., Sahin, I., Oghan, F., Ozturk, O.Nasopharyngeal aerobic bacterial flora and Staphylococcus aureus nasal carriage in deaf children. Int J Pediatr Otorhinolaryngol 2005; 69: 69-74.*

12. *Soysal, A., Sahin, H., Yagci, A., et al. The low rate of methicillin-resistant Staphylococcus aureus in Turkish children. Jpn J Infect Dis 2006;59:195-196.*

13. *Hussain, F.M., Boyle-Vavra, S., Daum, R.S. Community-acquired methicillin-resistant Staphylococcus aureus colonization in healthy children attending an outpatient pediatric clinic. Pediatr Infect Dis J 2001; 20: 763-767.*

14. *Lo, W., Lin, W., Tseng, M., et al. Nasal carriage of a single clone of community-acquired methicillin-resistant Staphylococcus aureus among kindergarten attendees in northern Taiwan. BMC Infect Dis 2007; 7:51-56.*

15. *Nakamura, M.M., Rohling, K.L., Shashaty, M., et al. Prevalence of methicillin-resistant Staphylococcus aureus nasal carriage in the community pediatric population. Pediar Infect Dis J 2002; 21:917-921.*

16. *Delialioglu, N., Aslan, G., Ozturk, C., et al. Inducible clindamycin resistance in Staphylococci isolated from clinical specimens. Jpn J Infect Dis 2005; 58: 104-106.*

17. *Lim, J.A., Kwon, A.E, Kim, S.K., et al. Prevalence of resistance to macrolide, lincosamide and strepto-*

gramin antibiotics in Gram-positive cocci isolated in Korean hospital. J Antimicrob Chemother 2002; 49:489-495.

18. *Siberry, G.K., Tekle, T., Caroll, K., et al. Failure of clindamycin treatment of methicillin-reistant Staphylococcus aureus expressing inducible clindamycin resistance in vitro. Clin Infect Dis 2003; 37:1257-60.*

Corresponding Author
Muge Oguzkaya Artan,
Erciyes University,
Halil Bayraktar Health,
Services Vocational College,
Kayseri,
Turkey
E-mail: martan38@gmail.com

Treatment incidence of orthopedic injuries among hiv-infected subjects in Taiwan: a dynamic cohort survey, 2005–2008

Nan-Ping Yang[1,2], Yi-Hui Lee[3,4], Nien-Tzu Chang[1,4], Yuan-Nian Hsu[5,6], Jin-Chyr Hsu[2,5], I-Liang Yu[2,7], Chien-Lung Chan[7]

[1] Institute of Public Health, National Yang-Ming University, Taipei, Taiwan,
[2] Department of Orthopedic Surgery, Tao-Yuan General Hospital, Department of Health, Executive Yuan, Taoyuan, Taiwan,
[3] Department of Nursing, School of Nursing, Chang-Gang University, Taoyuan, Taiwan,
[4] Institute of Nursing, College of Medicine, National Taiwan University, Taipei, Taiwan,
[5] Department of Internal Medicine, Tao-Yuan General Hospital, Department of Health, Executive Yuan, Taoyuan, Taiwan,
[6] College of Management, Central Taiwan University of Science and Technology, Taichung, Taiwan,
[7] Department of Information Management, Yuan-Ze University, Taoyuan, Taiwan.

Abstract

Background: The musculoskeletal system can be affected by a variety of abnormalities in association with HIV infection, and there is increasing concern regarding musculoskeletal trauma among the HIV-infected population.

Methods: Based on Taiwan's nationwide insurance dataset (22,315 X 10^3 claimants in 2005, increasing to 22,918 X 10^3 in 2008), all subjects matching the inclusion criteria of HIV-infected codes in the annual ambulatory data files or the admissive data files during 2005–2008 were selected as the annual dynamic cohort population. The concomitant ICD9-CM diagnosis codes and associated treatment codes were evaluated and used as the inclusion criteria of orthopedic fractures or dislocations. The diagnosis codes of orthopedic injuries were classified into four major categories: upper extremities fracture, lower extremities fracture, trunk fracture and orthopedic dislocation.

Results: In this dynamic cohort of HIV-infected Taiwanese, the treatment incidence of all orthopedic injuries (including fractures and dislocations) was 93.45 cases per 10,000 persons annually, with a 95% confidence interval (CI) of 84.15 to 102.77 per 10,000 during 2005–2008. The greatest annual incidence of various orthopedic injuries among HIV-infected Taiwanese was noted for radius/ulna or hand fracture (32.60/10,000), followed by femoral neck/femur fracture (18.60/10,000) and tibia/fibula or patella fracture (17.39/10,000); the incidence of upper/lower limb orthopedic dislocations was estimated to be 9.18 (95% CI 5.10–13.26) per 10,000. Males were at significant risk of clavicle/scapular fracture (RR: 4.15, 95%CI 2.15–6.15), femoral neck/femur fracture (RR: 2.43, 95%CI 1.42–3.44) and radius/ulna/hand fracture (RR: 2.35, 95%CI 1.58–3.12), and over 80% of these orthopedic fracture cases were treated using open methods.

Conclusions:The HIV-infected population in Taiwan has a noteworthy risk of orthopedic injuries, and in most cases operative treatment is required.

Key words: Orthopaedic injuries, HIV infection

Introduction

The life expectancy of individuals infected with the human immunodeficiency virus (HIV) has improved greatly since the institution of combination antiretroviral therapy (ART). However, many metabolic derangements have been discovered with long-term combination ART, including lipodystrophy, insulin resistance, and, more recently, abnormal bone metabolism [1]. Bone disorders such as osteopenia and osteoporosis have been recently reported in patients infected with HIV, but the prevalence estimates vary widely among different studies, and can be affected by concomitant factors such as the overlapping of other possible conditions inducing bone loss, advanced HIV disease, advanced age, low body weight or concomitant use of antiretroviral drugs or other drugs [2].

The musculoskeletal system can be affected by a variety of abnormalities in association with HIV infection, including infectious statuses such as cellulitis, abscesses, pyomyositis, septic arthritis, osteomyelitis, tuberculous spondylitis, spondylodiskitis, etc. [3]. Non-infectious musculoskeletal disorders are still associated with HIV infection, including polymyositis, drug-induced myopathy, avascular necrosis, bone marrow abnormalities, inflammatory and reactive arthropathies, etc. [4]. Some investigations have focused on another subsequent orthopedic problem – fracture or dislocation among the HIV-infected population. For example, a study of 2391 (1728 HIV-infected, 663 HIV-uninfected) participants with a median follow-up of 5.4 years, the Women's Interagency HIV Study, found that among HIV-infected women, an older age, white race, current cigarette use, and history of an acquired immune deficiency syndrome (AIDS)-defining illness were associated with the incidence of new fracture [5].

Similarly, in Taiwan, increasing concern regarding musculoskeletal trauma among the HIV-infected population is necessary, but information is still deficient. This study aimed to estimate the incidence of various orthopedic injuries and to evaluate some associated factors in the HIV-infected population in Taiwan. The results are expected to be valuable for health policymakers in terms of re-distributing resources for future HIV management.

Materials and methods

Source, security, and quality control of data

Taiwan launched a single-payer National Health Insurance (NHI) Program on March 1, 1995. As of 2007, 22.60 million of Taiwan's total population of 22.96 million were enrolled in this program; foreigners in Taiwan are also eligible for inclusion. This universal national health insurance, financed jointly by payroll taxes, subsidies, and individual premiums, commenced in Taiwan and its coverage expanded from 57% of the population (before the introduction of national health insurance) to more than 98% (after the year 2005). All the enrollees enjoy almost free access to healthcare, with a small co-payment by most clinics and hospitals.[6] In order to respond to current and emerging health issues rapidly and effectively, the National Health Research Institute (NHRI), in cooperation with the National Health Insurance Bureau (NHIB), established a nationwide research database. The NHRI safeguards the privacy and confidentiality of those included in the database and routinely transfers health insurance data from the NHIB to enable health researchers to analyze and improve the health of Taiwan's citizens. The NHI database contains registration files and original claims data for reimbursement, and access to the National Health Insurance Research Database (NHIRD), which was derived from this system by the NHIB and is maintained by the NHRI, is provided to scientists in Taiwan for research purposes [7]. The NHIB has established a uniform system to control the quality of medical services and coding. If the medical services provided to beneficiaries by the contracted medical care institution are determined by the Professional Peer Review Committee to be incompatible with the provisions of the NHI Act, the expenses thereof are borne by the contracted medical care institution themselves. Otherwise, the Disputes Settlement Board, established under the NHI scheme, settles disputes arising in cases approved by the insurer and raised by the insured, group insurance applicants, or contracted medical care institutions.

Data protection and permission

Data in the NHIRD that could be used to identify patients or care providers, including medical institutions and physicians, is scrambled before being sent to the NHRI for database inclusion, and is further scrambled before being released to each researcher. Theoretically, it is impossible to query the data alone to identify individuals at any level using this database. All researchers who wish to use the NHIRD and its data subsets are required to sign a written agreement declaring that they have no intention of attempting to obtain information that could potentially violate the privacy of patients or care providers. This study protocol was evaluated by the NHRI, who gave their agreement to the planned analysis of the NHIRD (Application and Agreement Number: 100047). This study was also approved by the Institutional Review Board (IRB) of Taoyuan General Hospital, which

has been certificated by the Department of Health, Taiwan (IRB Approval Number: TYGH99037).

Selection of target population and definition of human immunodeficiency virus (HIV) infection and orthopedic injuries

Every claimant of the NHI Program at any time during 2005–2008 was included in the studied population (22,315 X 10^3 people in 2005, increasing to 22,918 X 10^3 people in 2008).[8] As a retrospective cohort study population, the registration and claims data of these individuals collected by the NHI Program were traced and two separate categories of expenditure were used as below: (1) inpatient expenditure by admission (DD files); (2) ambulatory care expenditure by visit (CD files). In order to investigate the incidence of orthopedic injuries in the population with HIV infection in this study, the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) diagnosis codes were evaluated, and the major diagnosis codes of HIV-infection disorders were defined as coded as the 042 series (HIV infection) and the V08 series (asymptomatic HIV infection status). All subjects matching the inclusion criteria of HIV infection codes in the annual CD files or DD files during 2005–2008 were selected as the annual dynamic cohort population.

In order to investigate the incidence of orthopedic fractures or dislocations of the annual dynamic cohort population during 2005–2008 in this study, the concomitant ICD9-CM diagnosis codes and treatment codes were evaluated and used as the inclusion criteria. The diagnosis codes of orthopedic injuries were defined as those coded as one of four major categories. The first major orthopedic injury category, fractures of upper limbs, was defined as injuries coded in the 810–811 series (fracture of the clavicle or scapular), 812 series (fracture of the humerus), and 813–817 series (fracture of the radius, ulna or hand). The second major orthopedic injury category, fractures of lower limbs, was defined as injuries coded in the 820–821 series (fracture of the femoral neck or shaft), 822–823 series (fracture of the patella, tibia or fibula) and 824–826 series (fracture of the ankle or foot). The third category, fractures of the trunk, was defined as injuries coded in the 805–806 series (fracture of vertebrae) and 808 series (fracture of the pelvis). The fourth major orthopedic injury category was orthopedic joints dislocation, which was defined as upper limbs dislocation [coded as the 831 series (shoulder dislocation), 832 series (elbow dislocation), 833 series (wrist dislocation) and 834 series (finger dislocation)] and lower limbs dislocation [coded as the 835 series (hip dislocation), 836 series (knee dislocation), 837 series (ankle dislocation) and 838 series (foot dislocation)].[9, 10] The treatment codes of the orthopedic injuries mentioned above were classified as the 78 series (other operation on bones, except facial bones), 79 series (reduction of fracture and dislocation) and 81 series (repair and plastic operations on joint structures).[10, 11]

Statistical analysis

Descriptive statistics and the estimated annual cumulative incidence (ci) of specific orthopedic injury types (per 10,000 population) and the 95% confidence intervals (CI) for the estimated incidence were calculated based on the number of observed cases according to the following formula: $ci \pm 1.96 \sqrt{(ci)(1-ci)/N}$. As a dynamic cohort survey, the relative risk (RR) of various accumulative orthopedic injuries in both genders was evaluated and the 95% CI was calculated according to the following formula:

$$RR \pm 1.96\sqrt{[(1/a)-(1/(a+c))+(1/b)-(1/(b+d))]}$$

(a: orthopedic-injured and HIV-infected male cases; a+c: HIV-infected male subjects; b: orthopedic-injured and HIV-infected female cases; b+d: HIV-infected female subjects).

Results

Basic characteristics of the enrolled HIV-infected subjects in Taiwan, 2005–2008

In the present study, according to any ICD-9-CM coding of the two categories of HIV-infected disorders as the inclusion criteria, 6,110, 10,502, 11,903 and 12,898 Taiwanese people were enrolled as the annual dynamic cohort population in 2005, 2006, 2007 and 2008, respectively. The peak age stratum of the studied population was 20–39

years (ranging from 65.5% to 68.7%), followed by 40–59 years (ranging from 22.9% to 28.2%). The majority of these insured people with HIV-infected disorders were male (ranging from 77% to 90%) (Table 1).

The treatment incidence of various orthopedic injuries among the dynamic HIV-infected cohort in Taiwan, 2005–2008

Table 2 details the case distributions of the 10 individual categories of orthopedic fractures and dislocations of the selected dynamic cohort population during 2005–2008. In general, 59 cases of various orthopedic injuries occurred in 2005, and 106, 110, and 112 cases occurred in 2006, 2007 and 2008, respectively. On average, the treatment incidence of all orthopedic injuries (including fractures and dislocations) in the HIV-infected population in Taiwan was 93.45 cases per 10,000 persons annually, with a 95% Confidence Interval (CI) of 84.15 to 102.77 per 10,000. During 2005–2008, the greatest annual incidence of various orthopedic injuries among HIV-infected Taiwanese was noted for radius/ulna or hand fracture, estimated to be 32.60 cases per 10,000 persons, with a 95%CI of 27.10 to 38.10 per 10,000. Other estimated incidences for different locations of orthopedic injuries of the studied population are shown in Table 2, and ranged from 18.60 (95% CI 14.45–22.75) per 10,000 persons for femoral neck/femur fracture, 17.39 (95% CI 13.37–21.41) per 10,000 for tibia/fibula or patella fracture, 7.24 (95% CI 4.66–9.84) per 10,000 for clavicle or scapular fracture, 3.38 (95% CI 1.61–5.15) per 10,000 for humeral fracture, 3.14 (95% CI 1.43–4.85) per 10,000 for ankle or foot fracture to 1.93 (95% CI 0.39–3.76) per 10,000 for trunk fracture and 9.18 (95% CI 5.10–13.26) per 10,000 for upper/lower limb orthopedic dislocations.

Furthermore, the accumulative incident cases of the four major categories of orthopedic injuries indicated that the most common orthopedic injury type was upper limb fractures, followed by lower limb fractures, any joint dislocations and trunk fractures, and all three types of orthopedic fracture occurred more frequently in the age stratum of 20–39 years (Figure 1).

Comparison of the mean age, gender tendency and treatment methods of these orthopedic injury cases among the HIV-infected Taiwanese subjects

Table 3 shows the mean age, gender tendency and treatment methods of all the orthopedic-injured HIV-infected subjects during 2005–2008 in Taiwan, separately analyzed by the 10 individual categories of orthopedic fractures and dislocations. The mean age of the HIV-infected Taiwanese sustaining an upper extremity fracture ranged from 33- to 36-years-old, and that for lower extremity fracture and trunk fracture was 35–40-years-old and 31–43-years-old, respectively. The peak age of orthopedic dislocations occurring in the HIV-infected population was 34-years-old. In this dynamic cohort of HIV-infected Taiwanese, the male subjects had a significant risk of sustaining a clavicle/scapular fracture (RR: 4.15, 95%CI 2.15–6.15), femoral neck/femur fracture (RR: 2.43, 95%CI 1.42–3.44) and radius/ulna/hand fracture (RR: 2.35, 95%CI 1.58–3.12). Over 80% of these orthopedic fracture cases were treated using open methods, but more than half of the orthopedic dislocation cases could be managed by closed methods.

Table 1. Characteristics of the enrolled subjects in Taiwan, 2005–2008.

	2005	2006	2007	2008
	No. (%)	No. (%)	No. (%)	No. (%)
Total HIV-infected subjects with health insurance	6,110	10,502	11,903	12,898
Age stratum				
less than 20 y/o	431 (7.1)	280 (2.7)	239 (2.0)	248 (1.9)
20–39 y/o	4002 (65.5)	7068 (67.3)	8175 (68.7)	8612 (66.8)
40–59 y/o	1398 (22.9)	2757 (26.3)	3124 (26.2)	3631 (28.2)
60 y/o or over	279 (4.6)	390 (3.7)	365 (3.1)	407 (3.2)
Gender				
male	4698 (76.9)	9028 (86.0)	10363 (87.1)	11626 (90.1)
female	1412 (23.1)	1474 (14.0)	1540 (12.9)	1272 (9.9)

Table 2. Treatment incidence of various orthopedic traumas among the HIV-associated population in Taiwan, 2005–2008.

	2005		2006		2007		2008		annual
	cases	Inc.*	cases	Inc.*	cases	Inc.*	cases	Inc.*	cumulative inc.*(ci) (95%C.I.)
Total Incidence of Orthopedic Injuries	59	96.56	106	101.00	110	92.41	112	86.84	93.45 (84.15–102.77)
Orthopedic Fracture									
Upper limb									
clavicle or scapula	9		1		14		6		7.24 (4.66–9.84)
humerus	0		7		2		5		3.38 (1.61–5.15)
radius/ulna or hand	24		40		33		38		32.60 (27.10–38.10)
Lower limb									
femoral neck/femur	9		26		29		13		18.60 (14.45–22.75)
tibia/fibula or patella	8		18		16		30		17.39 (13.37–21.41)
ankle or foot	2		2		3		6		3.14 (1.43–4.85)
Trunk									
vertebrae	0		1		1		4		1.45 (0.39–2.61)
pelvis	0		1		1		0		0.48 (0.00–1.15)
Orthopedic Dislocation									
upper limb	6		10		4		5		6.04 (3.67–8.41)
lower limb	1		0		7		5		3.14 (1.43–4.85)

** 1/10,000 ; C.I.: Confidence Interval*

Table 3. Mean age, gender tendency and treatment methods of various orthopedic-injured subjects in the HIV-infected Taiwanese population, 2005–2008.

	Age (years)		Gender tendency		Treatment method	
	mean	S.D.	Relative Risk(RR) (male vs female)	(95% C.I.)	Closed method (%)	Open method (%)
Orthopedic Fracture						
Upper limb						
clavicle or scapula	**36.45**	**10.79**	**4.15**	**(2.15, 6.15)**	**14.8**	**85.2**
humerus	**33.19**	**5.55**	**0.36**	**n.s.**	**15.4**	**84.6**
radius/ulna or hand	**36.30**	**11.44**	**2.35**	**(1.58, 3.12)**	**20.9**	**79.1**
Lower limb						
femoral neck/femur	**39.92**	**15.51**	**2.43**	**(1.42, 3.44)**	**9.2**	**90.8**
tibia/fibula or patella	**35.13**	**10.07**	**1.69**	**n.s.**	**10.3**	**89.7**
ankle or foot	**37.44**	**10.33**	**1.75**	**n.s.**	**8.3**	**91.7**
Trunk						
vertebrae	**42.72**	**14.75**	**0.32**	**n.s**	**0**	**100**
pelvis	**31.05**	**10.93**	**N.A. (all male)**	**N.A.**	**0**	**100**
Orthopedic Dislocation						
upper limb	**34.32**	**10.63**	**1.91**	**n.s.**	**57.7**	**42.3**
lower limb	**34.26**	**9.12**	**N.A. (all male)**	**N.A.**	**50.0**	**50.0**

SD: standard deviation; C.I.: confidence interval; n.s.: not significant; N.A.: not available.

Discussion

Paradoxically, bone loss may occur not only due to HIV but also as a consequence of highly active antiretroviral therapy (HAART). The cause and mechanisms driving these distinct forms of bone loss, however, are complex and controversial [12]. Low bone mineral density (BMD) is prevalent in HIV-infected subjects. Initiation of antiretroviral therapy is associated with a 2–6% decrease in BMD over the first 2 years, a decrease that is similar in magnitude to that sustained during the first 2 years of menopause [13]. A prospective cohort study of 92 HIV+ and 95 HIV- postmenopausal subjects to check their serum levels of inflammatory cytokines, bone turnover markers, and calciotropic hormones showed that serum TNFalpha, N-telopeptide, and C-telopeptide were significantly higher in HIV+ than in HIV- women, particularly in those receiving ART [14]. A study compared HIV+ Canadian women with age- and region-matched control women (1:3) from a national population-based study of osteoporosis, and revealed that HIV+ women were more likely to have sustained fragility fractures (OR 1.7), but had BMD values that did not differ from those of women from a national population-based cohort [15]. From the viewpoint of orthopedic and trauma medicine, the orthopedist must face the increasing likelihood of treating orthopedic injuries of HIV-infected subjects, especially when this specific population now live to a much greater age.

In the present study, over 85% of the orthopedic-fractured HIV-positive subjects underwent operative treatment. How to manage these special cases following orthopedic surgery might be another important concern. A study following 36 HIV-positive patients who underwent surgery for orthopedic trauma revealed that 14 (39%) developed surgical wound infections (4 were deep and 10 superficial) that were significantly associated with HIV clinical category B, a $CD4^+$ T-lymphocyte category of greater than or equal to 2, and contaminated wounds [16]. Another study of 74 HIV-infected patients receiving implant orthopedic surgery for trauma compared with a control group of 572 showed that if prolonged prophylactic antibiotic therapy and systematic antiretroviral therapy are given to HIV immune-depressed carriers undergoing implant orthopedic surgery, their post-operative infection risk may be close to that of non-HIV carriers [17]. Patients infected with HIV presenting with an open fracture of a long bone are difficult to manage. A prospective case–control study showed the overall rate of severe pin-track infection in HIV-positive patients requiring removal of the external-fixation pins to be 7%, and there were significantly more pin-track infections requiring pharmaceutical or surgical intervention in the HIV-positive group [18]. More follow-up studies of the HIV-infected Taiwanese population after an orthopedic operation for fracture should be performed in the future.

A cohort study of patients treated with combination ART therapy in 1997–1999 revealed that the incidence density of bone fractures was 3.3 for 1000 patient-years [95% confidence interval (CI) = 2.0-4.6]. The rate was 2.9-fold (95% CI = 1.3-6.5) higher among patients with excessive alcohol consumption and 3.6-fold (95% CI = 1.6-8.1) higher in those with hepatitis C virus (HCV) coinfection [19]. Although no identical study has been performed, compared to another retrospective cohort study to estimate the incidence of orthopedic dislocation in the general population in Taiwan [10], the annual incidence of all orthopedic dislocations in the HIV-infected population was 2.2-fold higher (4.21/10,000 vs. 9.28/10,000, respectively).

Another population-based study was conducted in a large U.S. health care system. Among males, the fracture prevalence per 100 persons was higher in HIV-infected patients than in non-HIV-infected patients for wrist fractures (1.46 *vs*. 0.99; P=0.001), hip fractures (0.79 *vs*. 0.45; P = 0.001), vertebral fractures (1.03 *vs*. 0.49; $P < 0.0001$), and any fracture (3.08 *vs*. 1.83; $P < 0.0001$). Similarly, HIV-infected females had a higher prevalence of wrist (1.31 *vs*. 0.83; $P = 0.01$) and vertebral (0.81 *vs*. 0.45; P = 0.01) fractures per 100 persons than non-HIV-infected females [20]. Compared with the present study, the male HIV-infected Taiwanese were still at greater risk of sustaining wrist or forearm fractures (RR: 2.35, 95%CI = 1.58–3.12) and hip or femoral fractures (RR: 2.43, 95%CI = 1.42–3.44). Moreover, there was also a higher tendency to sustain a clavicle or scapular fracture (RR: 4.15, 95%CI = 2.15–6.15) in the male HIV-infected population in Taiwan.

In Taiwan, diagnosis of injury/poisoning is the most frequently noted diagnostic category in

emergency departments (EDs), which accounts for 26.4% of ED visits [21]. A study using data from the Universal Screening for HIV in the Emergency Room (USHER) Trial in Boston, US, showed that the proportion of HIV-infected cases that is undiagnosed in this ED-based setting was estimated to be 23.7% (95% CI: 11.6%, 34.9%) of the total HIV infections [22]. No investigation has been performed to study the possible under-diagnosis of HIV-positive visitors to EDs due to orthopedic injuries in Taiwan. However, more identified HIV+ subjects and a lot of incident cases of orthopedic fractures or dislocations requiring treatment were noted in the present study, which must be an important issue at ambulatory units, especially EDs, in Taiwan. More suspicion when dealing with the traumatic population at the ED and more consistent self-protective procedures when performing operations in these verified HIV-infected cases should be included in the education and training of medical staff in Taiwan. Achievement of the above-mentioned recommendations require the health authority of the Taiwan government to supply more medical resources.

Conclusions

The HIV-infected population in Taiwan has a noteworthy possibility of sustaining orthopedic injuries, and in most cases operative treatment is required. This is an important trend for orthopedists and policymakers to note.

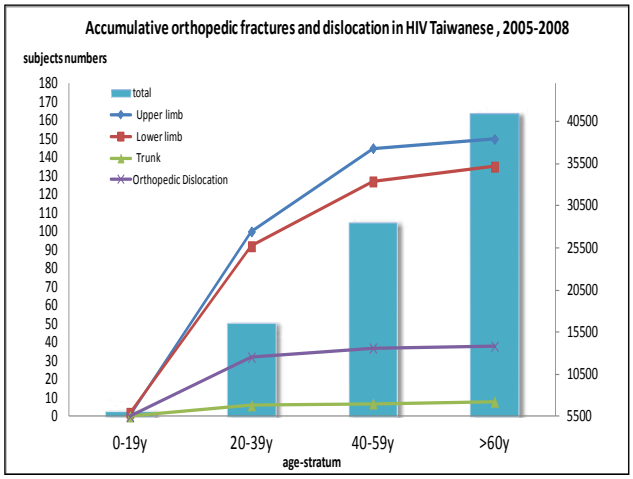


Figure 1. Accumulative subjects with three categorical orthopedic fractures and all orthopedic dislocations among different age strata in the HIV-infected Taiwanese population, 2005–2008.

References

1. *Warriner AH, Mugavero MJ. Bone changes and fracture risk in individuals infected with HIV. Curr Rheumatol Rep. 2010; 12: 163-9.*

2. *Bongiovanni M, Tincati C. Bone diseases associated with human immunodeficiency virus infection: pathogenesis, risk factors and clinical management. Curr Mol Med. 2006; 6: 395-400.*

3. *Tehranzadeh J, Ter-Oganesyan RR, Steinbach LS. Musculoskeletal disorders associated with HIV infection and AIDS. Part I: infectious musculoskeletal conditions. Skeletal Radiol. 2004; 33: 249-59.*

4. *Tehranzadeh J, Ter-Oganesyan RR, Steinbach LS. Musculoskeletal disorders associated with HIV infection and AIDS. Part II: non-infectious musculoskeletal conditions. Skeletal Radiol. 2004; 33: 311-20.*

5. *Yin MT, Shi Q, Hoover DR, Anastos K, Sharma A, Young M, Levine A et al. Fracture incidence in HIV-infected women: results from the Women's Interagency HIV Study. AIDS. 2010; 24: 2679-86*

6. *Wen CP, Tsai SP, Chung WS. A 10-year experience with universal health insurance in Taiwan: measuring changes in health and health disparity. Ann Intern Med. 2008; 148: 258-67.*

7. *Yang NP, Deng CY, Chou YJ, Chen PQ, Lin CH, Chou P, Chang HJ. Estimated Prevalence of Osteoporosis from a Nationwide Health Insurance Database in Taiwan. Health Policy 2006; 75: 329-37.*

8. *Bureau of National Health Insurance, DOH, Taiwan. Taiwan NHI Information for the public: essential data of ensured affair. [Available at : http://www.nhi.gov.tw/webdata/webdata.aspx?menu=17&menu_id=661&WD_ID=689&webdata_id=805] Accessed December 4, 2011*

9. *Yang NP, Chan CL, Yu IL, Lee CY, Chou P. Estimated Prevalence of Orthopaedic Fractures in Taiwan – A Cross-sectional Study based on Nationwide Insurance Data. Injury 2010; 41: 1266-72.*

10. *Yang NP, Chen HC, Phan DV, Yu IL, Lee YH, Chan CL. Chou P et al. Epidemiological Survey of Orthopedic Joint Dislocations based on Nationwide Insurance Data in Taiwan, 2000-2005. BMC Musculoskelt Disord 2011; 12:253.*

11. *Chiu HJ, Chan CL, Hsu JC, Chung CY, Yu IL, Renn JH, Chang NT et al. Nationwide retrospective cohort survey of orthopedic injuries in the Taiwanese population with various psychiatric disorders, 2000-2005. Unpublished data*

12. *Ofotokun I, Weitzmann MN. HIV-1 infection and antiretroviral therapies: risk factors for osteoporosis and bone fracture. Curr Opin Endocrinol Diabetes Obes. 2010; 17: 523-9.*

13. *McComsey GA, Tebas P, Shane E, Yin MT, Overton ET, Huang JS, Aldrovandi GM et al. Bone disease in HIV infection: a practical review and recommendations for HIV care providers. Clin Infect Dis. 2010; 51: 937-46.*

14. *Yin MT, McMahon DJ, Ferris DC, Zhang CA, Shu A, Staron R, Colon I et al. Low bone mass and high bone turnover in postmenopausal human immunodeficiency virus-infected women. J Clin Endocrinol Metab. 2010; 95: 620-9.*

15. *Prior J, Burdge D, Maan E, Milner R, Hankins C, Klein M, Walmsley S. Fragility fractures and bone mineral density in HIV positive women: a case-control population-based study. Osteoporos Int. 2007; 18: 1345-53.*

16. *Abalo A, Patassi A, James YE, Walla A, Sangare A, Dossim A. Risk factors for surgical wound infection in HIV-positive patients undergoing surgery for orthopaedic trauma. J Orthop Surg (Hong Kong). 2010; 18: 224-7.*

17. *Bahebeck J, Eone DH, Nonga BN, Kingue TN, Sosso M. Implant orthopaedic surgery in HIV asymptomatic carriers: management and early outcome. Injury. 2009; 40: 1147-50.*

18. *Norrish AR, Lewis CP, Harrison WJ. Pin-track infection in HIV-positive and HIV-negative patients with open fractures treated by external fixation: a prospective, blinded, case-controlled study. J Bone Joint Surg Br. 2007; 89: 790-3.*

19. *Collin F, Duval X, Le Moing V, Piroth L, Al Kaied F, Massip P, Villes V et al.: Ten-year incidence and risk factors of bone fractures in a cohort of treated HIV1-infected adults. AIDS. 2009; 23: 1021-4.*

20. *Triant VA, Brown TT, Lee H, Grinspoon SK. Fracture prevalence among human immunodeficiency virus (HIV)-infected versus non-HIV-infected patients in a large U.S. healthcare system. J Clin Endocrinol Metab. 2008; 93: 3499-504.*

21. *Yang NP, Lee YH , Lin CH , Chung YC , Chen WJ, Chou P. Utilization of and Direct Expenditure for Emergency Medical Care in Taiwan: a Population-based Descriptive Study. J Epidemiol 2009; 19:41-8.*

22. *Reichmann WM, Walensky RP, Case A, Novais A, Arbelaez C, Katz JN, Losina E. Estimation of the Prevalence of Undiagnosed and Diagnosed HIV in an Urban Emergency Department. PLoS One. 2011; 6:e27701*

Corresponding Author
Nan-Ping Yang,
Department of Orhtopedic Surgery,
Tao-Yuan,
General Hospital,
Taoyuan 330,
Taiwan,
E-mail: yang.nanping@gmail.com

Effectiveness and safety of Etanercept in treatment of arthritis

Olyaeemanesh A[1], Doaee Sh[1], Nejati M[1], Mobinizadeh M[1], Aboee P[1], Beyhaghi H[2]

[1] HTA office, Deputy of Curative Affairs, Ministry of Health and Medical Education (MOHME), Tehran, Iran,
[2] Center for Clinical Excellence, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

Abstract

Millions of people around the world are suffering from debilitating pain and physical limitations of more than a hundred forms of arthritis. Thus, this study aims at reviewing therapeutic evidence on Etanercept as an effective treatment for different forms of inflammatory arthritis in general and RA in particular.

Methods: In this study, databases including Cochrane Library (HTA database, DARE, NHS EED, Cochrane Database of Systematic Reviews and CENTRAL) and Google Scholar were searched for relevant secondary studies. Using specific search query, 33 hints were retrieved. After eliminating the irrelevant studies and duplications, 12 articles entered the review based on predetermined inclusion and exclusion criteria. Full-papers of all these 12 articles were also retrieved.

Results: Findings of 12 selected articles, all of them published between 2009 and 2011, were categorized in three groups, namely: safety, effectiveness and economic evaluations with 3, 6 and 3 articles respectively.

Conclusion: Based on different studies on safety of anti-TNF drugs, Etarnercept safety profile is acceptable particularly in treatment of Rheumatoid Arthritis. However, long-term complications including TB, Cancers and Heart diseases are in need of further investigation. Etanercept is effective in treating Rheumatoid Arthritis, Psoriatic Arthritis and Psoriatic Plaque and has been efficacious in alleviating signs and symptoms of early and severe Rheumatoid Arthritis. The review suggests that Etanercept is cost-effective in treating these three forms of arthritis compare to other relevant alternatives.

Key words: Rheumatoid Arthritis, Anti-TNF drugs Arthritis, Etanercept

Introduction

Millions of people are afflicted with debilitating pain and physical limitations caused by different forms of inflammatory arthritis. World Health Organization (WHO) suggested that the prevalence of different types of arthritis was between 0.7 and 4.01 in every 1000 children in 2003 [1]. Among all inflammatory arthritis, Rheumatoid Arthritis stands out as one of the most significant types of arthritis due to its highly disabling effects and being the most common form of multisystem inflammatory arthritis. The prevalence averages out at 0.3 to 1 and 0.3 to 0.5 in developed and developing countries respectively [2]. This figure is estimated to be 0.33 percent in Iranian urban population. The disease frequently leads to severe disability as 50 percent of patients with Rheumatoid Arthritis develop different levels of disability within 10 years from the diagnosis [3]. Although the major initiator of the disease is still remained unknown, a large body of evidence suggests that genetic predisposition and immunologic disturbances accompanied by environmental factors can cause the disease [4]. Tumor Necrosis Factor (TNF) is a molecule known to play a significant role in inflammatory processes. Technological advancement has allowed for development of pharmaceuticals that are able to selectively suppress TNF and are indicated in treatment and control of certain types of arthritis. These biologic medications are classified into two groups, namely Anti-TNF antibodies and TNF receptor inhibitors; Etanercept, Infliximab and Adalimumab are some of the drugs in the former group. In some of articles, they named Biologics .Biologics are large molecule and are often administrated by injection [5]. Etanercept (trade name Enbrel) is administered subcutaneously [6]. Etanercept is recombinant soluble TNF receptor that selectively fuses with TNF and inhibits it from binding to its receptors on the sur-

face of cells and consequently prevents inflammatory effects of TNF in diseases like Rheumatoid Arthritis. Although this drug became available in 1998, the price is still prohibitively high [7]. So this article aimed to review recent evidence on safety and effectiveness of Etanercept in different types of arthritis as many other medicines such as Infleximab and Insulin analogue had been studied similarly based on the Rapid review protocol of the Health technology Assessment office which is placed in deputy of curative affairs in MOHME to provide sufficient evidence for policy makers especially who are involved in drug insurance issues [8]. On the other hand, regarding budget limitation more efficient allocation of health technologies has become more critical recently as WHO has emphasized greatly on health technology assessment over about last two decades [9].

Methods

Due to the limitations of time, we adopt the rapid review method in this study. In the first stage, major medical databases were searched for background knowledge on Etanercept, its mechanism of action and alternative pharmaceutical therapies. Thereafter following databases were searched for the period of time between 2009 and 2011:

Cochrane Library (HTA databases, DARE reviews, NHS EED reports, Cochrane Systematic Reviews, CENTRAL) and Google Scholar

In this stage after reviewing the 33 hints retrieved by a specific query (table 1), irrelevant articles and duplications were excluded from the list and 12 articles entered the study considering the prespecified inclusion criteria. Based on the rapid review protocol, just relevant HTA reports, economic evaluation studies and systematic reviews and meta-analysis were selected; if more information was needed other types of studies e.g. Randomized Controlled Trials were also reviewed. All the data regarding safety, efficacy and cost-effectiveness of Etanercept was extracted.

Reports of studies that satisfy following criteria entered this review:

- Secondary studies including HTA reports, economic evaluation studies and systematic reviews
- Articles that investigate effects of Etanercept on different types of arthritis
- Studies that investigate the effects of different anti-TNF medications (including Etanercept) alone or in combination with other treatment regimens on patients with arthritis

Table 1. Keywords and search history in www.crd.york.ac.uk

Arthritis	995
Rheumatoid	643
#1 OR #2	999
Etanercept	141
Enbrel	12
#4 OR #5	141
#3 AND #6	107
(#3 AND #6), from 2009 to 2011	33

Results and discussion

All 12 articles that entered in this review were published between 2009 and 2011 (table 2). Findings of these studies were classified in three groups namely safety, effectiveness and economic evaluation. Three systematic reviews that cover the harms and complications of anti-TNF pharmaceuticals fell into the safety group. The reports of six secondary studies assessing the effectiveness of Etanercept were categorized in effectiveness group. Since each study considered specific type of disease and none of them assesses the therapeutic effects of Etanercept in all forms of arthritis, studies were classified based on the therapeutic indication in following diseases: Rheumatoid Arthritis, Psoriatic Arthritis, and Psoriatic Plaque. We also include 3 economic evaluation studies that assess the clinical and economic effects of Etanercept through cost-effectiveness and cost-utility analysis. Results of the included studies were assessed in three aforementioned groups.

Safety

The findings of articles that investigate safety of anti-TNF factors generally approved the Etanercept safety profile in treatment of Rheumatoid Arthritis; however, we did not find a head to head study determining safety of Etanercept in comparison

Table 2. Published articles between 2010-2011.

No.	Title of study	Year	Study design
1	Adverse effects of biologics: a network meta-analysis and Cochrane overview	2011	Systematic review
2	The safety of anti-tumor necrosis factor treatments in rheumatoid arthritis: meta and exposure-adjusted pooled analyses of serious adverse events	2009	Systematic review
3	A systematic review and meta-analysis of the efficacy and safety of Etanercept for treating rheumatoid arthritis	2009	Systematic review
4	A systematic comparison of combination DMARD therapy and tumor necrosis inhibitor therapy with Methotrexate in patients with early rheumatoid arthritis	2010	Systematic review
5	Efficacy and safety of treatments for childhood psoriasis: a systematic literature review	2010	Systematic review
6	Indirect comparisons of the efficacy of biological anti-rheumatic agents in rheumatoid arthritis in patients with an inadequate response to conventional disease-modifying anti-rheumatic drugs or to an anti-tumor necrosis factor agent	2011	Systematic review
7	Etanercept, Infliximab and Adalimumab for the treatment of psoriatic arthritis: a systematic review and economic evaluation	2011	HTA
8	Economic evaluation of Etanercept in the management of chronic plaque psoriasis	2009	Economic evaluation
9	Cost-effectiveness of sequential therapy with tumor necrosis factor antagonists in early rheumatoid arthritis	2009	Economic evaluation
10	Cost-effectiveness analysis of Rituximab treatment in patients in Germany with rheumatoid arthritis after Etanercept-failure	2010	Economic evaluation
11	Cost-effectiveness of Infliximab for the treatment of active and progressive psoriatic arthritis	2011	Economic Evaluation
12	Cost-effectiveness modeling of biological treatment sequences in moderate to severe rheumatoid arthritis in France	2010	Economic evaluation

with alternatives such as, for example, Infliximab and Adalimumab. All of included studies generally address the safety profile of anti-TNF drugs. Safety findings were normally based on the results of clinical trials that had investigated both harms and benefits of anti-TNF factors, thus mostly short-term harmful effects were detected, while long-term complications like Tuberculosis, cancers and cardiac diseases due to these pharmaceutical agents are in need of further investigations and studies with longer periods of follow-up. In their article, Singh et al suggested that like other 8 pharmaceuticals in anti-TNF group, short-term side effects and complications due to Etanercept showed no significant difference compare to placebo branch while long-term complications were limited for tuberculosis (TB) reactivation, lymphoma, and congestive heart failure. Adjusted for dose, biologics as a group were associated with a statistically significant higher rate of total adverse events (odds ratio (OR) 1.19, 95% CI 1.09 to 1.30; number needed to treat to harm (NNTH) = 30, 95% CI 21 to 60) and withdrawals due to adverse events (OR 1.32, 95% CI 1.06 to 1.64; NNTH = 37, 95% CI 19 to 190) and an increased risk of TB reactivation (OR 4.68, 95% CI 1.18 to 18.60; NNTH = 681, 95% CI 143 to 14706) compared to control. So they proved that there is an urgent need for more research regarding the long-term safety of biologics and the comparative safety of different ones [10].

The other study by Leombruno et al evaluated the safety of biologic treatments for rheumatoid arthritis (RA) and suggested that recommended doses of anti-TNFs (20 mg weekly)found no increase in the odds of death (OR=1.39, 95%CI 0.74-2.62), serious adverse events (OR=1.11; 95%CI 0.94-1.32), serious infection (OR=1.21; 95%CI 0.89-1.63), lymphoma (OR=1.26; 95%CI 0.52-3.06), non-melanoma skin cancers (OR=1.27; 95%CI 0.67-2.42) or the composite endpoint of non-coetaneous cancers plus melanomas (OR=1.31; 95%CI 0.69-2.48). They confirmed that anti-TNF drugs are safe

for treating Rheumatoid Arthritis but suggested that risk of complications like severe infections should be measured in future studies because High dose anti-TNF therapy may be associated with a twofold increase in the risk of serious infections [11]. Further, in their study of Etanercept in treatment of Rheumatoid Arthritis, Wines et al found that although the drug is efficacious in treating RA, there was no significant difference between Etanercept and placebo groups in term of the rate of serious adverse events like serious infections, malignancy and death, also loss to follow up due to adverse effects of Etanercept was virtually zero. They also showed that TNF-blockers were more efficacious than placebo at all time points but were comparable to MTX. TNF-blocker and MTX combination was superior to either MTX or TNF-blocker alone. Increasing doses did not improve the efficacy. TNF-blockers were relatively safe compared to either MTX or placebo [12].

As well, Food and Drug Administration has approved Etanercept for treating Rheumatoid Arthritis, Psoriatic Arthritis, Ankylosing Spondylitis and moderate to severe Psoriatic Plaque in 1998, 1999, 2003 and 2004 respectively [13]. Generally the Etanercept safety profile in treatment of Rheumatoid Arthritis is approved based on the findings (table 3).

Effectiveness

In searching for articles that evaluate the effectiveness of Etanercept, therapeutic indications of treating Rheumatoid Arthritis, Psoriatic Arthritis, Ankylosing Spondylitis and Psoriatic Plaque were considered in this review. Five studies that evaluated the therapeutic effects of anti-TNF drugs such as Etanercept included in this section. Anti-TNF drugs particularly Etanercept were effective in alleviating signs and symptoms of early and advanced Rheumatoid Arthritis. Salliot et al, Ma et al and Saraux et al studied the effects of anti-TNF factors on Rheumatoid Arthritis, while Wines et al has evaluated therapeutic effects of Etanercept in Rheumatoid Arthritis and approved the effectiveness of the drug. As In their article, Salliot et al suggested that In IR-MTX, anti-TNFs had the same probability of reaching an ACR50 compared to 'non-anti-TNF biologicals' taken together (OR 1.30, 95 % CI 0.91 to 1.86). However, when compared to specific biological agents, anti-TNFs demonstrated a higher probability of reaching an ACR50 than abatacept (OR 1.52, 95 % CI 1.0 to 2.28), but not in comparison to rituximab and tocilizumab. In IR-anti-TNF, rituximab demonstrated a higher probability of achieving an ACR50 than tocilizumab (OR 2.61, 95% CI 1.10 to 6.37), but no significant differen-

Table 3. Safety Index have been used in included articles

	Title	Author year	Sample size	Safety index	Results
1	Adverse effects of biologics: a network meta-analysis and Cochrane overview	Singh JA 2011	163 RCT 50,010	tuberculosis reactivation lymphoma congestive heart failure	OR=1.19 NNTH=30 (total adverse events)
2	The safety of anti-tumor necrosis factor treatments in rheumatoid arthritis	Leombruno 2010	18 RCT 8,808 RA subjects	Death lymphoma serious adverse events serious infection non-melanoma skin cancers the composite endpoint of non-coetaneous cancers, melanomas	OR 1.39; 95% CI 0.74 to 2.62 OR 1.26; 95% CI 0.52 to 3.06 OR 1.11; 95% CI 0.94 to 1.32 OR 1.21; 95% CI 0.89 to 1.63 OR 1.27; 95% CI 0.67 to 2.42 OR 1.31; 95% CI 0.69 to 2.48
3	A systematic review and meta-analysis of the efficacy and safety of etanercept for treating rheumatoid arthritis	Wines A 2009	8 RCT 2385 patients	Serious adverse events serious infections malignancy deaths	(RR = 0.48 [0.30, 0.78]) The RR values were not statistically significant for any of items respectively: (P = 0.38, 0.57, 0.32 ,0.58)

ces existed between golimumab and other biological [11]. Ma et al studied Patients with active RA that showed Compared with MTX monotherapy, both combination DMARDs and TNF/MTX increased ACR20–70 responses (OR 1.64–2.02 and 2.03–2.30, respectively), reduced withdrawals for inefficacy (OR 0.52 and 0.29), reduced HAQ (WMD −0.17 and −0.16) and reduced annual X-ray progression (WMD −1.20 and −0.84%). DMARD combinations increased withdrawals for toxicity (OR 2.69; there was no difference with TNF/MTX). So It seems that both combination DMARDs and TNF/MTX are more effective than MTX monotherapy In early active RA [14]. Whereas in their study, Saraux et al assessed four biologic treatment sequences over 2 years in patients failing to respond to at least one anti-TNF agent. the sequence representing the use of abatacept after an insufficient response to a first anti-TNF agent (etanercept) appeared significantly (P<0.01) more efficacious over 2 years(102 TEND, S.D. 1.12) compared with a similar sequenceusing rituximab (82 TEND, S.D. 1.2). Following an insufficient response to two anti-TNFagents (etanercept, and then adalimumab), abataceptused as a third biological agent that appeared significantly (P<0.01) more efficacious over 2 years (63 TEND,S.D. 15.0) compared with a similar sequence using inflix-imab (32 TEND, S.D. 1.39). Using the remis-sion criterion, the sequence using abatacept after a firstanti-TNF agent (etanercept) appeared significantly (P<0.01) more efficacious over 2 years (52 TEND, S.D. 0.2) compared with a similar sequence usingrituximab (32 TEND, S.D. 0.2) [15].

Wines et al, on the other hand evaluated the efficacy of Etanercept (ETA) for treating rheumatoid arthritis with attention to subcutaneous doses of ETA at25 mg twice a week or 50 mg weekly to a placebo group, with or without methotrexate. In the efficacy meta-analysis, a greater number of ETA-treated patients achieved the efficacy criteria within 6 months of treatment, where the relative risk (RR) was 2.94 [2.27,3.81] for achieving ACR20, 5.28 [3.12, 8.92] for ACR50 and 4.83 [1.74,13.47] for ACR70. After 1 year, the RR for achieving ACR20, ACR50 andACR70 were 1.14 [1.07, 1.23], 1.36 [1.21, 1.53] and 1.56 [1.30, 1.88], respectively. This response rates were higher for ETA-treated patients in comparison with control group patient [16]. Many authors believe that Etanercept effectiveness should be investigated more in future studies to provide definitive evidence.

Etanercept also is recognized as an effective therapy for other kinds of Arthritis like Psoriatic Arthritis. In their study, Rodgers et al showed the therapeutic effects of Adalimumab, Infliximab and Etanercept in relieving signs and symptoms of Psoriatic Arthritis. Findings of this study suggested that after 12 to 14 weeks of treatment, Infliximab had the best effect on cutaneous signs and symptoms while Etanercept was most effective in treating arthritis symptoms because they showed that The biologic treatment significantly reduced joint symptoms for etanercept [relative risk (RR) 2.60, 95% confidence interval (CI) 1.96 to 3.45], infiximab (RR 3.44, 95% CI 2.53 to 4.69) and adalimumab (RR 2.24, 95% CI 1.74 to 2.88), with 24-week data demonstrating maintained treatment effects. However, further studies with larger sample sizes are needed to provide better evidence in this regard.

After reevaluating NICE Appraisal Guidance 104 and 125 conducted in 2006 and 2007 respectively, Revision Committee concluded that based on clinical evidence and expert opinion, there was no sufficient evidence for declaring the dominance of any of these three pharmaceuticals and all of them seemed to be equally effective in treating Psoriatic Arthritis [17, 18]. Lloyd et al showed that treatment with 12-week of Etanercept 50 mg was both effective in treating Psoriatic Plaque because The gain in QALYs with 50 mg was found to be higher than with 25 mg, as more patients achieved response and so were eligible for continuing intermittent therapy. NHS has also approved this indication for Etanercept [19]. So Etanercept was found effective in alleviating signs and symptoms of Arthritis (table 4).

Cost-effectiveness

Further evidence is needed for determining incremental cost effectiveness of Etanercept in comparison with relevant pharmaceutical alternatives. However, Etanercept was generally shown to be cost-effective in treating Rheumatoid Arthritis, Psoriatic Arthritis and Psoriatic Plaque. As Rodgers et al suggested that Etanercept had the most cost-effective profile for treating Psoriatic

Table 4. Effectiveness indicators have been used in included articles

	Title	Author year	Sample size	Effectiveness Index	Results
1	Indirect comparisons of the efficacy of biological antirheumatic agents in rheumatoid arthritis…	Saliot 2011	19 RCT	ORs of achieving a 50% improvement according to American College of Rheumatology criteria (ACR50) response at 6 months	IR-MTX, anti-TNFs had the same probability of reaching an ACR50 compared to 'non-anti-TNF biologicals' taken together (OR 1.30, 95 % CI 0.91 to 1.86)
2	A systematic comparison of combination DMARD therapy and tumor necrosis inhibitor therapy with methotrexate…	MA 2010	15RCT 4200	ACR20–70 responses	both combination DMARDs and TNF/MTX increased ACR20–70 responses (OR 1.64–2.02 and 2.03–2.30, respectively
3	Cost-effectiveness modeling of biological treatment sequences in moderate to severe rheumatoid arthritis	Saraux 2010	-	low disease activity score (LDAS) based on DAS-28 scores	the use of abatacept after an insufficient response to a first anti-TNF agent (etanercept) appeared significantly (P<0.01) more efficacious over 2 years (102 TEND, S.D. 1.12) compared with a similar sequence using rituximab (82 TEND, S.D. 1.2)
4	A systematic review and meta-analysis of the efficacy and safety of etanercept for treating rheumatoid arthritis	Wines A 2009	8 RCT 2385 patients	achieving ACR20	(RR) was 2.94 [2.27, 3.81] for achieving ACR20, 5.28 [3.12, 8.92] for ACR50 and 4.83 [1.74, 13.47] for ACR70. After 1 year, the RR for achieving ACR20, ACR50 and ACR70 were 1.14 [1.07, 1.23], 1.36 [1.21, 1.53] and 1.56 [1.30, 1.88] respectively.
5	Comparisons of the efficacy of biological antirheumatic agents in rheumatoid arthritis… (HTA)	Rodgers 2011		a significant improvement in patients with PsA for all joint disease and functional status outcomes at 12–14 weeks' follow-up	The biologic treatment significantly reduced joint symptoms for etanercept (RR) 2.60, 95% confidence interval (CI) 1.96 to 3.45
6	Economic evaluation of etanercept in the management of chronic plaque psoriasis.	Lloyd 2009	3 RCT 94 patients	Quality of life	The gain in QALYs with 50 mg was found to be higher than with 25 mg,

Arthritis with £30000 per QALY. They designed economic model was developed by updating the model produced by the York Assessment Group for the previous NICE appraisal of biologics in PsA and showed that ICER of etanercept compared with palliative care is about £18,000, and the ICER of infiximab compared with etanercept is about £44,000 per QALY. Of the three biologic therapies, Etanercept had the highest probability of being cost effective at a threshold of between £20,000 and £30,000 per QALY, so recognized as the most cost effective strategy in 44% of simulations of the base-case model, at a threshold ICER of £20,000 and in 48% of simulations at a threshold of £30,000 per QALY [18]. Lloyd et al also constructed an economic model to estimate the incre-

mental cost per quality-adjusted life year (QALY) gained. The model considered patients with chronic plaque psoriasis who had both Psoriasis Area and Severity Index (PASI) and Dermatology Life Quality Index (DLQI) of 10 or higher who were unable to take standard systemic therapies. Quality of life gain was estimated from the DLQI responses of patients enrolled in three clinical studies. The model considered expenditure on drugs, monitoring visits, adverse events and inpatient stays. Costs were estimated from the perspective of the U.K. National Health Service over a time period of 10 years. The incremental cost per QALY for etanercept 50 mg biw compared with no systemic therapy was found to be £6217 (95% confidence interval £5396–7486). The cost-effectiveness of 50 mg dosing was more attractive in patients with baseline PASI ‡ 20 (£5163) or baseline DLQI ‡ 20 (£4599). A 12-week period of therapy with Etanercept 50mg seemed to be cost-effective for patients with Psoriatic Plaque compare to Etanercept 25mg with Incremental Cost Effectiveness Ratio of £11,710. They also mentioned that NHS has approved the use of Etanercept in this indication [19]. Moreover, Etanercept alone or therapeutic regimens containing Etanercept were shown to be cost-effective in treating Rheumatoid Arthritis. After 2-year follow up, Saraux et al reported that therapeutic regimen including sequential use of Etanercept, Adatacept and then Adalimumab had better cost-effectiveness profile than the sequence of Etanercept, Rituximab and Adalimumab [16].

On the other hand Merkesdal et al studied the effects of Rituximab in patients that failed to respond to primary treatment with Etanercept and found Rituximab cost-effective from providers' perspective [20]. Davis et al also studied different treatment regimens for Rheumatoid Arthritis and concluded that when Etanercept is added after the combination of Methotrexate and Adalimumab the treatment would be cost-effective with ICER 36,296$. [21, 22]. Although Etanercept was shown to be cost-effective in treating Rheumatoid Arthritis While further evidence is needed for determining incremental cost effectiveness of Etanercept in comparison with relevant pharmaceutical alternatives.

Conclusion

Based on the findings of this review, anti-TNF drugs specially Etanercept were safe in treating different kinds of arthritis, particularly RA. Nevertheless, long-term complications of anti-TNF medications including TB reactivation, cancers and cardiac diseases are in need of further investigation. Etanercept was found also effective in alleviating signs and symptoms of Arthritis and can be cost-effective in treating Rheumatoid Arthritis.

Acknowledgment

We appreciate to minister of health and undersecretary of curative affairs at MOHME in Iran for supporting this study.

References

1. *Manners PJ, Bower C. Worldwide prevalence of juvenile arthritis — why does it vary so much? J Rheumatol 2002; 29: 1520-30.*
2. *D.Woolf A, Pfleger. Burden of major musculoskeletal conditions. Special Theme – Bone and Joint Decade 2000 –2010. Bulletin of the World Health Organization 2003; 81: 646-656.*
3. *Khalvat A, Abdolrahman R, Najafizade SR. The comparison between monotherapy and combination therapy in Rheumatoid Arthritis. Tehran University Medical Journal 2007; 64 (11): 69-76*
4. *Nell VP, Machold KP, Eberl G, Stemma TA, Uffmann M, Smolen JS. Benefit of very early referral and very early therapy with disease-modifying anti-rheumatic drugs in patients with early rheumatoid arthritis. Rheumatology 2004; 43: 906-14.*
5. *Kasumagic-Halilovic E, Prohic A, Cavaljuga S. Alopecia areata: New treatment modalities. HealthMed 2010; 4(1): 163-7.*
6. *GUIPCAR Group. In: Clinical practice guideline for the management of rheumatoid arthritis. Madrid: Spanish Society of Rheumatology 2001; 146.*
7. *Anonymous [cited December 2012]. Available at: URL:http://www.ingentaconnect.com/content/subject? j_subject=196.*
8. *Mobinizadeh M, Oliyaeemanesh A, Doaee sh, Nejati M, Aboee P, Azadbakht M, et al. Health Technology Assessment of Infliximab: A Rapid Review of Type 2 Studies. Journal of Isfahan Medical School 2012; 30: 177*

9. *Wulsin L, Doughery A. A Briefing on Health Technology Assessment. California Research Bureau,California State Library Publishers ; 1 edition; First published in 2008;{Book}*

10. *Singh JA, Wells GA, Christensen R, Tanjong Ghogomu E, Maxwell L, Macdonald JK, et al. Adverse effects of biologics: a network meta-analysis and Cochrane overview. Cochrane Database Syst Rev. 2011; 16 :(2):CD008794.*

11. *Leombruno JP, Einarson TR, Keystone EC. The safety of anti-tumour necrosis factor treatments in rheumatoid arthritis: Meta and exposure-adjusted pooled analyses of serious adverse events. Annals of the Rheumatic Diseases 2009; 68(7): 1136-1145*

12. *Wiens A, Correr CJ, Pontarolo R, Venson R, Quinalha JV, Otuki MF. A systematic review and meta-analysis of the efficacy and safety of etanercept for treating rheumatoid arthritis. Scandinavian Journal of Immunology 2009; 70(4): 337-344*

13. *Anonymous [cited December 2012]. Available at: URL: http:// www.fda.gov/Drugs/default.htm*

14. *Salliot C, Finckh A, Katchamart W, Lu Y, Sun Y, Bombardier C, et al. Indirect comparisons of the efficacy of biological anti-rheumatic agents in rheumatoid arthritis in patients with an inadequate response to conventional disease-modifying anti-rheumatic drugs or to an anti-tumor necrosis factor agent: a meta-analysis. Ann Rheum Dis. 2011 Feb; 70(2): 266-71.*

15. *Ma MH, Kingsley GH, Scott DL. A systematic comparison of combination DMARD therapy and tumor necrosis inhibitor therapy with Methotrexate in patients with early rheumatoid arthritis. Journal of Rheumatology 2010; 49 (1): 91- 98*

16. *Saraux A, Gossec L, Goupille P, Bregman B, Boccard E, Dupont D, Beresniak A. Cost-effectiveness modelling of biological treatment sequences in moderate to severe rheumatoid arthritis in France. Rheumatology 2010; 49(4): 733-740*

17. *de Jager ME, de Jong EM, van de Kerkhof PC, Seyger MM. Efficacy and safety of treatments for childhood psoriasis: a systematic literature review. Journal of the American Academy of Dermatology 2010; 62(6): 1013-1030*

18. *Rodgers M, Epstein D, Bojke L, Yang H, Craig D, Fonseca T, et al Etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis: a systematic review and economic evaluation. Health Technol Assess. 2011 Feb; 15(10): i-xxi, 1-329.*

19. *Lloyd A, Reeves P, Conway P, Reynolds A, Baxter G. Economic evaluation of etanercept in the management of chronic plaque psoriasis. British Journal of Dermatology 2009; 160(2): 380-386*

20. *Merkesdal S, Kirchhoff T, Wolka D, Ladinek G, Kielhorn A, Rubbert-Roth A. Cost-effectiveness analysis of rituximab treatment in patients in Germany with rheumatoid arthritis after etanercept-failure. European Journal of Health Economics 2010; 11(1): 95-104*

21. *Cummins E, Asseburg C, Punekar YS, Shore E, Morris J, Briggs A, et al. Cost-effectiveness of infliximab for the treatment of active and progressive psoriatic arthritis. Value in Health 2011; 14(1): 15-23*

22. *Davies A, Cifaldi MA, Segurado OG, Weisman MH. Cost-effectiveness of sequential therapy with tumor necrosis factor antagonists in early rheumatoid arthritis. Journal of Rheumatology 2009; 36(1): 16-26*

Corresponding Author
Mina Nejati,
HTA office,
Deputy of Curative Affairs,
Ministry of Health and Medical Education (MOHME),
Tehran,
Iran,
E-mail: mnejati_m@yahoo.com

A study on the life and work values of health workers

Hasan Tutar, Aydin Yilmazer

Sakarya University Faculty of Economics and Administrative Sciences, Esentepe Campus Sakarya, Turkey

Abstract

This study was carried out to determine whether or not there is a relationship between the life and work values of private and public health workers in Ankara. Data about participants' perceptions of values was collected with a survey and then analyzed via a sampling scale that measures life and work ethics to identify the set of values according to which employees work. The results of the ***t*** test, variance/ANOVA, correlation, and analysis indicated that there was a significant difference between the life and work values of the sample and their demographic characteristics. The results of the correlation analysis carried out to determine the relationship between the life and work values revealed that just as there was a relationship between the sub-dimensions of these values, there was also a significant relationship between the participants' general life and work values.

Key words: Health workers, values, life values, work values, ethics, (JEL Code: M12 - Personnel Management; Executive Compensation)

Introduction

The concept of values in the field of social sciences, such as in sociology, social psychology, anthropology, psychology, and theology, has been taken up in different ways. Nonetheless, in all of these areas of study, it has been argued that values and beliefs cannot be approached independent of the individual (McCarty and Shrum, 1994) and that they are impacted not only by an individual's life but by work and social life as well. There are values behind an individual's attitudes and behavior and a person's attitudes and behavior vis-à-vis work are guided by those values. As argued by Stern et al. (1994), there are beliefs and values that underpin the attitudes that drive behavior. Thus the way to understand the behavior of individuals is to identify the values behind their behavior. Since values constitute one of the foundations of behavior, the differences in human behavior can be explained through different codes of value.

According to Güngör (1998), who has worked extensively on the psychology of values, the importance of values in psychology is not based on an objective foundation, but rather according to whether or not they guide human behavior. Güngör states that for a psychologist, it is sufficient to accept a value as a "belief." Additionally, Güngör notes that values are a particular type of belief which in fact constitutes a broader mental system. It is a commonly held notion that in the private and work lives of individuals, there is a need for values as they represent the given criteria for attitudes and behavior. In the process of using knowledge acquired by observing what is happening around them, people develop work and life values. In short, when people react to the developments in their environment, they make a number of evaluations of these occurrences and produce "value" judgments about them. This aspect of values has an impact on how these interiorized values are then revealed through attitudes and behavior. In this way, values can be perceived as a form of conduct in reaction to events.

Values are the underpinning criteria of private and work life because comprehending "uprightness" and "honesty" provide the motivation for being "upright" and "honest" in private and work life. For this reason, values are not simply an abstract concept; they play a functional role in the unfolding of daily life and in how individuals relate to events and to other people. The functional aspect of values can be understood from the effect they have on people and on human behavior.

1. Conceptual framework

The concept of value has been defined in numerous ways. According to Allport, it is a belief pertaining to how someone behaves vis-à-vis their

preferences (Herriot, 1976), while Williams defines it as a criterion for preferences or standards (Kilby, 1993). In Kluckhohn's terms, it is a form of action that either openly or in a concealed manner defines the quality of a group or the characteristics of an individual, or it is the prime factor that leads to a preference in achieving the means to an end (Kluckhohn, 1951).

According to Hofstede, it is the tendency to prefer one particular situation over another (Özen, 1996), whereas Güngör defines it as a belief about whether or not something is desired, or whether it is acceptable or unacceptable (Güngör, 1993). Rokeach defines a value as a permanent belief about preferences which are made to realize the goals of certain forms of behavior, as well as existence, at the level of the individual and society (Rokeach, 1973) Values are those criteria which, since an individual's birth, acquire permanence through cultural interaction; these criteria are then utilized in descriptions of beliefs, events, occurrences, objects, and other people. Values are criteria that are shared, adopted, approved of, and compromised socially and also at the individual level, and thus they reveal individual differences. It is for this reason that such differences are explained via differing value systems.Values and ethics are the guidelines and standards for the behavioral interactions between people.

These standards are comprised of traditions, beliefs, logical deductions, cultural interactions, and formal arrangements. The standards that organize behavior are the practical universal principles used in the evaluation of good and bad. In short, values are the foundational criteria that allow us to characterize anything as positive or negative, or right or wrong.

The concept of values is perceived in various ways; it has been discussed as a preference for particular lifestyles, sometimes as a foundational hypothesis about the place of humans in the world, sometimes as the goal of any need, attitude, or desire, and sometimes as a cultural or social value. Despite these varying perceptions, values can generally be defined as the foundational, unwritten morals and beliefs that have been accepted by individuals and which aim to secure the continuity of societies. Such definitions suggest that values are the foundational criteria that set apart individuals and society, as well as the guidelines which are utilized to make preferences among practical alternatives to distinguish between good and bad; they are also the set of normative principles used to represent not what *is*, but what *should be*. They thus constitute the organizational basis for all aspects of an individual's existence, and hence include work and private life.Rokeach approached values in a manner that encapsulated both the objectivist and subjective understandings of values.

For Rockeach, values are a type of belief that can be categorized in three ways. The first of these are descriptive and existentialist beliefs, and since they can be proven or disproven, they are tangible. Since they can be tested, they are objective or phenomenological. The second type of beliefs is evaluative, and as such they are related to judgments. When people define objects or events as good or bad, they rely on these beliefs; and, since they are bound up with personal evaluations, they are subjective. The third belief includes those that have been incorporated into our lives through custom and tradition. Beliefs of this type have an impact on decisions about whether an individual's behavior is desired or not desired.

According to Rockeach, values are more compatible with this third type of belief.There are common aspects of values, such as their being a belief, or a psychological state that is desired or has been approved of, or the means to explaining certain events or phenomenon, or as a guide utilized in the selection of behavior or reactions to events. When these shared aspects of values are brought together, they create a means of evaluation for people's personal and work lives. In this way, just as values constitute a source of behavior, at the same time they are also the criteria for decision-making. Additionally, values serve as a means for people to be cognizant of and understand themselves (Stein, 1985).

Within the framework of definitions of values, Rokeach (1973) categorizes the core suppositions concerning the nature of personal values as follows:

- The number of values to which people adhere is relatively few;
- People experience the same values with varying degrees of intensity;
- Values are shaped by beliefs and systems of values;

- Culture, society, and individuals have an impact on the development of systems of values; and,
- Values are inherent to the individual and appear in every aspect of life.
- Schwartz and Bilsky set forth the criteria for the particularities of values as follows (Kuşdil ve Kağıtçıbaşı, 2000):

Values are beliefs. However, unlike beliefs, values are not completely objective or purged of emotions; rather, when they come to the fore, they are embedded in one another.

Values are illustrative of aims and goals. Values are related to the particularly normative goals to which individuals aspire and to the types of behavior (such as dedication to equity or philanthropy) that are effective in attaining those goals.

Values are not just related to specific acts or phenomenon. For individuals who adhere to certain systems of values, those values are not restrained to just one aspect of life; rather, they appear in all aspects of a person's life. For example, the values "dutifulness" and "fidelity" not only shape a person's private life, but also her or his work and family life as well.

Values are standards. Values and beliefs are intertwined. Just as attitudes underpin forms of behavior, these attitudes are themselves shaped by beliefs and values. Values function as the standard of criteria for a type of behavior or a preference.

Values have an order of priority. Values are organized according to their level of importance. The priority of values is thus revealed by the manner in which they are ordered.

As suggested by the discussions above, values play a critical role in an individual's personal and work life, and one of the most important roles is how they serve as a means for motivation. Values, such as being industrious, productive, or philanthropic, are one of the factors that help people achieve their aims and goals, and as such values play a key role in providing the motivation to attain those goals. Additionally, values are utilized as criteria for judging attitudes and forms of behavior. When someone behaves according to their values, they acquire identity and personality. In this way, values play a role in the production of identity and in realizing the self by ensuring that they behave per their normative principles; in this way, they shape our attitudes and behavior, as well as serve as a guide. Without knowing the values that drive human thought, it is difficult to understand and explain their behavior because individuals act according to the values that they have adopted and to which they attach importance. In this way, work values constitute the main means of motivation that shapes attitudes and behavior.

2. The relationship between life and work values

Research about values has demonstrated that there is a relationship between individuals' life and work values, and it is generally accepted that there is a connection between people's values, attitudes, and beliefs, as well as their mental and physical efforts. Since values generate the criteria for measuring behavior and standards, they serve as a guide for behavior at work as well. It is assumed that while working, a person who acts according to her or his values will perform the job as required and act with a sense of responsibility vis-à-vis the effective use of time. In short, beliefs and values underpin all forms of action, including work.Work is not just a means to make a living; it is part of the act of understanding life and creating meaning for existence, and as such it is critical for the shaping of our lives as well as social status. Work is not just a technical activity that is stripped of values, but rather it is based on a person's individual, social, economic, and cultural activities. Just as it is not easy to separate work life from private life, it is difficult to separate life values and work values. Work values are an inherent part of life values, and the two are interdependent. Work values are a reflection of the value that a person ascribes to work, the meaning that a person attributes to that work, and a person's humanistic values. Work values are thus concerned with how an individual will demonstrate interest in the work at hand at the level of values. Research has illustrated that life and work values cannot be separated from one another and that in evaluating work values, humanistic criteria must be employed (see Rokeach, 1973); in this way, life and work values cannot be taken up not independently.

Work values are an important means for predicting how a person will respond to the work at

hand. Analyses of the relationship between work and life values have shown that life values are more comprehensive and complex than work values (Klenke, 2005). Life values are inclusive of home, social, group, and family life. As for work values, they are the criteria and standards that guide an individual's actions only when work is being carried out. As such, they serve as a guide in making decisions, applying decisions, and checking the results of those decisions.

It is generally accepted that life values are inherently involved in the production of work values. In this line of thinking, work values are derived from aspects of work within the larger field of general life values. However, some research (Kinnane and Gaubinger, 1963; Ros, Schwartz and Surkiss, 1999) has claimed that the relationship between life and work values is tenuous.

3. Literature review

Much research has been carried out on the issue of life and work values (Dose, 1997; Elizur, 1984; Elizur, Borg, Hunt, and Beck, 1991; Furnham, 1984, Hofstede, 1984; Schwartz, 1992), and it has been argued that overall there is a significant relationship between work and life values. However, studies of individual characteristics at the lower level have not always corroborated the existence of this relationship. In a study of hotel workers, Miller (2006) did not find a significant relationship between work and life values. Furnham et al. (2005) conducted a comparative study of more than five hundred workers in England and Greece which focused on personal characteristics and individual work values; the study did not find a significant relationship between age, gender, and work values. Other studies, however, have produced findings contrary to these results. Cherrington, Conde and England (1979) found that there was a significant relationship between age, education, moral importance of the work, importance of money, and work values. Lyons et al. (2006) examined work values by sector, and their study indicated that work values differed for workers in the public, private, and semi-public sectors. Researchers have also taken up the issue of values in a number of different manners. Hofstede (1984), Ralston et al. (1997) examined the factors that underpin work values from the perspective of culture, while Kaufman and Fetters (1980) focused on the relationship between demographic factors and work values. England and Lee (1974, 411) took up the issue from the perspectives of worker's value orientation, situational perceptions, perspectives on problems, decision-making and problem solving, group and interpersonal management, evaluation of organizational and individual success, and assessment of ethical behavior. In the comparative studies carried out by England and Lee (1974) in the United States, Japan, India, and Australia as regards the relationship between the personal values of administrators and levels of success, a significant and positive relationship was found.

Beutell and Brenner (1986) conducted a study which focused on identifying the differences between work values and demographic variables. They found that for women, physical working conditions and emotional attachment were more important, whereas men were concerned about the values of development and risk-taking; the study thus demonstrated that there were significant differences from the point of view of the demographic variable of gender. The study carried out by Sagie et al. (1996), which focused on the relationship between demographic variables and work values, indicated that there were differences as regards demographic characteristics. In the comparative study conducted by Şener and Hazer (2007), it was found that there were differences concerning point averages from the point of view of gender variables. Rosener (1990) found that the behavior of male managers dwelt more on work (economic value), while the behavior of female managers was focused more on relationships (social value).

The study carried out by Bulut and İşma (2004) indicated that there was a difference between administrators' personal values and demographic characteristics. Naktiyok (2003) found that there were differences in terms of the averaging of the extent of values, and the same study noted differences between demographic characteristics and work values. While this overview of the literature demonstrates that some studies have indicated that, from the point of view of life values, work values, and demographic characteristics, there are differences, other research has demonstrated that there were not significant differences between

certain demographic variables and work values. Nonetheless, the studies discussed above indicate that there is a significant relationship among the sub-dimensions of work values. In this study, individual values are categorized according to five sub-dimensions: theoretical, economic, aesthetic, social, and political. These are as follows: theoretical values concern the search for the real and for knowledge; economic values are about financial profit and the means for acquiring income; aesthetic values are those that pertain to experiences and preferences regarding style and taste; social values relate to private and public relations with others; and, political values are those associated with power and effective leadership. The research at hand takes up work values in the dimensions of comfort and security, skills and development, and status and independence. Comfort and security are discussed in terms of comfortable working conditions, job security, and regular routines. Skills and development are examined in light of those characteristics pertaining to work, such as sustainable development of skills and a sense of success. Status and independence refer to such issues as high salary, managing others, and working on important problems.

4. Methods

4.1. Aims of the study

This study, which compares the life and work values of employees at private and public health in Ankara, aims to identify the relationship between the political, aesthetic, social, theoretical, and economic life values of workers vis-à-vis their work values as regards comfort and security, skills and development, and status and independence. Another aim of the study is to make a contribution, based on the findings concerning the values of health workers, for future studies on the issue, as well as for the implementation of policies in the health sector.

4.2. Research model

The figure below, which depicts the relationships between health workers' life and work values, was developed in line with the study's aims and for the analysis of the findings.

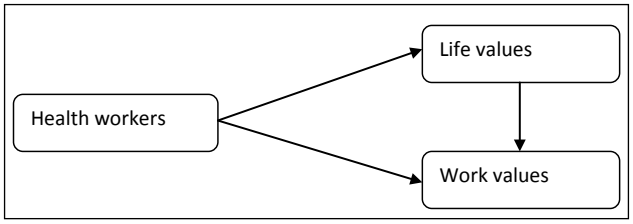


Figure 1. Research model

The following hypotheses have been developed based on the theoretical framework and research model.

H1. There are significant differences between the life and work values of employees in the private health sector and employees in the public health sector.

H2. In terms of demographic characteristics, there are differences between health sector workers' life and work values.

H3. There is a significant relationship between health sector workers' life and work values.

4.3. Research sample

The sample for the study was comprised of workers employed at private and public health in Ankara. 350 surveys were distributed, of which 293 were returned; 285 of the completed and returned surveys were evaluated, 123 (43%) of which were from private health workers, and 162 (57%) were from workers at public health.

4.4. Means of data collection

The measure for Personal Value Statement (PVS) developed by Oliver (1985) was utilized in the identification of participants' personal values. A total of 20 questions were asked, each of which were based on sub-dimensions of the concepts; for the scale, respondents were asked, "Indicate your responses as a 1…, 2…, 3…, placed in front of the expressions according to how important they are to you." The reliability based on Oliver's scale was (α=0.83), and our reliability analysis indicated that the alpha coefficient of the survey was (α=0.81). The inner consistency coefficient for expressions of personal values was found to be (α_{ort} =0.63). To determine the construct validity of the scale, we carried out principal component analysis, the results of which were between 0.67 and 0.81. The content validity was acceptable as indicated by experts in both the domestic and international literature.

The scale for personal values was represented by 12 expressions of value for each dimension. In the scale, there were 20 separate word groups consisting of 3 words which reflect the shared characteristics of the value systems represented. In the survey, respondents gave a score of 3 (most important), 2 (average importance), and 1 (least important) based on the level of importance for the 60 words as regards the question group; for each dimension, a minimum of 12 and a maximum of 36 points was possible.

Work values of the sample were measures using the 21-item scale developed by Manhardt (1972). Following Manhardt, three dimensions were utilized, which were "comfort and security," "skills and development," and "status and independence." Comfort and security included expressions such as "comfortable working conditions," "job security," and "regular routines." Skills and development were inclusive of work-related characteristics such as "sustainable development of skills" and "a sense of success." Status and independence included such expressions as "high salary," "managing other workers," and "working on problems which are important for the organization." In previous studies, reliability analysis produced values between 0.68 and 0.84 for measurements of life values (Meyer et al., 1998); in our study, the reliability tests for the dimensions on the survey resulted in the following values: comfort and security, 0.73; skills and development, 0.81; and, status and independence, 0.77. The reliability test for the scale of work values resulted in an inner consistency coefficient of (α_{ort}=0.63). To determine the construct validity of the scale we carried out principal component analysis, the results of which were between 0.69 and 0.83. The representative validity was determined to be acceptable by experts. Variations in personal value scores were analyzed, ANOVA analysis was used to identify the statistical significance between dimension scores, a ***t*** test was used for independent samples, and correlation analysis was used to identify the relationship between the dimensions of life and work values.

5. Analysis and findings

5.1. Findings regarding the research sample

Table 3 indicates the measurements for work values, the highest of which was "comfort and security" (X=4.1, SD 5617) for the lower dimension of public workers, and private health workers reported the lowest value (X=3.0, SD 5828) for "status and independence." The average perception of the sample regarding the criteria of work values was higher for public workers (X=3.4, SD 6257) than for private health workers (x=3.2, SD 6112).

5.2. Findings on Dimension Averages

An analysis of Table 2 demonstrates that, from the perspective of gender variables, the lowest score was for women working in public health as regards the dimension of economics (x=22.76), and the highest average score was for the theoretical dimension for men working in private health. The lowest score as regards the age variable was for employees at private health for the age group 20-27 vis-à-vis the dimension of social value (x=22,31), and the highest value, (x=28.42), was for the sub-dimension of economic value for employees at private health aged 52 and above. As regards the education variable, the lowest avera-

Table 1. Descriptive Statistics on Demographic Variables

Demographic Characteristics									
Age	Frequency		Percentage		Education	Frequency		Percentage	
	Public	Private	Public	Private		Public	Private	Public	Private
20-25	25	24	15.4	19.7	High school	8	3	4.9	2.6
26-30	47	38	29	30.8	Voc. Sch.	32	19	19.6	15.4
31-40	53	34	32.7	27.6	Undergrad.	63	57	39.2	46.3
41-50	22	17	13.5	13.8	Grad.	38	31	23.4	25.2
51+	15	10	9.4	12.1	PhD	21	13	12.9	10.5
Wom.	89	74	54.9	72.3					
Men.	73	49	45.1	39.7					
Total	162	123	100	100	Total	162	123	100	100

Table 2. Dimension Averages and Standard Deviation Values

Variables		Political		Aesthetic		Social		Theoretical		Economic	
		Average (X)		Average (X)		Average (X)		Average (X)		Average (X)	
		Pub.	Priv.	Pub.	Priv.	Pub.	Priv.	Pub.	Priv.	Pub.	Priv.
Sex	Female	26.80	24.18	23.87	25.33	24.06	25.47	23.93	25.45	22.76	24.32
	Male	26.05	25.44	23.41	24.31	25.31	24.44	22.85	26.23	23.51	24.21
Age	20-27	26.10	26.41	23.72	23.33	25.35	22.31	25.08	25.24	22.89	23.45
	28-35	26.64	24.23	23.22	22.46	25.02	24.22	23.21	26.32	23.32	26.41
	36-43	26.10	24.41	24.43	24.33	25.00	23.33	23.03	25.44	23.40	27.34
	44-51	26.45	25.23	24.35	25.23	25.35	24.45	23.05	27.43	23.80	26.25
	52+	28.00	25.21	23.71	26.32	25.42	26.31	23.42	24.41	22.57	28.42
Education	H.S.	24.80	25.44	24.47	26.43	25.61	23.12	24.28	24.45	22.85	26.22
	Voc. Sc.	26.28	25.22	25.83	24.48	25.05	24.18	23.03	26.44	23.77	27.23
	Underg.	26.53	24.41	26.93	25.41	25.55	21.46	24.75	27.24	22.73	26.32
	MA/ DR.	27.32	25.27	25.77	24.32	25.03	25.32	24.19	26.21	23.25	25.21
Total		26.47	25.04	24.52	24.72	25.16	24.06	23.71	25.90	23.16	25.94

Table 3. Dimension Averages and Standard Deviation Values

	Public		Private	
Dimensions of Research	X	SD.	X	SD.
Comfort and security	4.1	0.5617	3.2	0.5813
Skills and development	3.7	0.7930	3.4	0.6547
Status and independence	3.1	0.7453	3.0	0.5828
Work Values (GENERAL)	3.4	0.6257	3.2	0.6112

ge value was recorded for the dimension of social value for individuals holding a high school diploma who worked in private health (x=21.46); the highest average (x=27,32) was for the value of politics for workers employed in public health who held a graduate or doctoral degree.

The highest average score for the sub-dimension of life values was (x=26.47) for political values for public health employees, and the second highest was (x=25.94) for economic value for workers in private health. The lowest average score was (x= 23.16) for economic value for employees at public health. This supports hypothesis H1 of this study which stated: *There are significant differences between the life and work values of employees in the private health sector and employees in the public health sector.*

The one-way variance/ANOVA analysis carried out to determine if there was a significant difference from the perspective of life and work values in the variables of age and education indicated that there was a significant difference between the dimensions of age and education, and life and work values. The ANOVA table below demonstrates the differences between the age variable and the dimension of life values.As Table 4 demonstrates, there was a significant difference of $p<0.05$ in the average value between the age variable and political value ($F=3.224$; $p=0.005$). The table also indicates that there was a significant difference of $p<0.05$ in the average value between the age variable and economic value ($F=3.324$; $p=0.022$) and that there was a significant difference of $p<0.05$ in the average value between the age variable and sub-dimension work value of comfort and security ($F=3.465$; $p=0.004$). It was also determined that the significant differences between workers' educational status and personal values pertained to the dimensions of politics and economics. There was a significant difference of $p<0.05$ in the total average value between education and the dimension of political value ($F=2.946$; $p=0.013$) and there was a significant difference of $p<0.05$ in the average value between education and economic value

(F=3.349 ve p=0.016). In terms of the values for education and comfort and security, there was a significant difference of p<0.05 in the average value between them (F=2.789 ve p=0.002). The results of the ANOVA test, as regards H2 of our study (*In terms of demographic characteristics, there are differences between health workers' life and work values*), corroborated the hypotheses in terms of the variables of age and education, as well as the sub-dimensions of the values of economics and politics and comfort and security.

Correlation analysis was carried out to determine if there was a significant relationship among the dimensions of workers' personal values. The correlation table below shows the relationships between the dimensions of life and work values, and general life and work values. The aim of the correlation analysis was to identify the relationships between life and work values, which constitute the main hypothesis of this study. As is known, a correlation coefficient has a value of 0 to 1, and values approaching 1 indicate a stronger relationship, while values approaching zero indicate a weakening relationship. Pearson correlation analysis was found to be the most useful approach for the analysis of the data in this aspect of the study.As Table 5 illustrates, there was a negative and significant relationship between the following: political and aesthetic dimensions of value (r=-.323; p=.000), with a significance of p<0.05; political and social dimensions (r=-.324; p=.000), with a significance of p<0.05; political and theoretical dimensions (r=-.288; p=.000), with a significance of p<0.05; and, political and economic dimensions (r=-.266; p=.007), with a significance of p<0.01. The analysis also revealed that there was a negative and significant relationship between the aesthetic and social dimensions (r=-.273; p=.033), with a significance of p<0.05, as well as between the aesthetic and theoretical dimensions (r=-.239; p=.000), with a significance of p<0.05. There was also a negative and significant relationship between the social and economic dimensions (r=-.233; p=.002), with a significance of p<0.01, and between the theoretical and economic dimensions (r=-.347; p=.000), with a significance of p<0.01. The fact that a relationship is negative means that when there is an increase in dimensions of value between which exists a signifi-

Table 4. ANOVA Table for Age and Education Variables and Life Values

	Source of Variance		SD	Box Total	Box Average	F	P
Age	Political	**General**	285	1623.311		3.224	0.005
		Among groups	5	123.434	24.258		
		Within groups	280	1481.371	12.4412		
	Economic	**General**	285	1231.280		3.374	0.022
		Among groups	5	130.471	25.543		
		Within groups	280	1323.409	6.625		
	Comfort and security	**General**	285	1423.212		3.465	0.004
		Among groups	5	132.236	37.454		
		Within groups	280	1341.474	14.484		
Education	Political	**General**	285	1623.611		2.946	0.013
		Among groups	5	163.651	29.228		
		Within groups	280	1797.377	13.542		
	Economic	**General**	285	1738.280		3.349	0.016
		Among groups	5	133.451	33.434		
		Within groups	280	1514.529	9.249		
	Comfort and security	**General**	285	1423.344		2.789	0.002
		Among groups	5	143.439	24.228		
		Within groups	280	1681.671	14.572		

cant relationship, this will result in a decrease in the other dimensions of value. An analysis of Table 5 corroborates the hypothesis upon which this study was based, which was that there is a relationship between life and work values. In following, there was a significant relationship between: the sub-dimensions of the work values of comfort and security, and life values (r=.329; p=.000) with a significance of p<0.01; the sub-dimensions of the work values of skills and development, and life values (r=-.258; p=.004) with a significance of p<0.05; and, the sub-dimensions of the work values of status and independence, and life values (r=.358; p=.000) with a significance of p<0.01. As for general life values and general work values, a positive and significant relationship was found (r=.453; p=.002), with a significance of p<0.05. These results corroborate H3 of this study, which posited, *There is a significant relationship between health workers' life and work values*.

Conclusion and discussion

In this study, in which we comparatively analyzed the relationship between the life and work values of workers at public and private health in Ankara, it was found that there was a positively directed and mid-level relationship (r=.453) between their life and work values. This finding, just as in the hypotheses put forward by previous theorists, indicates that it is not possible to divide life into two separate categories of private life and work life. The results of the study demonstrate that health workers are concerned not only with the dimension of economic value, but also with the dimensions of social, aesthetic and theoretical value. Furthermore, the fact that there is a mid-level, positively directed relationship between the sub-dimensions of life and work values suggests that workers perceive life as a whole and that the associated values are not severable, and also that they do not draw a clear line between work and private life. The findings of this study indicate that, on the one hand, there is the dimension of aesthetic value which is associated with beauty, symmetry, harmony, structure and coherence, and, on the other hand, there is the dimension of economic value which prizes economic benefit, regards life as a struggle, and views others as rivals; if there is a meaningful relationship between these

Table 5. Pearson Correlation Coefficient Table for Research Variables

Sub-dimensions		A	B	C	D	E	F	G	H	I	J
A- Life values	Pearson r	1									
	Significance	.,									
B Political	Pearson r	-.231	1								
	Significance	.000	,.								
C Aesthetic	Pearson r	-.342	-.323*	1							
	Significance	.012	.000	,.							
D Social	Pearson r	-.143	-.324*	-.273*	1						
	Significance	.012	.000	.013	,.						
E Theoretical	Pearson r	-355	-.288*	-.239*	-.121	1					
	Significance	.002	.012	.000	.126	,.					
F Economic	Pearson r	-.361	-.266*	-.044	-.233*	-.347*	1				
	Significance	.002	.003	.502	.004	.000	,.				
G-Comfort and security	Pearson r	.329**	.427*	.533**	.332*	.243**	.576**	1			
	Significance	.000	.001	.001	.002	.003	.004	,.			
H-Skills and develop.	Pearson r	.258*	.566*	.231*	.465**	.346*	.573**	.336*	1		
	Significance	.004	.000	.003	.021	.012	.002	.003	,.		
I-Status and independ.	Pearson r	.358**	.413*	.535**	.547*	.341*	.443**	.434*	.547*	1	
	Significance	.000	.003	.013	.003	.003	.000	.002	.002	,.	
J-Work Values (General)	Pearson r	.453*	.467**	.365*	.573*	.451**	.449*	.435*	.339*	.449**	1
	Significance	.002	.009	.006	.003	.000	.003	.004	.000	.000	.,

** Significant at the level of 0.05*

two dimensions, however, health professionals do not evaluate their lives solely in terms of economic value but also place life values at the center of their professional and private lives. However, the basis for the furthering of political value, which is represented by effort, obtaining power, impacting others, garnering personal recognition, and acquiring control and authority, must be situated in its relationship (r=-,324) to social value, which is represented by an individual's humanistic values, including a sense of belonging, appreciation for emotional sympathy, politeness, refinement, and charitableness.

Similar studies have also identified a relationship between life values and work values. Furnham noted that since life and work values are constitutive of a whole, then values, attitudes, and beliefs are the parts of a larger unity which are interrelated both at the mental and at the emotional levels. It is then expected that there would be a relationship between life values and work values. For Furnham, the relationship between life and work values is bound to the hypothesis that belief in organized work, a stimulating life, equality and honesty, and the values of obedience and politeness exist in a positive relationship.

In conclusion, this study is significant from the perspective that, in an environment of cosmopolitanism and popularization brought about by globalization, life and work values are a matter of concern. Even if it is mid-level (r=.453; p=.002), the relationship between life and work values is significant because, as this study has shown, health workers continue to bring their personal life values into the workplace. The statistical analysis carried out for this project has corroborated the hypothesis that there is a mid-level and positive relationship between life and work values, as well as between sub-dimensions of both life and work values.

Contributions, limitations, and future research

The aim of this study, which focused on health workers in Ankara, was to contribute to academic discussions concerning life and work values through a comparative study of the life and work values of these workers. Within this framework, this study sought to focus on the relationship between workers' life and work values, and it contributes to the field in three regards. The first of these is that, through an emphasis on the significance of work and private values as they impact behavior, such knowledge will be useful in particular for organization administration. Secondly, this study underscores the bringing of personal values to work life, and this will be beneficial from the perspective of institutionalization, professional management, and image management. As the last contribution, through a comparison of workers at private and public health, this study comments on these institutions' organizational climate, culture, and, more broadly speaking, work life. In this regard, the study provides useful data for evaluating how life and work values reflect on the ethical management principles of health.

It should be pointed out that this study on workers at private and public health has its limitations. The first of these is that it was limited to workers at private and public health in Ankara; in order to expand on the results of this study, it could be repeated in other regions and provinces. Related to this is the fact that a limited number of workers in public and private health participated in the study. Since the study was carried out only in Ankara, it may not be possible to draw more general conclusions about the common characteristics of health workers in all of Turkey; nonetheless, the study does provide a framework for considering these in terms of life and work values.

The assertions made in this study are based on tests of the three hypotheses set forth, and these tests were carried out per the terms of the theoretical framework research model. The results, however, concerning the relationship between the life and work values of health workers are insufficient; for this reason, it is necessary to carry out further studies on the issue with other samples to further universalize the claims set forward.

The constraints discussed above limit the generalizations that can be made about the results of the study, which other research could build upon through a comparison of larger samples drawn from other cities and regions. Furthermore, the use of different criteria and variables would also be beneficial in such further research. The development of other hypotheses, the results of which could then be comparatively analyzed, would reinforce the statistical claims set forth. Lastly, rather than em-

ploying a survey to collect data, the use of other observational methods and qualitative techniques would offset the limitations incurred during the course of this study.

References

1. *Beutell, N. J. and Brenner, O. C. (1986). "Sex Differences in Work Values," Journal of Vocational Behavior, 28, 29 - 41.*

2. *Bulut, D., Isma, C. (2004). "Muğla İli Sağlık Yöneticilerinde Kişisel Değer Analizi" ["Personal Values Analysis of Health Administrators in the Province of Muğla"], Hacettepe Sağlık İdaresi Dergisi, 7 (3), 282.*

3. *Cherrington, Conde and England, (1979), "Age and Work Values", Academy Of Management Journal, C.22, ss.617-623.*

4. *Dose, J. J. (1997). Work values: An integrative framework and illustrative application to organizational socialization. Journal of Occupational and Organizational Psychology, 70, 219–240.*

5. *Elizur, D., Borg I., Hunt R., & Magyari-Beck, I. (1991) 'The Structure of Work Values: A Cross Cultural Comparison', Journal of Organizational Behavior, 12: 21-38.*

6. *Elizur, D. (1984) 'Facets of Work Values: A Structural Analysis of Work Outcomes', Journal of.Applied Psychology, 69: 379-389.*

7. *England, George W. & LEE, Raymond (1974). "The Relationship Between Managerial Values and Managerial Success in the United States, Japan, India and Australia" , Journal of Applied Psychology, V. 59, pp. 411-419.*

8. *Furnham A. (1987). "Work Related Beliefs and Human Values," Journal of Personality and Individual Differences 8: 627-637.*

9. *Furnham, A., K.V. Petrides, I. Tsaousis, K. Pappas and D. Garrod (2005). "A Crosscultural Investigation Into the Relationships Between Personality Traits and Work Values," The Journal of Psychology, 9 (l), 5-32.*

10. *Goodstein, L. D. (1983). "Managers, Values, and Organization Development Group and Organization Studies," 8 (2): 203.*

11. *Gungor, E., (1998). "Değerler Psikolojisi Üzerine Araştırmalar" ["Research on the Psychology of Values"], 2. Baskı, Ötüken Yayınevi, İstanbul.*

12. *Herriot, Peter (1976). Essential Psychology. Values, Attitudes and Behaviour Change, Methuen Co. Ltd., New York.*

13. *Hofstede, G. (1984). Culture's consequences: International differences in work-related values. Beverly Hills, CA: Sage Publications.*

14. *Kaufman, D. and Fetters, M. I., (1980). "Work Motivation and Job Values Among Professional Men and Women: A New Accounting," Journal of Vocational Behavior, 17, 251-262.*

15. *Kilby, R. W. (1993). The study of human values. Lanham, MD: University Press of AmericaKinnane, J.F. and Gaubinger, J.R. (1963) 'Life Values and Work Values', Journal of Counseling Psychology, 10(4): 362-372.*

16. *Klenke, K. (2005). Corporate values as multi-level, multi-domain antecedents of leader behavior. International Journal of Manpower, 26(1), 50-66.*

17. *Kluckhohn, Clyde & Others (1951). "Values and Value-Orientations in the Theory of Action", Toward A General Theory of Action, Ed.: T. Parsons & E. A. Shils (Harvard University Press, 1951), pp. 388-433.*

18. *Kusdil, E. M., C. Kagitcibasi, (2000). "Türk Öğretmenlerin Değer Yönelimleri ve Schwartz Değer Kuramı" ["Value Orientation for Turkish Teachers and the Schwartz Value Theory"], Türk Psikoloji Dergisi, 15 (45), 59-76.*

19. *Manhardt, P.J.(1972), "Job Orientation of Male and Female Collage Graduates in Business", Personel Pyschology, C.25. ss.361-368.*

20. *McCarty, J.A., and L.J. Shrum, (1994). "The Recycling Of Solid Wastes: Personal Values, Value Orientations, and Attitudes About Recycling As Antecedents of Recycling Behavior," Journal of Business Research, 30, 53–62.*

21. *Meyer, P.J., P.G. Irving and N.J.Allen, (1998), "Examination of the Combined Effects of Work Values and Early Work Experiences on Organizational Commitment, C.9, ss.29-52.*

22. *Miller, J.E.(2006), "The Effect of Reward, Commitment, Organizational Climate and Work Values on Intention to Leave: Is There aDifference Among Generation?", Doctoral Dissertation, State University of New York Collage of Business Department of Organizational Studies, Albay.*

23. *Naktiyok, Atılhan (2003). "Yönetici Değerleri ve Pazar Yönlülük Bir Uygulama" ["Administrative Values and their Application in a Market Setting"], Erciyes Üniversitesi İktisadi ve İdari Bilimler Fakültesi Dergisi, 20, 95-116.*

24. *Özen, Şükrü (1996). Bürokratik Kültür 1: Yönetsel Değerlerin Toplumsal Temelleri, TODAİE Yayınları, Yayın No: 272, Ankara.*

25. *Lyons, S. T., L. E. Duxbury and C. A. Higgins, (2006), "A Comparison of The Values and Parapublic Sector Employees", Public Administration Deview, ss. 605-618.*

26. *Ralston (1997). "The Impact, Of National Culture And Economic Ideology On Managerial Work Values: A Study Of The United States, Russia, Japan, and China," Journal Business International Business Studies, First Quarter, 177-207.*

27. *Rokach, Milton (1973). The Nature of Human Values, The Free Press, New York.*

28. *Rosener, J.B. (1990). "Ways Women Lead," Harvard Business Review, 68 (6), 119-125.*

29. *Ros M., Schwartz S. H., and Surkiss S. (1999) 'Basic Individual Values, Work Values, and the Meaning of Work', Applied Psychology, 48(1): 49-71.*

30. *Sagie, A., D. Elizur and M. Koslowsky (1997). "Work Values: A Theoretical Overview And A Model of Their Effects," Journal of Organizational Behaviour, 17, 503-514.*

31. *Schwartz, S. H. (1992). "Universals In The Content And Structure Of Values: Theoretical Advances And Emprical Tests in 20 Countries," Advances in Experimental Social Psychology, 25, 1-65.*

32. *Schwartz, S. H. (1994). "Are There Universal Aspects in The Structure and Content of Human Values?". Journal of Social Issues 50 (4), 19–45.*

33. *Sener A, Hazer O.(2007). Values and Sustainable Consumption Behaviour of Women: a Turkish Sample. Sustainable Development Early View. DOI: 10.1002/sd.329*

34. *Stein, H. F. (1985) Therapist and family values in a cultural context. Counseling and Values, 30, 35-45Stern, P. C., Dietz, T., (1994). "The Value Basis of Environmental Concern", Journal of Social Issues, Vol. 50, No.3.*

Corresponding author
Hasan Tutar,
Sakarya University Faculty of Economics and Administrative Sciences,
Esentepe Campus,
Sakarya,
Turkey,
E-mail: htutar@sakarya.edu.tr

The satisfaction levels of patients health services to apply university hospital inTurkey

Seyda Dulgerler[1], Gul Ertem[2], Serap Ozer[1]

[1] Ege University Faculty of Nursing, Psychiatric Nursing Department, Izmir, Turkey,
[2] Ege University Odemis School of Health, Gynecology and Obstetrics Nursing Department, Odemis, Izmir, Turkey.

Abstract

Objective: This study was conducted to evaluate patient satisfaction and its related factors.

Designs: A cross-sectional design was used in this study.

Setting and Participants: Sample size was determined as 390 from 3900 by randomized sampling in several phases according to the proportion of hospitalized and out-patient. Participants were interviewed privately face to face in the hospital time. The scale developed by Ercan et. Al in order to measure patient satisfaction in associations that are in secondary health-care services include components evaluating clinical-policlinical health care services, staff, patient-rights, hospital appearance, cafeteria services.

Results: Over 25% of the participants (n=105) were in age group 29-39 years and 64.4% were female. Mean age was 38.95±8.95. Patient satisfaction differentiates according to socioeconomic, demographic, functional conditions and health. There were the significant among satisfied with patients' with hospitalized, personal relationship, patients' rights and general physical structure of the a large university hospital in Izmir, Turkey.

Conclusions: The majority of out-patients were quite satisfied, with their satisfaction include mostly time related with laboratory, radiology services and bureaucratic procedures and cleanliness, hygiene, physical conditions, prices and service quality of cafeteria and quality and amount of the food given to the patients, behavior of the staff.

Keywords: patient satisfaction, hospital care, nursing, Turkey.

Introduction

Determination of patient satisfaction levels is critical for improving the quality of services and providing more sophisticated services fulfilling the expectations of patients. A patient, who is satisfied with the provision of health-care services in a facility, would admit to the same facility when he/she seeks (Esatoğlu-Ersoy 1996; Andaleb 2001).

Measurement of patient satisfaction is expected to play an increasingly important role in the growing push toward accountability among health care providers overshadowed by measures of clinical processes and outcomes in the quality of care equation (Aldana and et all. 2001). In order to address daily problems encountered during production in advance and to evaluate and improve services, research on services should be carried out (Şahin-Eğri 1999; Özer-Çakıl 2007). To achieve this, educational and research administrations should collaborate with health-care organizations and undertake responsibility and appropriate funds should be spared for research on services. Data about patient opinions obtained by systematical follow-up of consumers of health-care resources would be a valuable guide towards improving quality of services. In order to obtain information about and improve quality of health-care system, major variables of interest such as extent of service use, percentage of attainment and satisfaction scores should be assessed. Patient satisfaction finding regarding inpatient and ambulatory care play a significant role in hospital's strategies and tactics in delivering patient services. Patient satisfaction survey is an instrumental component in hospital's quality of care monitoring, in relation to cost and services. Many studies have been carried out throughout the world to determine the patient satisfaction and its related factors (Merkouris and at all 1999; Yılmaz M 2001; Quintana 2006; Özer-Çakıl 2007;). In a study conducted in Turkey, satisfaction with physicians, nurses, equipment and food services were the main determinants of overall satisfaction in hospitalized patients. Gender, sex and education play a major role in patient satisfaction.

In Iranian surveys, satisfaction level of patients who were treated by male doctors was greater than females and an inverse relationship between patient satisfaction and education was observed (Bahrampour-Zolala 2005). There is a lack of studies about patient satisfaction among patients admitted in hospitals in Izmir/Turkey. Therefore the aim of this study was to find out-patient satisfaction with care in a large university hospital in Izmir/Turkey and explore the associated factors. Findings from this study will be presented to national authorities to be used as a framework to improve health services (Kuosmanen L at all 2006).

Methods

Sample, Setting and Design

The cross sectional design was used to perform the study. Sample size was determined as 390 from 3900 by randomized sampling in several phases according to the proportion of the hospitalized and out-patient. This research was performed patients who admitted to a large university hospital in Izmir/Turkey. Implementation of the study lasted for three month including face-to-face interview with subjects. Scale was applied to 390 subjects. A socio-demographic form and the scale which was applied to measure non-technical dimension of service satisfaction from services provided by a secondary health-care unit, was used.

A socio-demographic form included questions about age, gender, education, marital status, health insurance.The scale which was developed and reliability and validity analyses were done by Ercan et. All (2004), was applied to measure non-technical dimension of service satisfaction from services provided by a secondary health-care unit. The scale developed by Ercan et. All in order to measure patient satisfaction in associations that are in secondary health-care services include components evaluating clinical-policlinical health care services, staff, patient-rights, hospital appearance, cafeteria services. The scale is composed of 43 items. Each respondent was asked to rate each item on a Likert's 0-4 response scale: where 0 corresponds to ever disagree, 1 partly agree, 2 agree, 3 largely agree, 4 completely agree. Alpha coefficient reliability of the scale was 0.97. In this study, alpha coefficient reliability of the scale was 0.94.

Characteristics of the sample

Over 23.8% of the participants were in age group of 40-50 years and 66.4% were female. Mean age was 38.95±8.95 years (Table 1). Out of all participants, 39% were high school graduates, 69.2% married and 97.2% had a health insurance (Table 1).

Statistical Analysis

Statistical analyses of the data were made with statistical package for the social science (SPSS Chicago, II, USA) and percanteges, variance analysis, and Pearson's Q-Square.

Ethical considerations

Approval was obtained from the ethical committee of the Odemis School of Health and the University Hospital. All patients provided written informed consent.

Table 1. Characteristics of the Participants

Age Group	N	(%)
18 – 28 age	103	25.41
29- 39 age	105	26.40
40 – 50 age	93	23.84
51 – 61 age	39	10.00
62 and over	60	14.35
Gender		
Female	259	66.4
Male	131	33.6
Education		
Elementary	52	13.3
secondary	76	19.5
High School	152	39.0
University	110	28.2
Marital status		
Single	79	20.2
Married	270	69.2
Other	41	10.5
Social guarantee		
Yes	379	97.17
No	11	2.83
Income status		
Below $ 103	3	0.8
Between $ 103 - 206	4	1.0
Between $ 206 - 412	68	17.4
Between $ 412 - 687	158	40.5
Between $ 687 - 1375	130	33.3
Above $1375	27	6.9
Total	**390**	**100.0**

Results

The 35.89% of patient were quite satisfied with their care and 25.12% was trusted the knowledge of physician (Table 2).

There was no significant relation between education and total satisfaction ($p>0.05$). There was significant relation between patient whose hospital stay and total satisfaction ($p<0.05$). There was also statistically significant relation between recourse of patients and local health clinics, hospitalization, bureaucratic procedure, health staff communication, knowledge and application patient's right, hospital's general physical structure, quality of cafeteria ($p<0.05$) (Table 3).

There was also statistically significant relation between age groups and local health clinics, hospitalization, bureaucratic procedure, health staff communication, knowledge and application patient's right, hospital's general physical structure, quality of cafeteria ($p<0.05$) (Table 4).

Discussion

This study revealed that in general, patients were quite satisfied with their hospital care. This is in line with previous studies (Bahrampour-Zolala 2005; Kuosmanen et all. 2006). In our study there was significant relationship between age and total satisfaction. Consistently with our finding many studies have pointed out the importance of certain variables including age which consistently shows that elderly patients are more satisfied (Crow et all. 2002). Age, gender, income and formal education have shown no clear connection with the patient satisfaction (Kelstrup et all. 1993; Leavy et all. 1997; Walker-Mclnerny 1998). The effect of the age variable on satisfaction was not significant in Japipaul study, but it showed interesting results. The greatest level of satisfaction was in the group 15-24 years old, then it decreased gradually and increased again in the group who were over 60 years old (Japipaul-Rosenthal 2003). Rahmqvist (2001) reported that patient age had the greatest explanatory value regarding the Patient Satisfaction Index. Determining the level of patient satisfaction, improving quality of service and patient expectations are important for the more qualified to serve. 66.4% of the patients participating in research were women, 39.0% of high school graduates and 97.17% of social protection such as a large majority were determined to be. In Turkey, however, is look at the income level to which hunger and monthly income limit, which is a TL 601-1000. In 2004, the income level of a similar study was found between TL 301-600. (Ercan–Ediz 2004). Although the figures differ, the level of inflation is associated with income levels of the two research groups on similar and low levels of refinery operations. 40.3% is often the primary school level education in Ercan et all. (2004) study group. In our study, level of the high school was majority. Finding from our study showed that there was no significant relationship between education and total satisfaction. Levels of education were inversely correlated with satisfaction in Ayatollahi study (1999). Observation and perception of socio-economic level, education level of our expectations of the patient is a high level of impact. Indeed, the study of a private hospital in the Aegean region the high income level was found to affect the perception of the quality (Demirtaş et all 1999; Devebakan 2002). We have found that perception of the quality is the mid-level, that similar with Ercan et all.'s (2004) results. Our research findings obtained from a large university hospital in the majority of patients (35.89%) and that they have chosen to give good service. Patient have been the last choice, cause of physicians are knowledgeable. This case illustrates the importance of patients' quality of service. Maral et all. (1998) the results were similar in their work. Associated different studies have shown different results (Maral et all 1998). Jenkinson et all. (2002) in a study of patients' experiences and satisfaction with health care reported that major determinants of patient satisfaction were physical comfort, emotional support, and respect for patient prefe-

Table 2. University Hospital Preference Reasons of Patients

Reasons of Preference	N	(%)
To give good service	140	35.89
Advice on	70	17.95
Easy access	35	8.97
Physicians are more confident	98	25.12
Other	47	12.07
Total	390	100.0

Table 3. Patient Satisfaction According to the Recourse of Patients

Unit The Scale	Internal Disease Polyclinic n = 97	Internal Clinic n = 54	Obstetric and Gynecology Polyclinic n = 48	Obstetric and Gynecology Clinic n = 59	Orthopaedy Polyclinic n = 77	Orthopaedy Clinic n = 55	F	Sig.
	X ± SD	X ± SD	X ± SD	X ± SD	X ± SD	X ± SD		
Evaluation Score of Outpatient Treatment	20.94 ± 7.75	18.41 ± 11.47	19.54 ± 6.37	10.64 ± 12.09	22.75 ± 7.93	22.55 ± 12.56	13.095	.000*
Evaluation Score of Hospitalization Treatment	4.86 ± 8.07	17.33 ± 6.27	5.35 ± 8.70	20.68 ± 7.73	9.58 ± 13.84	28.75 ± 6.79	66.797	.000*
Evaluation Score of Bureaucratic Process	19.89 ± 7.16	21.63 ± 6.12	18.04 ± 5.23	22.02 ± 7.09	20.61 ± 6.20	26.11 ± 4.18	10.480	.000*
Hospital Staff Evaluation score	12.37 ± 4.13	13.91 ± 2.47	11.35 ± 4.21	13.88 ± 4.70	17.79 ± 3.33	16.05 ± 3.45	11.516	.000*
Evaluation Score of Patients' Rights	13.78 ± 5.45	15.28 ± 3.71	14.06 ± 3.87	15.68 ± 4.79	15.34 ± 4.77	18.36 ± 2.33	8.240	.000*
Physical Environment Evaluation Score	9.44 ± 3.84	9.65 ± 3.48	8.94 ± 2.80	11.41 ± 3.94	10.68 ± 3.91	13.56 ± 2.98	12.807	.000*
Cafeteria Environment Evaluation Score	5.58 ± 3.97	5.22 ± 4.57	3.90 ± 4.03	6.36 ± 5.72	6.23 ± 4.15	8.36 ± 4.28	5.877	.000*
Overall Situation Assessment Score	8.60 ± 3.38	9.11 ± 2.15	8.21 ± 2.41	10.44 ± 2.34	9.47 ± 2.79	11.58 ± 1.96	12.815	.000*

*$p \leq 0.05$

Table 4. Patient Satisfaction According to Age Groups

Age Group The Scale	18-28 n = 103 X ± SD	29-39 n = 93 X ± SD	40-50 n = 105 X ± SD	51-61 n = 39 X ± SD	61 ve ↑ n = 60 X ± SD	F	Sig.
Evaluation Score of Outpatient Treatment	16.17 ± 10.85	17.84 ± 9.65	20.35 ± 10.69	23.12 ± 6.79	18.58 ± 10.94	3.687	.001 (*)
Evaluation Score of Hospitalization Treatment	10.17 ± 11.45	8.24 ± 11.19	14.18 ± 10.13	9.52 ± 11.58	13.58 ± 13.05	5.103	.000 (*)
Evaluation Score of Bureaucratic Processes	20.81 ± 6.25	18.52 ± 7.09	19.90 ± 6.86	21.29 ± 6.62	20.92 ± 7.17	4.976	.000 (*)
Hospital Staff Evaluation Score	13.72 ± 5.09	12.59 ± 3.81	12.61 ± 3.89	14.07 ± 4.03	13.13 ± 4.01	3.216	.004 (*)
Evaluation Score of Patients' Rights	13.00 ± 5.31	13.33 ± 4.65	14.98 ± 4.19	15.98 ± 4.35	15.71 ± 4.85	5.719	.000 (*)
Physical Environment Evaluation Score	10.56 ± 4.62	8.66 ± 3.41	9.63 ± 3.46	11.00 ± 4.15	10.76 ± 3.68	4.455	.000 (*)
Cafeteria Environment Evaluation Score	6.19 ± 4.56	4.47 ± 3.03	6.02 ± 4.90	6.21 ± 5.07	5.44 ± 4.27	2.292	.035 (*)
Overall Situation Assessment Score	8.97 ± 3.55	7.88 ± 3.11	9.92 ± 2.36	9.69 ± 2.66	9.71 ± 2.55	5.107	.000 (*)

$p \leq 0.05$

rences. In the study of Koşucu et all. (1998), reason for referral and medical profile of the surplus as possible was to the fore. All these results in Turkey are not yet fully recognized the service of patients and patients do not have enough information about rights and not in the form of comments. In the study of Önsüz et all. (2008), patient satisfaction results were similar, 28.1% of patients only because they were better served by this hospital have indicated they prefer. Hospital's being close to places of work and home has been identified as the reason for preference. The results of this study are similar with the results of our study. But relatives have received good service to communicate with the service work is to show preference for the hospital. The results were in line with this effort in the study of Filik et all. (2007) and Önsüz et all. (2008). In our study patients who stayed in hospital for 11-15 days were more satisfied than patient with a hospital stay of less than five days or over 16 days. Patients may have become familiar with the hospital care as this finding is in line with the study of Bahrampour & Zolala (2005). Study by Kuosmanen et all. (2006), showed that female patients with short duration of hospitalization were less satisfied with staff's care than men.

The results obtained from this research, referral, or social security institutions such as the preference of patients with more binding factors is left out, institutions, and close the preference of patients for their trust has been identified by the request. Health protection is associated with survival; patients' trust in their good services to be delivered to dry has emerged as a fact that cannot be denied.

Conclusions

University hospitals have more advanced technological facilities, to develop open, scientific; that the employees provide services in this direction, the addition of services as possible in satisfying the execution, both in terms of preference and satisfaction

is high is important. Research of our group, while patients in the hospital with calm satisfaction of the conditions of service they were examined and discussed with the scale of assessments of the difference between all the units and were determined to be significant ($p<0.05$). Long-term in-patient services for the satisfaction of the senses were found to be higher. At the same time, in research patients were preferred (35.89% of the patients) for a large university hospital in Izmir/Turkey is good service and for the physician to be more secure. Why choose of patients were preferred a large university hospital in Izmir/Turkey, this hospital have the advanced technological, that is an important factor.

All these results be treated with the lowest satisfaction level in the field (out-patient treatment, the bureaucratic process and the staff, patients and the approach) should be given weight, satisfaction levels are high in the area at this level to maintain and further increase should be working for. Employees' satisfaction in mind, quality work should be accelerated. The data in line with the health care institutions and employees, to ensure patient satisfaction and improve service quality and falls is a great responsibility.

As a result, patient satisfaction, as seen above, the service's presentation, the patient services provided by the interaction, the presence of services, continuity of service, adequacy of services provided and communication features, including multi-dimensional concept. Therefore, as a result of patient satisfaction, health services, and often the quality of care is considered as an indicator. Patient satisfaction on a regular basis with valid and reliable measurement tools to evaluate the patient are detected by monitoring the level of quality and results in line with expectations for patients to make appropriate arrangements to allow the quality of services will effect.

Limitations of the study

There are certain limitations in this study, which should be considered when the results of this study are examined. Firstly we used cross sectional data to identify relationships. Secondly only in-patients were included in this survey. Future studies using longitudinal data may provide stronger evidence of this relationship.

Acknowledgments

The authors would like to thank University Hospital in Izmir/Turkey and participants.

References

1. *Aldana, JM., Pieckulek, H., Al-Sabir, A. (2001). Client satisfaction and quality of health care in rural Bangladesh. Bulletin of the World Health Organisation; 79(6): 512-517.*
2. *Andaleb, S. (2001). Service quality perceptions and patient satisfaction a study of hospitals in a developing country. Social Science & Medicine; 52: 1359-1370.*
3. *Ayatollahi, SMT. (1999). Patient satisfaction from their consultant physicians in Shiraz. J Kerman Univ Med Sci; 3: 149-56.*
4. *Bahrampour, A., Zolala, F. (2005). Patient satisfaction and related factors in Kerman hospitals. Eastern Mediterranean Health Journal; 11: 905-12.*
5. *Crow, R., Gage, H., Hampson, S., Hart, J., Kimber, A., Storey, L. (2002). The measurement of satisfaction with health care: Implication for practice from a systematic review of the literature. Health Technology Assessment; 32: 1-244.*
6. *Demirtaş, T., Karacasu, G., Tunayürek, P., et all. (1999). Başkent Üniversitesi Zübeyde Hanım Uygulama ve Araştırma Merkezi hemodiyaliz ünitesinde tedavi gören olguların memnuniyet düzeylerinin araştırılması. Haberal Eğitim Vakfı: 49-55 (in Turkish).*
7. *Devebakan, N. (2005). Sağlık işletmelerinde algılanan hizmet kalitesi ve ölçümü. D.E.Ü. Sağlık Bilimleri Enstitüsü, İzmir, Türkiye (in Turkish).*
8. *Ercan, İ., Ediz, B., Kan, İ. (2004). Hastaların sosyoekonomik durumlarına göre sağlık hizmetlerinden memnuniyetlerinin incelenmesi. İnönü Üniv. Tıp. Fak. Dergisi; 11(3): 161-166 (in Turkish)*
9. *Ercan, İ., Ediz, B., Kan, İ. (2004). Sağlık kurumlarında teknik olmayan boyut için hizmet memnuniyetini ölçebilmek amacıyla geliştirilen ölçek. Uludağ Üniv. Tıp Fak. Dergisi; 30 (3): 151-157 (in Turkish).*
10. *Esatoğlu, EA., Ersoy, K. (1996). Hasta tatmininin ölçülmesi sağlık hizmetlerinde toplam kalite yönetimi ve performans ölçümü, Ankara, Haberal Eğitim Vakfı; 61-71 (in Turkish).*
11. *Filik, T., Ünalan, D., Çetinkaya, F. (2007). Erciyes Üniversitesi Gevher Nesibe Hastanesi Polikliniklerine basvuran erişkin hastalarda memnuniyet duru-*

mu. V. Ulusal Sağlık Kuruluşları Yönetimi Kongresi 19-23 Nisan, Antalya (in Turkish).

12. *Japipaul, CK., Rosenthal, GE. (2003). Are older patient more satisfied with hospital care than younger patient. J General Internal Medicine; 1: 23-30.*

13. *Jenkinson, C., Coulter, A., Bruster, S. et all. (2002). Patients' experiences and satisfaction with health care: results of a questionnaire study of specific aspects of care. Quality and Safety in Health care; 11: 335-339.*

14. *Kelstrup, A., Lund, K., Laritsen, B., Bech, P. (1993). Satisfaction with care reported by psychiatric inpatients. Relationship to diagnosis and medical treatment. Acta Psychiatric Scandinavica; 87: 374-9.*

15. *Koşucu,S., Maral, I., Bumin, MA. (1998). Ankara Hastanesi Dahiliye Polikliniği'nde muayenesi tamamlanan hastaların hastaneden memnuniyet durumları. Gazi Kalite Günleri, Özet Kitabı, Ankara; 112-118 (in Turkish).*

16. *Kuosmanen, L., Hatonen, H., Jyrkinen, AR., Katajisto J., Valimaki M. (2006). Patient satisfaction with psychiatric inpatient care. J Adv Nurs; 6: 655-63.*

17. *Leavy, G., King, M., Cole, E., Hoar, A., Johnson-Sabine E. (1997). First-onset psychotic illness: patient's and relative's satisfaction with services. British J Psychiatry; 170: 53-7.*

18. *Maral, I., Aycan, S., Özkan, S., Yıldırım, A., Baran, FN. (1998). Gazi Hastanesi Polikliniklerinden hizmet alanların temel özellikleri, hastaneyi seçme nedenleri ve poliklinik hizmetlerini seçme nedenleri ve poliklinik hizmetlerine yardımcı olan birimlerden memnuniyet durumları. Gazi Kalite Günleri Özet Kitabı, Ankara: 83-99 (in Turkish).*

19. *Merkouris, A., Ifantopoulos , Lanara, V., Lemomdou, C. (1999). Patient satisfaction. A key concept for evaluation and improving nursing services. Journal of Nursing Management; 7 (1): 19-28.*

20. *Önsüz, FM., Topuzoğlu, A., Cöbek, UC., Ertürk, S. ve ark. (2008). İstanbul'da bir tıp fakültesi hastanesinde yatan hastaların memnuniyet düzeyi. Marmara Medical Journal; 21 (1): 33-49 (in Turkish).*

21. *Özer, A., Çakıl E. (2007). Sağlık hizmetlerinde hasta memnuniyetini etkileyen faktörler. Tıp Araştırmaları Dergisi; 5 (3): 140-143 (in Turkish).*

22. *Quintana, JM., González, N., Bilbao, A., Aizpuru, F., Escobar, A., Esteban, C. et all. (2006). Predictors of patient satisfaction with hospital health care. BMC Health Services Research; 6: 102.*

23. *Rahmqvist, M. (2001). Patient satisfaction in relation to age, health status and other background factors: a model for comparisions of care units. International Journal for Quality and Health Care; 13 (5): 385-390.*

24. *Şahin, M., Eğri, M. (1999). Malatya Yeşilyurt ilçesinde hastane hizmetlerinin kullanımı ve etkileyen faktörler. Toplum ve Hekim Dergisi; Eylül-Ekim, 14: 332-337 (in Turkish).*

25. *Walker-Brooksby, A., Mclnerny-Taylor, A. (1998). Patient perceptions of hospital care: building confidence, faith and trust. Journal of Management; 6 (4): 193-200.*

26. *Yılmaz, M. (2001). Sağlık bakım kalitesinin bir ölçütü: hasta memnuniyeti, C.Ü.H.Y.O Dergisi; 5 (2): 69-74 (in Turkish).*

Corresponding Author
Seyda Dulgerler,
Ege University Faculty Of Nursing,
Psychiatric Nursing Department,
Bornova,
Izmir,
Turkey,
E-mail: Seydadulgerler@Yahoo.Com

The comparison of the effects of fennel extract and vitamin e on the intensity of primary dysmenorrhea

Moslemi L[1], Bekhradi R[2], Galini Moghaddam T[3], Gholamitabar Tabari M[1]

[1] Department of midwifery, Islamic Azad University, Sari Branch, Sari, Iran,
[2] Researcher at the Research at Development Unit of Barij Essence Kashan, Iran,
[3] Department of Obstetrics and Gynecologist, Mazandaran University of Medical Sciences, Sari, Iran.

Abstract

Introduction: primary dysmenorrhea is described as pelvic pain around the time menstrual bleeding in the absence of an identifiable pathologic lesion. It is a common gynecologic problem among women in reproductive age groups. Our objective was to compare the effect of vitamin E and Fennel extract on intensity of primary dysmenorrhea.

Materials & Method: A randomized single blind, Placebo-controlled trial among 65 single female students who suffered from primary dysmenorrhea that divided into 3 groups: Fennel extract, vitamin E and placebo. Groups used treatment four times a day from the onset of bleeding and continued through three days for two consecutive menstrual periods.

Result: In the Fenalgin group, pain severity was lower in compare to before treatment (P<0/000) and vitamin E group either cycle (P<0/02). Comparison 3 groups showed that there was significant difference in pain severity in second cycle and reduction was greater in Fenalgin group (P<0/019). Painkiller using was lower in compare to before treatment in Fenalgin and vitamin E groups but reduction in both drugs was not significant in compare to placebo.

Conclusion: Fenalgin, which has few side effects, can be taken for treatment of primary dysmenorrhea. More clinical trial needed to establish the efficacy of this herbal drug.

Key word: primary dysmenorrhea, vitamin E, Fennel extract.

Introduction

Dysmenorrhea refers to cramp-natured menstrual pains [1, 2] located in lower abdominal areas. The most common of cyclic pains, dysmenorrheal is categorized – depending on anatomical and pathological cases – into primary and secondary types [1]. Primary Dysmenorrhea involves menstrual pain without pelvic pathology, whereas in the secondary type, painful menstruation is accompanied with pathology. [3] Occurring one or two years after the beginning of menstruations and during ovulation, dysmenorrhea is more common in ages 13 to 19, and becomes rare after the age of 30, particularly after 35. [4] Primary Dysmenorrheal pains usually begin a few hours before or just after menstruating starts, and last for 48 to 72 hours. [1, 3] Primary Dysmenorrhea shows a 50 to 90 percent occurrence in various societies, and is, according to an epidemiological study, %91 common in Iran. [5] Another report shows that almost 15 percent of women suffer from intense pain during menstrual bleeding. [6] Although not fatal, dysmenorrhea affects the quality of women's life, and at times produces incapability and inefficiency, which in turn leads to absence from work or school for at least 3 or 4 days a month, an annual average of around 36 to 48 days for fertile women – a great damage to the community's business cycle [8, 5]. In the United States, 60 million hours of work and 2 billion dollars are thus wasted every year. [5, 9] The cause of primary Dysmenorrhea is the increase in the synthesis of prostaglandins, particularly the E2 and F2a types. [10, 11] Several treatments have been suggested for dysmenorrhea, such as using prostaglandin control drugs, nonsteroid anti-inflammatory painkillers, birth control pills, vitamins, herbal drugs, etc. [4, 12] In about 80 percent of women suffering from dysmenorrhea, pain is relieved by using prostaglandin controllers including proponics and fenamates. The most frequent side effects brought about by drugs controlling prostaglandins are slight digestive dis-

orders such as nausea, indigestion and vomiting. Kidney disorders, ulceration, dizziness, buzzing in ears, headaches, insomnia, depression, allergic reactions, blood and liver disorders can be named as other side effects. [12] Due to the undesirable side effects these treatments have besides their curative effects, researchers recommend that herbal remedies and vitamins be used instead in order to prevent side effects. In Iran, a wide variety of herbal remedies – fennel, chamomile, evergreen, and many others – have been used in order to treat dysmenorrhea. [13] Indeed, research has proven the anti-spasm effects of fennel upon spasms caused by oxytocin and prostaglandin E2 in uteruses dissected from mice. [8] Many researchers attribute the effects fennel extract has on the female reproductive system and mammary glands to the estrogenic characteristics of the anetol existing in fennel extract; they believe that anetol polymers such as dianethol and photoanethole act as phytoestrogens. [4] There is a lost of research on the effect of fennel essence on dysmenorrhea, whereas little study has been done upon fennel extract, which is extracted from fennel seeds and not only contains, in addition to the essence, all of the contents of the fennel fruit, but also eliminates the strong smell of the essence, thus making it easier to consume. Various recent studies have pointed out the effect of vitamins such as E and B on menstrual pains; apparently, the anti-oxidant quality of vitamin E can prevent the formation of prostaglandin [14], which decreases dysmenorrhea. Thus, the present study focuses upon a comparison of fennel extract – a new form of this plant, which contains both the essence and all of its nutrients – with vitamin E and a placebo on dysmenorrhea in an effort to present a more effective remedy for this frequently-occurring disorder in women.

Material and Method

This research is a single blind clinical trial. The subjects of the study were all of the female medical students at the Sari Branch of Azad University who suffered, based on multi-dimensional speech criteria, from mild or acute dysmenorrhea. Sample volumes were estimated as 75 individuals based on the test capability – 80 percent – and the range of certainty – 95 percent – and based on the comparison mean in the two groups. Study samples included single, female students with regular menstrual cycles; the lack of any known diseases, allergies to drugs or herbal remedies and the occurrence of stress-creating factors (the divorce or death of parents or family members) in the last 6 months made them qualify for the research. Once the contract with the Sari Branch of Azad University's Research Deputy was finalized, individuals who qualified as study samples were included to their own consent and after they had received sufficient information on the procedures and goals of the study. Prior to starting the treatment, all participants were asked to provide a history of the type, intensity and duration of their dysmenorrhea and other diseases; they were given a questionnaire on their personal information and menstrual characteristics. The intensity of dysmenorrhea was determined by multi-dimensional speech criteria. This system involves four degrees: in Degree 0, menstruation is not painful, and thus does not have any effect on one's life. Degree 1 involves menstruation with slight pain which rarely inhibits one's daily tasks and very little need for painkillers exists. In Degree 2, the pain is moderately intense and affects one's daily tasks, but absence from work or school is unnecessary. In Degree 3, the pain is so strong that the individual is unable to do her daily tasks, and systemic symptoms are acute. [16] Students who had qualified filled out the multi-dimensional speech criteria prior to random categorization. Each student was placed randomly in one of three groups – vitamin E, fennel extract or placebo (each group consisted of 25 individuals) – by means of 1:1:1 randomness and the table of random numbers. 100-unit vitamin E capsules were purchased from local drugstores, and fennel extract capsules called Fenalgin and placebos with completely identical appearances and special coding for researchers were provided by Barij Essence Pharmaceutical Company. Each capsule of Fenalgin contained 46 milligrams of hydro-alcoholic fennel fruit extract mixed with starch. In order to prepare Fenalgin, powdered fennel fruit was turned into extract by means of soaking overnight for three times in 96 percent ethanol and without contact with heat or any solvent; mild temperatures and vacuum was used to collect the extract and mix it with starch. Drugs

and placebos in exactly identical covering with codes only known to the researchers were given to the study samples. Each box of drugs contained 24 capsules or placebos. Each student was instructed to take the pills every 6 hours for 3 days after their menstruation started for two consecutive menstrual cycles. In addition, samples were instructed not to use any other prescribed drugs – even those similar or generically equivalent to the drugs given to them. Also, they were allowed to take the painkillers they regularly used only 2 hours after their pains persisted. At the end, individuals who failed to take the drugs regularly or lost one of the conditions needed to qualify for the research were removed from the study. Eventually, 63 individuals remained in the study (22 in the Fenalgin group, 20 in the vitamin E group and 21 in the placebo group). Having collected the data and fed them into the SPSS software, data analysis was carried out by means of KI-score, Mann Whitney, Kruskal-Wallis, and Friedman tests.

This study was undertaken with the approval of the Mazandran Medical University Ethics Committee (registration letter 90-5) and registered in Iranian Registration Clinical Trial (201106046705N1).

Results

Table 1 shows the individual characteristics and menstrual situations for 3 studied groups of students suffering from dysmenorrhea. As the results imply, no significant difference is seen between the three groups in terms of variables such as age, age of beginning of menstruations, age of occurrence of dysmenorrhea, duration of bleeding, average pads used and the interval between menstrual cycles.

The average intensity of pain in the Fenalgin group decreased from 2.73 ± 0.93 before treatment down to 2.18 ± 0.66 in the first cycle and 1.59 ± 0.66 in the second cycle; these figures were, respectively, 2.95 ± 0.6, 2.55 ± 0.88 and 2.15 ± 0.93 for the vitamin E group, showing a significant statistical difference in the average intensity of pain before and after the consumption of Fenalgin ($P<0.00$) and vitamin E ($P<0.02$).

A comparison of the intensity of pain between the three groups shows a significant difference of between them in the second treatment cycle ($P<0.019$) – the number of individuals suffering no pain in the Fenalgin, vitamin E and placebo group was respectively 50, 25 and 4.8 percent. A separate comparison of each of the treatment groups with the placebo shows a significant statistical difference in the average intensity of pain in the second cycle between the Fenalgin and the placebo group ($P<0.006$). Fenalgin and vitamin E were able to decrease the consumption of painkillers compared to before the treatment; in comparison with the placebo in each group, however, no significant difference is seen.

Discussion

Results show a decrease in the intensity of menstrual pains due to the consumption of vitamin E as compared to before the treatment. In the study carried out by Akhlaghi et al, the average intensity of pain in the second month decreased from 5.18 down to 3.4. [7] Moreover, Ziaei et al found that consuming 500 units of vitamin E in two periods of treatment can lower the intensity of pain from 5.5 to 3.5. [17] Another study by the same researcher showed that the consumption of 400 units of vitamin E for 5 days during 4 periods of treatment decreases the intensity of pain from 5 to 3 in the

Table 1. Characteristics of the students on entry to the trial

Groups Demographic criteria	Fenalgin (M±SD)	Vitamin E(M±SD)	Placebo (M±SD)	p-Value
Age	16/2 ±	14/2 ±	12/2 ±	0/24
Age of menarche	95/0 ±	99/0 ±	33/1 ±	0/16
Duration bleeding	7/1 ±	27/1 ±	77/1 ±	0/13
Age of dysmenorrhe	43/1 ±	77/1 ±	42/1 ±	0/24
Interval cycles	26/2 ±	73/1 ±	89/3 ±	0/42

Table 2. Comparison of mean of intensity Dysmenorrhea before and after treatment

Groups Intensity	Fenalgin(M±SD)	Vitamin E(M±SD)	Placebo(M±SD)	p-Value (Kreskas-Wallis)
Before use	93/0±73/2	6/0±95/2	79/0±86/2	61/0
Cycle 1	66/0±18/2	88/0±55/2	68/0±52/2	23/0
Cycle 2	66/0±59/1	93/0±15/2	67/0±24/2	019/0

Table 3. Comparison of mean of intensity Dysmenorrhea between the Fenalgin and the placebo group

Groups Intensity	Fenalgin(M±SD)	Vitamin E(M±SD)	p-Value (Mann Whitney)
Before use	93/0±73/2	6/0±95/2	53/0
Cycle 1	66/0±18/2	88/0±55/2	11/0
Cycle 2	66/0±59/1	93/0±15/2	006/0

second month and down to 0.5 in the fourth month. [18] In an article review in the January 2005 issue of *American Family Physician*, consuming 2500 units of vitamin E daily for 5 days (2 days prior to menstruating and the first three days of the menstrual cycle) proves much more effective than the placebo. [19] By studying these articles, we found that despite the decrease in the intensity of pain brought about by vitamin E in this study, the lack of significant statistical difference compared to the placebo can be attributed to the time of initiation, the amount of drug and the duration of the treatment period; apparently, the consumption of vitamin E 2 days prior to menstruating or during a longer period (4 months) and with a higher dosage can prove to be much more effective.

Fenalgin also lessens the intensity of pain, and the average difference in the intensity of pain before and after the treatment is considerable. In (Khodakarami's study on the effect of a combination of herbs (fennel, saffron and celery) on dysmenorrhea, the intensity of pain decreased from 5.3 to 3 in the second month and to 0.5 in the third month. [10] Torkzahrai's study also shows a decrease in the intensity of pain from 2.217 before treatment down to 0.364 after the treatment in the second cycle in the fennel extract group [13], which agrees with the results obtained in this study. According to the results of this study, a comparison of the groups treated with placebo implies that the Fenalgin and vitamin E groups prove to be more effective in pain relief than the placebo, which is apparently connected with the potential pain relief mechanism it follows. The effect of fennel may secondarily be due to its spasmolytic nature, which arises from the structural similarity between the anetol existing in fennel and dopamine; through connecting to dopamine, pain relief is brought about. [20] Moreover, studies have shown that fennel extract can control contractions of uterus muscles due to oxytocin and prostaglandin E2, thus enabling it to also relieve pain. [8, 21] Recent studies, furthermore, have proven that the anti-spasm effects of fennel extract arise from its ability to control the contractions caused by acetylcholine and histamine. [4] The only mechanism offered for vitamin E, on the other hand, is controlling the release of arachidonic acid, thus preventing its conversion into prostaglandin through acting on the enzyme phospholipase A2 and cyclooxygenase. [17, 7]

Conclusion

In comparison to vitamin E and the placebo, Fenalgin proved more effective in pain relief, and can therefore be used as a remedy with fewer side effects for treating primary Dysmenorrhea. Further research, however, using higher amounts, more time and longer treatment periods is recommended, however.

Acknowledgments

I would like to express my gratitude toward the Research Deputy of the Sari Branch of Azad University for his financial support of the project, and also toward the students who assisted me in this study.

References

1. *Irvani M. (The effect Zataria Multiflora on primary Dysmenorrhea. Herbal Drugs Journal 2009; 11(2):55-60. [Persian].*
2. *Daniels S, ROBBINS j, West CR,Nemeth MA. Celecoxib in the treatment primary Dysmenorrhea:Result from two randomized, double-blind,active and placebo-controlled,crossover studies.Clinacal Therapeutics 2009.31(6):1192-1208.*
3. *Berek J. Novaks Gynecology,13th ed.USA: Lippincott Williams& Wilkins, 2002:4*
4. *Nazarpoor S, Azimi H. The comparison Fenelin and Mefenamic acid on primary Dysmenorrhea. Journal of Mazaandran University of Medical Sciences 2007; 17(61): 54-61.*
5. *Molazem Z, Alhani F, Anooshe M, Vagharseyyedin S.A. Epidemiology of Dysmenorrhea with dietary habits and exercise. Researchs Journal of Zahedan University of Medical Sciences. 2011; 1393): 41-5.*
6. *O Connell K, Davis A, Westhoff C. Self treatment patterns among adolescent girls with Dysmenorrheal. Pediatr Adosc Gynecol Journal 2006; 19: 285-289*
7. *Akhlaghi F, Zirak N, Nazemian SH. The effect vitamin E on primary Dysmenorrhea.Hayat Journal 2009; 15(1): 13-19.*
8. *Modarsnezhad V, Motamedi B, Asadipoor M. The comparison Fennel and mefenamic acid on Dysmenorrhea. Journal of Rafsanjan University of Medical Sciences 2006; 5(1): 1-6.*
9. *Kermanshahi S, Hosseinzadeh Sh, Elhani F.The effect of the group counseling program on the status dysmenorrhea, dietary condition and exercise in Shahrreyar girls high school. Journal of Zanjan University of Medical Sciences 2008; 16(65):49-60.*
10. *Khodakarami N, Moatar F, Ghahari A,Soloki S. The effect of Iranian Herbal Drug on primary Dysmenorrea: A clinical controlled trial. J midwifery & women health 2009; 54(5): 401-404*
11. *Nagata C, Hirokawa K.Shimizu N, Shimizu H. Associations of menstrual pain with intake of soy,fat and dietary fibr in Japanese women. European Journal of clinical Nutrition2005; 59:88-92*
12. *Azgeli G, Goli M, Moatar F, Valai N. The comparison zangebil, mefenamic acid and ibubrofen on dysmenorrhea. Journal of Research in medicin 2008; 31(1):61-5. [Persian].*
13. *Tork zahrai Sh, Akhavanamjadi M, Mojab F, Alavimajd H. The effect Foeniculum vulgare on primary dysmenorrhea.Journal of productive and infertility 2007:45-51. [Persian].*
14. *Zakeri M, Ziaei S, Kazemnezhad A. The effect vitamin E on gastrointestinal symptoms with primary dysmenorrheal Journal Ardebil medical science university.2006; 6(4):374-378. .*
16. *Wall PD, Melzack R. Text book of pain. 5th ed. London: hurchill Livingstone; 1999.786-79*
17. *Ziaei S, Zakeri M. Kazemnezhad A. A randomized controlled trial of vitamin E in treatment of primary dysmenorrhea. BJOG2004; 112(4): 466-9*
18. *Ziaei S, Zakeri M. Kazemnezhad A. A randomized controlled trial of vitamin E in treatment of primary dysmenorrhea. BJOG200; 108:1181-83*
19. *French l. Dysmenorrea. Am Fam physician 2005; 71(2): 285-91*
20. *Decherney A.H. Current obstetrics & gynecologic diagnosis & treatment, 9th ed. New York: Mc Grow-Hill; 2003*
21. *Ostad SN, Soodi M, Shariffzadeh M, Khorshidi N, Marzban H. The effect of Fennel essential oil on uterine contraction as a model for dysmenorreal, pharmacology and toxicology study. J Ethnopharmacol 2000; 76:299-304*
22. *Farahmand M, Zahediasl S, Abaspoor Z, Rasekh A. The effect vitamin E and ibubrofen on mount,duration and interval bleeding in dysmenorrheal women. Journal of Medicin kosar 2009; 14(1): 49-52.*

Corresponding Author
Gholamitabar Tabari M,
Sari,
Mazandaran,
Iran,
E-mail: maryam_tabari@yahoo.com

Autonomy and submissive behaviour among students at the college of nursing

Leman Senturan[1], Selmin Kose[2], Necmiye Sabuncu[2], Fatma Ozhan[2]

[1] Halic University School of Health Sciences, Istanbul, Turkey,
[2] Halic University School of Nursing, Istanbul, Turkey.

Abstract

Introduction and Aim: This research was conducted to define and analyze the levels of and relationship between autonomy and submissive behavior among nursing students.

I**nstrument and Method:** The research sample consisted of 229 students who agreed to participate in the study. Three instruments were utilized to collect the data: student information forms, Submissive Behavior Scale, and the Autonomy Scale. Average and percentage distributions, Mann-Whiney U test, the Kruskal-Wallis Test, Tukey's Test and the Spearman Correlation Analysis were used to evaluate the data collected at the end of the academic year.

Findings: The students' average score on the autonomy scale was 66.16 ± 19.46 (min: 14 max: 119). The average score on the scale of submissive behavior was 32.87± 7.54 (min:16 max: 62). A meaningful difference was found in the students' average total scores for autonomy according to class (x^2 =16.261 p=0.001) (p<0.01). No meaningful correlation was found between the average scores on the autonomy scale and the submissive behavior scale (r=0.14).

Result: Nursing students are expected to have a high level of autonomy and a low level of submissive behavior. Improvement in these concepts during nursing education may play an important role in students' nursing caregiver role.

Keywords: Nursing students, Autonomy, Submissive Behavior

Introduction And outline

Autonomy

The word autonomy is derived from the Greek *auto* (self) and *nomos* (law) and means self-management (1). Autonomy, which emphasizes the need for freedom and the achievement of specific goals for individuals, is defined as a means of increasing and protecting individuals' personal rights and independence (2,3). Furthermore, autonomy includes self-management, independence, privacy and personal preference in behaviors and manners (1,4,5,6,7). Individuals who have high autonomy are generally successful and able to achieve their goals, control their environment and shape their activities (3).Autonomy is an important concept in nursing. In healthcare, respect for autonomy is the basis for the client's right to self-determination (8). Historically, descriptions of nurses as obedient and adaptable have been obstacles to increasing their professional autonomy (4). Autonomy in nursing has also been affected by changing roles and has primarily been discussed theoretically. Applying these discussions to practice requires nurses to be able to take the responsibility and authority to make decisions (1). In broad terms, nursing autonomy involves not only an individual's independence but also the ability to make nursing decisions (8). Autonomous individuals can implement their decisions without requiring permission (9). The philosophy of nursing requires that nurses should have the autonomy to control situations that affect the individuals under their care (8). Nursing education should allow nurses to use their autonomy (9) because education is the primary means of developing occupational autonomy. The literature indicates that education and autonomy are positively and powerfully correlated (10). Increasing nurses' autonomy is a topic of management and professional development research, which can broadly apply to the undergraduate level. However, in a study conducted among nursing students have shown that nursing students are less autonomous than are other college students. Nursing students often exhibit obedient and submissive features and do not tend to demand autonomy and initiative in their positions (11).

Submissive Behavior

Submissive behavior, which is an undesirable type of behavior in nursing, involves a person denying his/her own feelings, needs and thoughts, ignoring his/her rights or allowing another person to treat him/her unfairly (12). In other words, submissive behavior involves a set of personality traits in which submissive people aim to avoid hurting other people's feelings, attempt to satisfy everyone, have difficulties expressing negative thoughts, require approval and are unable to express their thoughts and assert their rights (13). The concept of submissive behavior (or "obedience") may be mistaken for respect and may be used in place of it (14). Whereas obedience implies obeying or submitting, respect allows one to behave attentively, carefully and temperately to those who are elder, helpful, valuable or superior and to avoid disturbing others (15). It is clear that these two concepts have opposite meanings. Both of these concepts are important to personal relationships. However, it is important for the predominant concept to be "respect" rather than "obedience" or "submissive behavior" (16). Individuals and societies cannot be improved if "obedience" dominates in interpersonal relationships (14). A person who acts submissively cannot act freely and feels less valuable or important than others. Submissive people take blame even if the event in question is not their fault and listen silently to what is said about them. Even if they believe differently, they cannot express their thoughts and have difficulty saying "no". They cannot defend themselves against blame, unfair treatment, insults, or interruptions. Submissive people attempt to behave warmly toward others even if they do not want to, and they apologize for small mistakes. If "respect" is predominant in a relationship, individuals are free, independent, creative, and productive; they think, object, and offer alternatives (16). Hence, submissive behavior is a concept that negatively affects personal development (12,16).

Environmental factors often determine the occurrence of submissive behaviors. There are different opinions regarding these environmental factors. Some arguments suggest that that the childhood family environment is the primary determinant, whereas others assert that the individual's current social environment and perceptions are the main determinant. Many researchers think that individuals exhibit submissive behavior because they were treated authoritatively, strictly and oppressively by their parents (17). In addition to parents, educators' approaches and types of communication with children are important. Teachers' approaches can maintain or stop submissive behavior (18).

University education generally begins around age 20 in most countries. In addition to career training, a university education contributes to the development of personality and self-confidence among young people. Nursing is a job that requires professional individuals who are modern, informed, curious, rational, decisive, and effective (19). Nursing programs attempt to encourage their graduates to be open-minded, open to criticism and improvement, competitive, and research-oriented and to have strong interpersonal communication skills (20). Members of this profession should develop autonomy by the end of the nursing education. Nurses who have autonomous characteristics will effectively participate in fulfilling occupational criteria (3). In contrast, individuals who display submissive behavior cannot express their feelings freely and encounter difficulties. They do not show leadership or entrepreneurial skills, and they avoid taking responsibility and making changes in their lives. Their self-esteem is low. In addition to having comprehensive knowledge, nurses are expected to have skills such as leadership, research and good communication. In addition, nurses who are enterprising and not submissive can make good connections with patients, care for patients and their relatives with integrity, support the rights of patients and show leadership in the workplace. In other words, nurses should not show submissive behavior (12,19).

Accordingly, this research examined levels of autonomy and submission among nursing students and whether there is a correlation between these levels. This research was conducted in two stages. In the second stage, first-year students will observe throughout their education and the results will evaluate after four year.

Method And Materials

The scope of this study comprised 244 nursing students (67 first-year; 63 second-year; 59 third-year; 55 senior students) who received education

at Halic University School of Nursing during the 2008-2009 academic year. The study sample included 229 students. The sampling choice was not preferred; it was based on voluntary participation and attempted to reach the entire student population. With the exception of five students in the pilot study and ten students who declined to participate or completed the data collection tools incorrectly, the entire population was reached.

Tools: Three tools were used to collect data: the "Student Information Form", "Autonomy Scale" and "Submissive Behaviour Scale".

Student Information Form

The Student Information Form consisted of 19 questions and was prepared by the researchers in accordance with the literature. The information form consisted of independent variables regarding decision making, family and demographic characteristics.

Autonomy Scale

This study used the autonomy section of the "Sociotropy–Autonomy Scale", which was developed by Beck et al (1983) and translated into Turkish by Şahin et al (21,22). The autonomy section consisted of 30 items that asked, "How much does this describe you?" Answers were provided on a 5-point scale ranging from "It does not describe me at all " to "It describes me perfectly". There were three sub-dimensions of the scale: individual achievement, independence and preference for solitude. The 12-item Individual Achievement Autonomy sub-dimension included questions about autonomy, the 12-item Independence sub-dimension examined independent decision making, and the 6-item Preference for Solitude reflected the ability to be independent and self-sufficient. The total score for the 30-item Autonomy scale was obtained by calculating the scores of the sub-dimensions. The maximum points for the overall evaluation and the subdimensions of "individual achievement", "independence" and "preference for solitude" were 120, 48, 48 and 24, respectively. High scores showed a high level of autonomy. The average response time was 15 minutes. The Cronbach's alpha coefficient was 0.81 for the student group in a reliability study conducted by Şahin et al (21,22). In our study, the Cronbach's alpha coefficient was 0.89.

Submissive Behaviour Scale

The Submissive Behaviour Scale was developed by Gilbert and Allan in 1984. Originally named the Submissive Acts Scale, the scale was translated into Turkish by Sahin et al in 1992 (21,22). The scale consists of 16 items, and individuals determine how well the items describe them. The responses on the scale are "does not describe me at all", "slightly describes me", "describes me well.", "describes me very well", and "describes me perfectly". The answers are evaluated with scores ranging between 1 and 5. The minimum and maximum scores that can be obtained are 16 and 80, respectively; there is no break point. High scores show that an individual has more submissive behavioral characteristics (21,22). The internal consistency Cronbach's alpha coefficient for the original scale is 0.89. In Sahin's adaptation, Cronbach's alpha coefficient was 0.74 (22). The alpha coefficient in our study was 0.74.

Data Collection

After receiving permission from school management, the pre-application was conducted with five students. At the end of the academic year, the scales were administered to students. Approximately 30 min were needed to administer the scale. The students who completed the pre-application were removed from the study.

Ethical Consideration

Initially, an information form that explained the aim and content of the study was sent to the management that collected the data, and approval was obtained for the ethical suitability of the research. At a convenient time for the management, the aim of the research and the participants' roles in the study were explained to the students. The students were told that they were free to choose to participate in the research. The students verbally agreed to participate.

Data Analysis

Data evaluation was conducted with SPSS statistical analysis packaged software. Descriptive statistical methods, such as frequency distribution, mean, standard deviation, Kruskal-Wallis variance analysis for comparing more than two groups and Spearman Correlation analysis to observe the relationships between numeric variables were used in

the evaluation. The further analysis of the significance between more than two groups was evaluated by Tukey's test. The level of significance was set at $p<0.05$ in the analysis.

Findings

The socio-demographic characteristics of the participants are shown in Table 1. Most of the students' mothers (35.8% n=82) graduated from primary school, and the fathers graduated from high school (35.4% n=81). Of the participants, 93.9% (n=82) had social security, 58.5% (n=134) had an adequate level of income and a family that was democratic (74.2%; n=170), concerned (72.9%; n=167), and core- parents and children (86%; n=197). Additionally, 69% of the nursing students made decisions with all family members and considered others' opinions, and 48.9% consulted their mothers on decisions. The average scores obtained by the students on the scales of autonomy and submissive behavior are shown in Table 2. The average total scores on the autonomy scale for first-year, second-year, third-year, and senior students were 71.06±15.47; 69.15±19.62; 66.09±20.70; and 57.41±19.80, respectively. For all nursing students, the average score was 66.16±19.46. According to the students' class, when comparing the students' average scores on the autonomy scale, a significant difference was found between the individual achievement ($x^2=14.9$ $p=0.002$) and independence ($x^2=17.545$ $p=0.001$) sub-dimensions and the average score of the total scale ($x^2=16.261$ $p=0.001$) ($p<0.01$). The average score for submissive behavior for all students was 32.87±0.54 (min:16 max:62). There was no statistically significant difference between the distribution of average scores on the submissive behavior scale by classes ($x^2=1.908$ $p=0.592$). Table 3 shows the relationship between the means of the scores obtained on the autonomy scale and the submissive behavior scale. A significant positive correlation was found between the sub-dimension of independence and submissive behavior ($r=0.173$ $p=0.009$). The other significant positive correlation was between the average autonomy score and submissive behavior score ($r=0.141$ $p=0.033$).

Discussion

This research was conducted as a pilot study to analyze the relationship between nursing students' autonomous characteristics and their level of submissive behavior. This study had two limitations. First, a descriptive study was used to examine the nursing students' current situation; they were not observed during their 4-year education. However, the second part of the study, which began in the 2008-2009 academic year, is ongoing. Thus, it is possible to observe the students' development and evaluate the results longitudinally. The second limitation is that this study did not examine the factors believed to affect autonomous or submissive behavior. This study examined autonomous and submissive behaviors of nursing students who displayed similar success on university entrance exams and received the same education. The scores obtained by the nursing students on the autonomy scale varied from 14 to 119, with an average score of 66.16±19.46. Considering that the range of possible scores on this scale is 0–120, the nursing students in this study obtained scores that reflected the "upper intermediate" level of autonomy (Table 2). Karagözoğlu (2009) found the average of general autonomy scores to be 83.03±14.51 in a study that evaluated nursing students' autonomy in the 2003-2004 academic year (23). Additionally, Kaya et al (2006) found an average general autonomy score of 77.25±14.45 in a similar study (3). In Turkey, the results of various studies evaluating students' levels of autonomy are similar. However, the average score found for nursing students in other studies is higher than the scores in the current study. This situation can be explained by the fact that colleges that offer a nursing curriculum have differing scores required for acceptance. The literature shows that studies that directly evaluate the autonomy of nursing students are limited. Studies have commonly compared the autonomy of nursing students and other student groups. The common point in these studies is that the autonomy level of nursing students is lower than that of other students (23). For instance, Boughn's (1988) study, which compared the autonomy levels of nursing students and other students in other fields, such as economics, education, linguistic determined that education and nursing students

had the lowest levels of autonomy (24). Similarly, nursing students' level of autonomy was lower in a study of nursing students and other health areas conducted by Karagözoğlu (2008) (25). Another remarkable result of this study was the finding of students' autonomy levels according to their class. For both the sub-dimensions and the average of the total scores, the average scores of senior nursing students were lower than those of other classes, and a decrease was observed from first-

Table 1. Socio-demographic characteristics of the students (N=229)

	I.Class* (n=64)		II.Class * (n=57)		III.Class * (n=53)		IV.Class * (n=55)		Total* (n=229)	
	n	%	n	%	n	%	n	%	n	%
Mother's education level										
Literacy	4	6.3	3	5.3	8	15.1	3	5.5	18	7.9
Graduated from primary school	20	31.3	23	40.4	19	35.8	20	36.4	82	35.8
Graduated from junior high school	13	20.3	6	10.5	8	15.1	10	18.2	37	16.2
Graduated from high school	18	28.1	19	33.3	12	22.6	12	21.8	61	26.6
Graduated from university	9	14.1	6	10.5	6	11.3	10	18.2	31	13.5
Father's education level										
Literacy	3	4.7	2	3.5	2	3.8	1	1.8	8	3.5
Graduated from primary school	17	26.6	13	22.8	13	24.5	17	30.9	60	26.2
Graduated from junior high school	8	12.5	8	14.0	5	9.4	6	10.9	27	11.8
Graduated from high school	20	31.3	20	35.1	21	39.6	20	36.4	81	35.4
Graduated from university	16	25	14	24.6	12	22.6	11	20	53	23.1
Family's income										
Good	26	40.6	20	35.1	17	32.1	23	41.8	86	37.6
Sufficient	36	56.3	33	57.9	35	66	30	54.5	134	58.5
Adequate	2	3.1	4	7	1	1.9	2	3.6	9	3.9
Family type										
Core family	54	84.4	50	87.7	44	83	49	89.1	197	86
Large family	9	14.1	6	10.5	7	13.2	5	9.1	27	11.8
Separated family	1	1.6	1	1.8	2	3.8	1	1.8	5	2.2
Attitude toward the children of the family										
Very concerned	20	31.3	15	26.3	14	26.4	13	23.6	62	27.1
Concerned	44	68.8	42	73.7	39	73.6	42	76.4	167	72.9
Family composition										
Authoritarian	13	20.3	16	28.1	19	35.8	11	20	59	25.8
Democratic	51	79.7	41	71.9	34	64.2	44	80	170	74.2
The person who makes decisions in the family										
Father	4	6.3	5	8.8	10	18.9	3	5.5	22	9.6
Mother	1	1.6	3	5.3	-	-	1	1.8	5	2.2
Parents together	10	15.6	13	22.8	10	18.9	11	20	44	19.2
All family together	49	76.6	36	63.2	33	62.3	40	72.7	158	69
The person who is consulted during decision making										
Mother	34	53.1	21	36.8	25	47.2	32	58.2	112	48.9
Father	8	12.5	11	19.3	5	9.4	7	12.7	31	13.5
Friend	4	6.3	6	10.5	6	11.3	3	5.5	19	8.3
Sister or brother	9	14.1	8	14	4	7.5	6	10.9	27	11.8
Mother or father	4	6.3	6	10.5	5	9.4	7	12.7	22	9.6
Form of decision making Do not consider others' opinions	15	23.4	15	26.3	9	17	16	29.1	55	24
Always consider others' opinions	45	70.3	39	68.4	40	75.5	34	61.8	158	69
Prioritize others' opinions	4	6.3	3	5.3	4	7.5	5	9.1	16	7
Age	21.49± 1.65 (16-23)									

***** *The column was a percentage.*

year to senior-year students. Moreover, this difference was statistically significant for the individual achievement and independence sub-dimensions and the average total score (p<0.001) (Table 2). A similar result was observed in Karagözoğlu's study (2009) (23). Although the findings were not significant, the study by Karagözoğlu (2009) showed that the autonomy levels of nursing students decreased through senior class. The decrease in average scores can be interpreted in different ways. Do students' thoughts and actions become more limited with increased professional responsibility? Does the consistent decrease in the dimensions of individual achievement and independence reflect this limitation? The lack of an increase in nursing students' autonomy levels throughout their educational problem has two implications. First, the curriculum should be examined to determine whether it is effective for improving autonomous behavior. Second, changes in autonomy should be evaluated through longitudinal studies. Nursing students are expected to graduate as productive, creative, autonomous, optimistic, knowledgeable members of the profession rather than as individuals who exhibit submissive behaviors. This goal is necessary for nurses to make rational and responsible decisions in patient care, to apply these decisions and to defend patients' rights (19,26). The examination of the features of submissive behavior is important to determine deficiencies related to students' autonomy. When students' submissive behaviors were evaluated, the average scores by class were similar (32.87±0.54) (Table 2). Considering the minimum and maximum scores (16-80), this value seems low. There was no statistically significant difference between the mean scores according to students' year in school (x^2=1.908 p=0.592; Table 2). The result in table 1 that 7% of the students prioritized others' opinions indicates this finding (Table 1). In the national nursing literature, only one study evaluated students' submissive behaviors (12). In that study, the scores of nursing students on the "Submissive Behaviour Scale" were found to be as low as 34.4 for first–year students, 31.6 for second-year students, 32.5 for third-year students and 29.3 for the senior class (12). In a study by Mete and Çetinkaya (2005), a significant decrease in autonomy was found from the first-year class to the senior class (p<0.05). In a study by Kaya (2004) of medical students, female students had lower levels of submissive behavior. However, their total mean scores were

Table 2. Autonomy and submissive behavior score means according to students' current year in school

Scales		mean ± ss (min-max) according to school year					*
		I. Class (n=64)	II. Class (n=57)	III. Class (n=53)	IV. Class (n=55)	Total (n=229)	
Autonomy	Individual achievement	30.34±7.64 (6-46)	29.49±8.44 (10-48)	28.20±8.79 (12-44)	24.36±8.63 (5-40)	28.20±8.61 (5-48)	X^2=14.906 **p=0.002**
	Independence	27.67±6.70 (15-41	27.08±8.12 (13-47)	25.33±8.65 (9-41)	21.85±7.85 (5-40)	25.58±8.08 (5-47)	X^2=17.545 **p=0.001**
	Preference for solitude	13.04±4.67 (2-23)	12.57±4.88 (3-24)	12.54±5.06 (3-23)	11.20±4.84 (3-24)	12.37±4.87 (2-24)	X^2=6.041 p=0.110
	Total	71.06±15.47 (34-104)	69.15±19.62 (28-119)	66.09±20.70 (24-104)	57.41±19.80 (14-102)	66.16±19.46 (14-119)	X^2=16.261 **p=0.001**
Submissive Behaviors		32,93±7,51 (22-56)	33.57±8.38 (16-58)	33.52±7.77 (20-62)	31.45±6.35 (19-49)	32.87±7.54 (16-62)	X^2=1.908 p=0.592

**Kruskal Wallis Test p<0.01 * Tukey Test*

Table 3. Relationship between autonomy and submissive behavior scores of students

Scales		Submissive Behavior	
Autonomy	Individual achievement	r=0.088	p=0.186
	Independence	r=0.173	**p=0.009****
	Preference for solitude	r=0.126	p=0.057
	Total	r=0.141	**p=0.033***

** p<0.05 ** p<0.01*

higher than our findings (27). Considering the findings in the current study and other studies, the low level of submissive behavior can be considered positive. However, nursing students should have similar or lower scores than other health science students; this is urgent in terms of nursing philosophy and professional values. A nurse who thinks critically, investigates and cares for patients in a traditional and progressive role should not perform submissive behaviors (9,19).In our country, nursing students generally do not have a high level of income, and most prefer this profession because employment opportunities are high. Nursing students are a group that is at risk for submissive behavior because they are mostly female, do not have significant loyalty to the field, have a low socio-economic level and have family with a low level of education. The sample in this study consisted of students with these features (Table 1). When developing a nursing curriculum, these characteristics should be considered. In contrast to submissive behavior, autonomy is an indication of individuality, independence, self-control, and the ability to reach goals and solve problems (28). As effective members of a healthcare group, not only to implement doctors' orders but also to be creative, responsible, curious, collaborative and decisive are expected from nurses. Nurses should show autonomous and confident behaviors rather than submissive behaviors when performing these roles. Submissive behaviors affect nurses' decision-making abilities and autonomy and may have a negative effect on patient care and nurses' professional status (12).When the relationship between students' level of autonomy and submissive behavior was compared, there was a positive correlation between the average scores on the autonomy scale and submissive behavior (r=0.141; p=0.033) (Table 3). This finding of a positive correlation between the average scores was an unexpected result. The findings may be affected by the fact that levels of autonomy decreased from the first-year class to the senior class, and submissive behaviors did not change significantly. However, our findings show that students wanted to behave autonomously, but understandings of strict discipline continue to influence our educational system. In the previous studies that compared nursing students with other types of students, nursing students had higher levels of obedience but lower levels of autonomy, entrepreneurship, and independence (24,25). Therefore, there is a need to strengthen these concepts in nursing curricula. Furthermore, longitudinal studies are needed.

Result

Autonomy and submissive behaviors are crucial concepts in nursing education. This study found that nursing students had low levels of autonomy and submissive behavior. Consequently, research on submissive behaviors, autonomy and contributing factors would offer an opportunity to implement an education program that could improve students' autonomy and decrease their submissive behaviors.

References

1. *Karagözoğlu Ş, Kangallı P. Autonomy levels among nurses:professional-ınstitutional factors that affect autonomy. Turkiye Klinikleri J Med Sci 2009; 29 (5): 1085-1097.*
2. *Kabakçı E. Üniversite öğrencilerinde sosyotropik/ otonomik kişilik özellikleri, yaşam olayları ve depresif belirtiler. Sociotropic/autonomic personality characteristics, life events and depressive symptoms among university students. Turkish Journal of Psychiatry 2001; 12 (4): 273-282. (in Turkish)*
3. *Kaya N, Aştı T, Acaroğlu R, Kaya H, Şendir M. Hemşire öğrencilerin sosyotropik-otonomik kişilik özellikleri ve ilişkili faktörlerin incelenmesi. Determination of Sociotropic /Autonomic Personality Characteristics and Related Factors among Nursing Students. Cumhuriyet University Journal of School of Nursing. 2006; 10 (3): 1-11. (in Turkish)*
4. *Seren, Ş. Hemşirelerin Otonomi Seviyelerinin Belirlenmesi. Determination of The Nurses Autonomy Levels. The Institute of Health Sciences. Department of Nursing. Master Thesis. Dokuz Eylül University: 1998 (in Turkish)*
5. *Ballou KA. A concept analysis of autonomy. J Prof Nurs 1998; 14 (2): 102-10.*
6. *Berman A, Snyder S, Kozier B, Erb G. Values, Ethics and Advocacy In: Kozier B, Erb G, (Eds), Kozier & Erb's fundamentals of nursing: concepts, process, and practice. 8th ed, New Jersey; Pearson Ed. Inc; 2002:80-97.*
7. *Potter PA, Perry, GA. Fundamentals of nursing: concepts, process, and practice. 4th ed. Missouri; Mosby camp; 2003: 313-324.*

8. *Craven RF, Hirnle CJ. Fundamentals of Nursing; Human Health and Function. 6th ed. Philadelphia; Wolters Cluwer Health/Lippincott Wiliams&Wilkins; 2008.*

9. *Lewis FM, Sterling E. Autonomy in Nursing. Ishikawa Journal of Nursing 2006; 3 (2): 1-5.*

10. *Wade GH. Professional nurse autonomy: concept analysis and application to nursing education. Journal of Advanced Nursing 1999; 30 (2): 310-318.*

11. *Dwyer DJ, Schwartz RH, Fox ML. Decision making autonomy in nursing. Journal of Nursing Administration 1992; 22 (2); 17-23.*

12. *Mete S, Çetinkaya E. Probleme Dayalı Öğretim Modelinin Hemşire Öğrencilerin Boyuneğici Davranışlarına Etkisi. The Effect of Problem Based Leaming to Nursing Students' Submissive Acts. Zonguldak Sağlık Yüksekokulu Dergisi, 2005; 1 (3): 49-55. (in Turkish)*

13. *Gilbert P, Allan S. Assertiveness, Submissive Behaviour and Social Comparison. The British Journal of Clinical Psychology. 1994; 33: 295-306.*

14. *Yıldırım İ, Ergene T. Lise son sınıf öğrencilerinin akademik başarılarının yordayıcısı olarak sınav kaygısı, boyun eğici davranışlar ve sosyal destek. Social support, submissive acts, and test anxiety as predictors of academic achievement among high school students. Hacettepe Üniversitesi Eğitim Fakültesi Dergisi 2003; 25: 224-234. (in Turkish)*

15. *Şenturan L, Ecevit Alpar Ş. Hemşirelik Öğrencilerinde Eleştirel Düşünme. Critical Thinking in Nursing Students. Cumhuriyet University Journal of School of Nursing 2008; 12 (1): 22-31. (in Turkish)*

16. *Yıldırım İ. Lise öğrencilerinde boyun eğici davranışların yaygınlığı. Prevalence of submıssıve acts among hıgh school students. Hacettepe Üniversitesi Eğitim Fakültesi Dergisi, 2004; 26: 220-228. (in Turkish)*

17. *Tekin M, Filiz M. Beden eğitimi ve spor yüksekokullarının antrenörlük eğitimi ve spor yöneticiliği bölümlerinde öğrenim gören öğrencilerin umutsuzluk ve boyun eğici davranış düzeylerinin çeşitli değişkenlere göre incelenmesi. Analysis of humiliating and hopelessness behaviour level of stududents who attend at education of training and sport management department of physical education and sport faculty in respect of different values. Spormetre:Beden Eğitimi ve Spor Bilimleri Dergisi 2008; 6 (1): 27-37. (in Turkish)*

18. *Dönmez B, Demirtaş H. Lise öğretmenlerinin boyun eğici davranışa yönelik algıları. Lise teachers' perceptıons regardıng submıssıve acts. Kastamonu Eğitim Dergisi 2009; 17 (2); 445-456. (in Turkish)*

19. *Özkan İA, Özen A. Öğrenci hemşirelerde boyun eğici davranışlar ve benlik saygısı arasındaki ilişki. The Relation Between Submissive Behaviours and Self Esteem State Among Nursing Students. TAF Prev Med Bull. 2008; 7 (1): 53-58. (in Turkish)*

20. *Erbil N, Yılmaz A. Hemşirelik öğrencilerinin meslek seçme kararlarını ve bakış açılarını etkileyen faktörlerin belirlenmesi. The determination of the factors that nursing students' decisions to choice vacotional and perspectives Hemşirelik Forumu 2008; 11 (1): 47-52. (in Turkish)*

21. *Öner, N. Examples of psychgological tests used in Turkey. Expanded second edition. Boğaziçi Ünv. Publishing 2008.*

22. *Şahin NH, Ulusoy MS, Şahin N. Sociotropy – Autonomy Scale. In: Savaşır I, Şahin N.H. (Eds.), Tools Frequently Used in Cognitive and Behavioral Therapy. Turkish Psychologists Society Publication, Ankara, 1997: 54–60 (in Turkish).*

23. *Karagözoğlu Ş. Nursing students' level of autonomy: A study from Turkey. Nurse Education Today 2009; 29: 176–187.*

24. *Boughn S. A lack of autonomy in the contemporary nursing student: a comparative study. Journal of Nursing Education 1988; 27 (4): 150–155.*

25. *Karagözoğlu Ş. Level of autonomy of Turkish students in the final year of university baccalaureate degree in health related fields. Nurs Outlook 2008; 56 (2): 70-7.*

26. *Dil Derneği Yayınları (2005) Türkçe Sözlük, Dil Derneği Yayınları No 9. Ankara*

27. *Kaya, M., Güneş, G., Kaya, B., Pehlivan, E. Tıp fakültesi öğrencilerinde boyun eğici davranışlar ve şiddetle ilişkisi.Submissive behaviors and its relationship with violence among students of medical school Anadolu Psikiyatri Dergisi, 2004; 5: 5-10. (in Turkish).*

28. *Keskin, G., & Yıldırım, G.Ö. Yapısalcı yaklaşım normlarında üniversite öğrencilerinin problem çözme, otonomi, çoklu zeka durumlarının değerlendirilmesi. İnönü Üniversitesi Eğitim Fakültesi Dergisi, 2008; 9(16): 67–88. (in Turkish).*

Corresponding author
Leman Senturan,
Halic Universitesi Saglık Bilimleri Yuksekokulu,
Mecidiyekoy,
Istanbul,
Turkey,
E-mail: lemansenturan@halic.edu.tr

Chemotherapy plus hematopoietic growth factors for refractory paroxysmal nocturnal hemoglobinuria: diminishing PNH clone and stimulating hematopoisis

Xi-feng Dong, Rong Fu, Hua-quan Wang, Zong-hong Shao

Department of Hematology, General Hospital, Tianjin Medical University, People's Republic of China

Abstract

To investigate the efficacy and safety of chemotherapy plus growth factors in patients with refractory and relapsed PNH.10 patients were enrolled in this study. These patients receivd either DAG or HAG (DNR 40mg/d, $d_{1\text{-}2}$; 20mg/d, d_3 or HHT 2-3mg/d, d1-5; Ara-C 100mg/d, d1-5 plus G-CSF) regimen chemotherapy. The primary end points were the improvement of hemoglobin level, decreased proportion of PNH clone and dosage of corticosteroid. Biochemical indicators of intravascular haemolysis and adverse events were also assessed. All patients responded well. Elevation of hemoglobin from (58.1±12.12) g/L to (90.20±21.55) g/L (P=0.000) was achieved in the 10 patients. The dosage of corticosteroid decreased significantly from (45.84±19.05)mg to (13.00±6.75) mg (P=0.000). $CD59^-$ and $CD55^-$ granulocytes in peripheral blood decreased significantly in 8 patients [(68.25±26.05)% vs (59.53±24.60)%, P=0.007 for $CD59^-$ granulocytes; (81.47±26.13)% vs (68.14±26.53)%, P=0.003 for $CD55^-$ granulocytes]. Indicators for haemolysis also improved. Most common adverse events were infection, nausea, vomiting and fatigue. DAG/HAG regimen chemotherapy was an effective, safe and promising therapy for PNH patients.

Key words: PNH; Chemotherapy; Anemia; Immunology

Introduction

Paroxysmal nocturnal hemoglobinuria (PNH) was a clonal hematopoietic stem cell disease originating from a somatic mutation of the X-linked PIG-A gene. PIG-A mutations can cause an early block in the synthesis of glycosylphosphatidylinositol (GPI) anchors, which gather many proteins to the cell surface. Two of these proteins, CD55 and CD59, were complement regulatory proteins; the absence of these proteins was fundamental to the pathophysiology of the disease[1,2]. CD59 blocked the formation of the terminal complement complex on the cell surface, thereby preventing erythrocyte lysis and in vitro platelet activation. CD55 inhibits C3 convertases and CD59 blocks formation of the membrane attack complex (MAC) by inhibiting incorporation of C9 into the MAC. The loss of complement regulatory proteins renders PNH erythrocytes susceptible to both intravascular and extravascular haemolysis[3]. Expansion and differentiation of the PIG-A mutant stem cell lead to clinical manifestations of the disease, including anemia, hemoglobinuria, and complications related to the presence of plasma free hemoglobin[4].

As to the treatment for PNH, corticosteroids was the classic drug, improving hemoglobin levels and reducing haemolysis in some patients, but with long-term toxicity and limited efficacy[5]. Then based on the pathophysiology of PNH, Eculizumab was developed, directing against the terminal complement protein C5. Some clinical trials showed that the new target drug was promising, however, it still on the way with its own drawbacks, such as the expansion of PNH clone that can cause ultimate severe haemolysis onset[6]. From another view, eradication or diminishing of deficient cells may cure the disease. Evidences have been provided by the success of allogeneic bone marrow transplantation (BMT) for PNH[7]. In light of the GVHD and GVH related to BMT and principle of eradication or diminishing of PNH clone, chemotherapy may be a promising treatment for PNH. We have employed OAP, CP, CMAP and MP regimen chemotherapies for

PNH inhibiting lymphocytes mainly, however, the effect was not as good as we expected[8]. Therefore, DA or HA regimen chemotherapy was used to treat relapsed and refractory PNH patients between 2006 to 2010, aiming at investigating whether the regimens could diminish PNH clone, stabilize hemoglobin level and reduce the dosage of corticosteroids. Moreover, safety was also assessed.

Methods

Patients

10 patients from 2006 to 2010 diagnosed as PNH according to the standard criteria were enrolled in this study. They were 4 males and 6 females with age range from 11-51 years, and the median age was 33.4 years. All the enrolled patients had been treated with corticosteroid and shown some severe side effects of corticosteroid, such as diabetes, hypertension, gastrointestinal bleeding and so on. The characters of chemotherapy were illustrated to the patients clearly and all patients gave their written informed consent. Patients with an active bacterial or fungal infection, or a history of lung or heart diseases and those who had undergone bone marrow transplantation were excluded.

Chemotherapy regimens

DA or HA was the regimens patients received, the detail for which was DNR 40 mg/d, d_1 or d_{1-2}; 20 mg/d, d_{2-3} or d_3; Ara-C 100mg/d, d_{1-5} or d_{1-7} or HHT 2-3 mg/d, d_{1-5}; Ara-C 100 mg/d, d_{1-5}. The chemotherapy regimens were administrated intravenously every 4 weeks for one to five cycles. Concomitant administration of erythropoietin, G-CSF, immunosuppressive drugs, vitamin E , sodium bicarbonate, corticosteroids in decreased dosage, iron supplements, and folic acid were permitted throughout the chemotherapy.Other supportive therapies were also given, including isolated wards, transfusion when necessary, antibiotics when infection occurred, vital signs and blood routine test and other treatment aiming at alleviating symptoms.

Clinical Efficacy

The primary end points included stabilization or elevation of hemoglobin levels; proportion of PNH clone and the dosage of corticosteroid. Other end points included transfusion independence; haemolysis measured by TBIL and IBIL level, LDH, plasma free hemoglobin level, Rous test and Ham ‘s test.

Safety

Adverse events and blood counts were documented. Adverse events were coded with the preferred terms from the Medical Dictionary for Regulatory Activities (MedDRA)

Statistical Analysis

SPSS 17.0 and SigmaPlot 12.0 were used to cope with data and design graphs. The data were descripted as $x \pm s$ and paired T test was used to analysis at alpha level of 0.05. All reported P values were two-sided.

Results

Patients’ Characteristics

A total of 10 patients with PNH underwent DA or HA regimen chemotherapy between 2006 and 2010. The dosage of chemotherapy drug and number of cycles were adjusted according to the severity of bone marrow depression or haemolysis. Baseline characteristics of the patients were summarized in Table 1.The duration of disease from diagnosis to chemotherapy ranged from 0.04 to 17 years. All of the patients had accepted corticosteroid treatment. However, the clinical efficacy of corticosteroid was not as good as expected, and some had developed renal disease, diabetes, hypertension and gastric mucosal bleeding, which might be related with high dosage of corticosteroid. Some of them also used androgen, EPO and cyclosporine before chemotherapy (table 1). But none of the patients had experienced thrombosis or used anticoagulant agents as a preventive therapy. All of these patients were included in the analyses.

Improvement of anemia

In 10 patients, anemia was improved apparently. Transfusion independence was achieved in 4 patients, one of them achieved normal hemoglobin level. Another 4 patients who hadn’t need transfusion got elevated hemoglobin level. 1 of the left 2 patients who still need transfusion got prolonged transfusion interval from 15 days when HB 45 g/L to 16 days when HB 53 g/L. The left 1 patient got shorted transfusion interval despite of improved hemoglobin level because of sudden attack

of heart disease. Overall improvement of anemia was achieved with elevation of hemoglobin from (58.1±12.12) g/L to (90.20±21.55) g/L(P=0.000).

Effects on PNH clone

The proportion of $CD59^-$ and $CD55^-$ granulocyte in peripheral blood were monitored by flow cytometry. Results showed that the proportion of $CD59^-$ and $CD55^-$ cells decreased significantly in 8 patients, with (68.25±26.05)% and (81.47±26.13)% at the baseline to (59.53±24.60)% and (68.14±26.53)% after chemotherapy for deficient granulocyte (P=0.007 and P=0.003 respectively) (Table 3). In another 2 patients, the proportion of $CD59^-$ and $CD55^-$ erythrocytes and granulocyte did not decrease as we expected.

Table 1. Baseline Characteristics of the Patients

Characteristic Sex−no	Patients (N=10)
Male	4
Female	6
Age−yr	
Median	33.4
Range	11−51
Duration of PNH−yr	
Median	4.9
Range	0.04−17
Time from diagnosis to chemotherapy-yr	
Median	4.9
Range	0.04−17
Reticulocyte counts−%	
Median	0.66-11.58
Range	7.12
History of aplastic anemia−no. (%)	50
History of myelodysplastic syndrome −no.(%)	100
History of thrombosis−no. (%)	100
Total no. of thrombotic events	0
Use of erythropoietin−no. (%)	8
Use of cyclosporine−no. (%)	4
Use of anticoagulant agents(coumarins or heparins)−no. (%)	10
Use of corticosteroids −no. (%)	1
Use of androgenic steroids−no. (%)	6

Table 2. The hemoglobin level of patients before and after chemotherapy(g/L)

Patients	Before chemotherapy	After chemotherapy	P
Enrolle from 2006 to 2010	58.1±12.12	90.20±21.55	P=0.000

The dosage of corticosteroid

The dosage of corticosteroid used for those patients decreased gradually after the chemotherapy without onset of severe haemolysis. After chemotherapy, the dosage of corticosteroid decrease significantly, from (45.84±19.05) mg at baseline to (13.00±6.75)mg (P=0.000) (Table 4).

Effect on Haemolysis

IBIL as an indicator of intravascular haemolysis was assessed. In 10 patients, apart from 1 patient with normal IBIL and TBIL all the time, IBIL decreased significantly from (36.8±29.2) U/L at baseline to (18.1±12.4) U/L in the other 9 patients (P=0.015). However, TBIL was (48.8±36.15) U/L and (27.2±15.8) U/L before and after the chemotherapy (P=0.065), which may be related to the hepatitis E infection in 1 patient during chemotherapy(table 5). The value of LDH decreased in 6 patients monitored all the time (1656.12 vs 1269.33 U per liter; P=0.103). As another indirect biochemical measure of haemolysis, reticulocyte decreased from (7.13±3.88)% to (5.59±4.96)% (P=0.35).

Plasma free hemoglobin level, Rous test, Ham ‘s test were carried out only in some of the patients. As to concentration of free hemoglobin in serum, which was monitored in 4 patients, it keep normal in 1 patients, decreased a lot in other patients, the mean level was 72.50±61.31 and 32.50±22.17 before and after chemotherapy (P=0.134). Rouse test was monitored in 1 patient who kept negative before and after chemotherapy. Ham ‘s test was carried out in 1 patient, It was positive before chemotherapy and turned out to be negative after chemotherapy.

Safety

No patient died during chemotherapy. The most common adverse events during chemotherapy were infections, nausea, vomiting and fatigue. Hepatitis E was diagnosed in 1 patient. Inefficient transfusion of platelet occurred in 1 patient. High fever without confirmed focal infection happened in 2 patients. Upper respiratory tract infection occurred in 3 patients, 1 of whom developed pneumonia, 1 developed sepsis, 1 dental ulcer, 1

Table 3. The variation of PNH clone in peripheral blood cells(%)

Blood cells	Before chemtherapy		After chemotherapy		P1(CD59-)	P2(CD55-)
	CD59-	CD55-	CD59-	CD55-		
granulocytes	68.25±26.05	81.47±26.13	59.53±24.60	68.14±26.53	P=0.007	P=0.003

Table 4. Decline of corticosteroid dosage after chemotherapy(mg)

Patients	Before chemotherapy	After chemotherapy	P value
corticosteroid dosage	45.84±19.05	13.00±6.75	P=0.000

Table 5. Variation of TBIL and IBIL before and after chemotherapy

	Before chemotherapy		After chemotherapy		
patients	TBIL	IBIL	TBIL	DBIL	P value
	48.8±36.15	36.8±29.2	27.2±15.8	18.1±12.4	P=0.065, P= 0.015

perianal infection, 1 skin herpes and 1 suspected pancreatitis and acute myocardial infarction. All of these side effects was cured with corresponding drugs or recovered as bone marrow hematopoiesis reestablished. The minimum value of platelet was (1-60)×10^9/L, none of the patients experienced severe bleeding. The minimum values of WBC and granulocyte were (0.2-4.68)×10^9/L and (0-1.8)×10^9/L respectively. The duration of bone marrow depression in each cycle ranged from 10 to 23 days, with 19.76 days as the mean value. 1 patient had hepatitis E, none of other patients experienced liver or renal dysfunction.

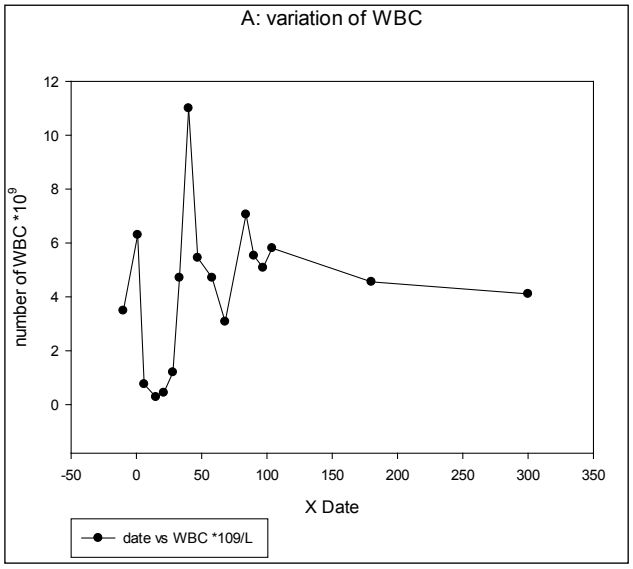
Report of a case

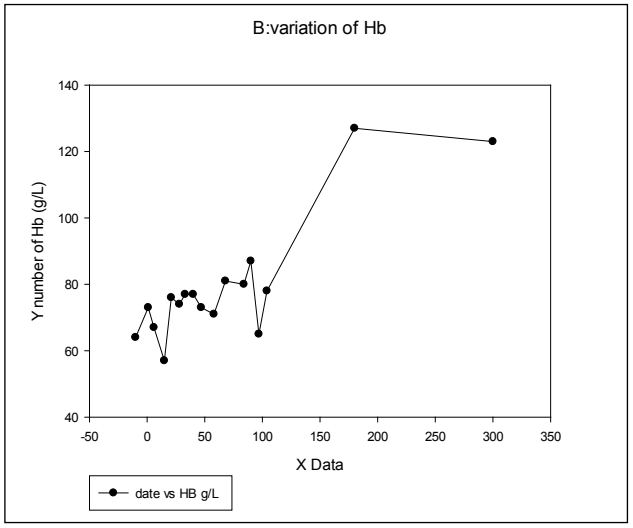
A 30-year-old female patient was admitted to the department of hematology at our hospital with complain of deep color of urine, dizziness and fatigue for 6 months. The patient reported that 6 months ago she had experienced deep color urine, dizziness and fatigue. Hematological findings were: hemoglobin concentration, 80g/L; platelets, 70×10^9/L and normal number of white blood-cells. Bone marrow smears showed hypercellularity with 70% nucleated erythrocyte , 14.4% granulocyte, 37 megakaryocytes; results of flow cytometry showed that CD59 and CD55 negative erythrocyte and granulocyte in peripheral blood were 33.2% and 4.3%, 20.9% and 12.7% respectively. Ham's test was positive, Coomb's test was negative. Then the patient was diagnosed as having PNH. Therefore, high dosage of dexamethosone(6mg ivdrip qd×6 days) followed by maintain dosage of prednisone to control heamolysis. HB could maintain 80-90 g/L and PLT 80-90×10^9/L when prednisone 40mg/d. However, 3 months ago, when the dosage of prednisone decreased to 10mg/d, HB decreased to 40 g/L, and RBC transfusion was given. Then cyclosporine with dosage of 150mg per day was given for 14 days before liver dysfunction occurred. After that, cyclosporine was discontinued and dosage of prednisone was added to 20mg/d again, then the disease was controlled again with HB 80-90g/L, RET 6.7%-8.76%, WBC 3.5-6.1×10^9/L, PLT 57-67×10^9/L. One month ago, the patient experienced deep color of urine once again after hard work and HB decreased to 40g/L. The same therapy as high dose of dexamethosone(6mg ivdrip qd×1 month) followed by maintain dose of prednisone were given to her. And blood routine showed that RBC 2.54×10^{12}/L, HB 89×10^9/L, RET 1.0%, WBC 3.45×10^9/L , PLT 40×10^9/L without RBC and PLT transfusion. In order to get confirmed diagnosis and further treatment, the patient came to our hospital. Before these symptoms started his medical history was unremarkable. A physical examination showed no pathological findings except for anemic face and icteric sclera. Laboratory analyses of hematological, bone marrow and biochemical parameters showed abnormalities. In particular, concentrations of TBIL, DBIL and LDH were not in normal range. Besides, abdominal percentage of CD59 and CD55 negative blood cells in peripheral and bone marrow supported the diagnosis of PNH. Furthermore FLARE test of bone marrow cells also confirmed PNH diagnosis.

Then chemotherapy regimen DAG including daunorubicin(DNR)400 mg/d, d_1; 20 mg/d, $d_{2\text{-}3}$; cytosine arabinoside(Ara-C) 100mg/d, $d_{1\text{-}5}$ plus

hemapoietic growth factors G-CSF were given to her. Concomitant administration of erythropoietin, immunosuppressive drugs, vitamin E, sodium bicarbonate, iron supplements, and folic acid were given to her throughout the chemotherapy. Other supportive therapies were also given, including isolated wards, transfusion, antibiotics, vital signs and blood routine test monitored and other treatments aiming at alleviating symptoms. And then after the chemotherapy, corticosteroid at low dosage and cyclosporine were given to her as maintain therapy.

After one cycle of chemotherapy, clinical efficacy was presented. Anemia improved and transfusion independence was achieved at thirty-third day, and then hemoglobin level increased gradually from 70g/L to 87 g/L three months after the chemotherapy and got to normal level as 127 g/L six months and kept normal till now (Figure 1).





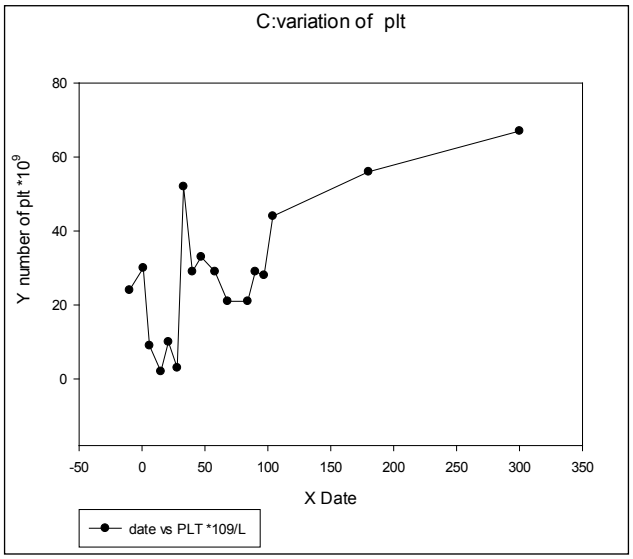


Figure 1. Variation of blood routine(A WBC; B Hb; C Plt) before and after chemotherapy. The horizontal ordinate represent the day before and after chemotherapy. 0 was difinted the first day of chemotherapy

The proportion of $CD59^-$ and $CD55^-$ erythrocytes and granulocytes in peripheral blood monitored by flow cytometry decreased to 0.13%,2.95% and 7.69%,10.35% one month after chemotherapy, which kept the reduced level till now(Figure2). The dosage of prednisone decreased gradually from 30 mg/d to 5 mg/d after chemotherapy without onset of severe haemolysis. As to the effect on haemolysis, TBIL, IBIL and LDH as indicators of intravascular haemolysis also decreased (Figure 3, 4). Plasma free hemoglobin level, Rous test, Ham ‘s test was carried out. As to concentration of free hemoglobin in serum, it was 0.09 g/L and 0.05 g/L before and after chemotherapy. Rous test kept negative before and after chemotherapy. Ham ‘s test was positive before chemotherapy and turned out to be negative after chemotherapy. During the chemotherapy, the most severe adverse events was inefficient transfusion of platelet, other adverse effects included infections, nausea, vomiting, fatigue. All of these side effects cured with corresponding drugs or recovered as bone marrow reestablished. The duration of bone marrow depression was 30 days with minimum values of WBC, granulocyte and platelet 0.2×10^9/L, 0×10^9/L and 1×10^9/L respectively. Neither liver nor renal dysfunction happened.

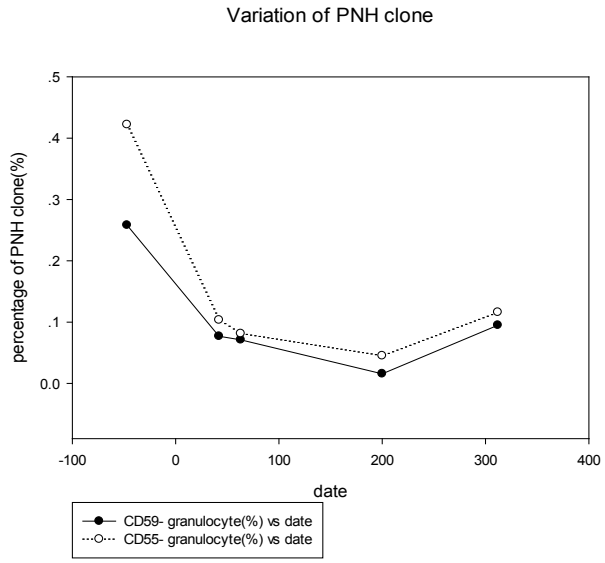


Figure 2. Variation of PNH clone in peripheral blood. The horizontal ordinate represent the day before and after chemotherapy. 0 was difined as the first day of chemotherapy

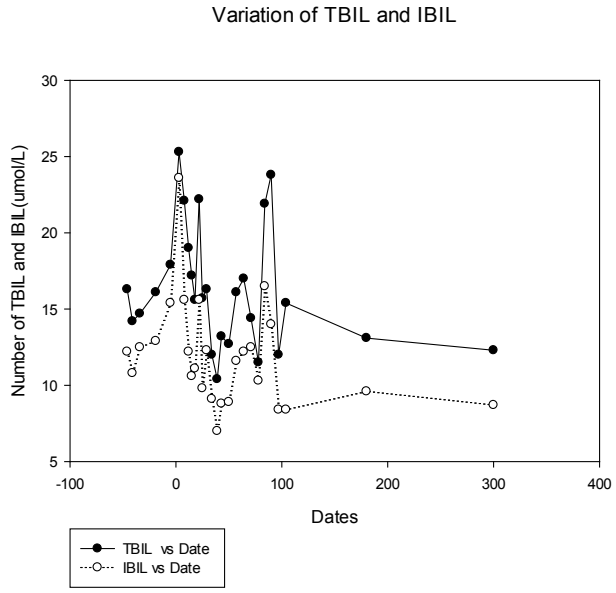


Figure 3. Variation of heamolysis indicators TBIL and IBIL. The horizontal ordinate represent the day before and after chemotherapy. 0 was difinted the first day of chemotherapy

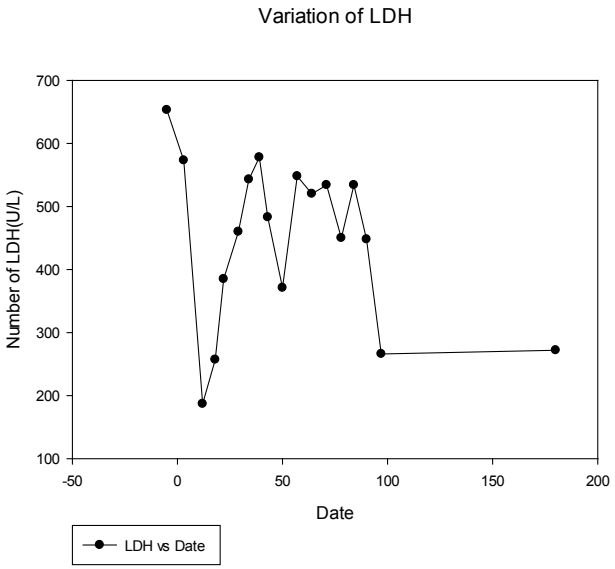


Figure 4. Variation of heamolysis indicators LDH. The horizontal ordinate represent the day before and after chemotherapy. 0 was difinted the first day of chemotherapy

Discussion

PNH was a refractory disease with both PNH clone and normal cells in the bone marrow. Patients with PNH have chronic intravascular haemolysis with acute exacerbations. Anemia and transfusions of RBC to sustain hemoglobin levels occured frequently. Despite remarkable progress in understanding the pathogenesis, treatment options for PNH have remained supportive, including red blood cell (RBC) transfusions, immunosuppressive therapy, or both[9]. Allogeneic hematopoietic cell transplantation (HCT) after high-dose conditioning regimens was the probable curative therapy currently available; however, it was associated with considerable morbidity and mortality[10]. Corticosteroid was a traditional drug for PNH with safety concerns. In order to prevent the adverse events caused by corticosteroid, the minimum dosage of corticosteroid should be taken to control haemolysis. In light of PNH clone mainly arising from myeloid hematopoietic cells, DA or HA regimens chemotherapy in moderate dosage with less side effects targeting at myeloid cells were employed to treat some corticosteroid resistant refractory severe PNH patients.

In this study, all patients achieved improved hemoglobin level, 4 patients got transfusion inde-

pendence, moreover, 1 patient has achieved normal hemoglobin level gradually. Even for 2 patients without transfusion independence, the interval of transfusion of packed red cells was prolonged. The proportion of $CD59^-$ and $CD55^-$ erythrocytes and granulocyte in peripheral blood(table 2) monitored by flow cytometry decreased significantly in 8 patients. Besides, the dosage of corticosteroid, a traditional therapy for PNH by protecting deficient cell from haemolysis, decreased gradually after chemotherapy without onset of severe haemolysis. Moreover, corticosteroid was discontinued in 2 patients. Intravascular haemolysis was central to the occurrence of serious coexisting conditions in patients with PNH and contributed to the risk of death among these patients. Biochemical markers of haemolysis, including IBIL, Lactate dehydrogenase, Plasma free hemoglobin level, Rous test and Ham 's test, were reduced to some extent after the chemotherapy, reflecting the effect of chemotherapy on haemolysis.

The controlled haemolysis may be achieved by diminishing deficient PNH cells, which was the basic principle of chemotherapy. There was no death during bone marrow depression, but only some common adverse events happened, including nausea, vomiting and fatigure. One patient infected hepatitis E during the chemotherapy, which was an acute infective disease cured with appropriate therapy. Suspected pancreatitis and acute myocardial infarction happened in 1 patient. Another 2 patients experienced severe bone marrow depression with inefficient transfusion of platelet, the recovery time was as long as 23 days. Prevention procedures as well as corresponding treatment aiming at alleviating symptoms were taken to minimize the risks, such as isolating clean ward, EPO, sometimes TPO, and antibiotics. None of the patients experienced severe liver or kidney damage related to the chemotherapy directly. The time for bone marrow returned to normal cellularity ranged from 10 to 23 days. No thrombotic or severe bleeding events occurred in these patients. The results indicated that DAG or HAG regimen chemotherapy could reduce PNH clone, control haemolysis, improve hemoglobin level and lessen corticosteroid dosage effectively without severe fatal adverse events.

GPI deficient cells were more sensitive to chemotherapy drugs and normal clones grew faster than PNH clone during recovery time. It might be explanations for effectiveness of chemotherapy. Therefore, we could get some "remission " of the disease. A lot of laboratory and clinical findings indicated that PNH clone did not possess endogenous predominance[11]. In vitro study, hematopoietic stem/progenitor cell with PNH phenotype and its differentiated GPI negative cells had inferior growth activity compared with normal cells. In PIG-A gene knockout mouse model, GIP-A deficient clone did not have endogenous superiority of growth, however, the number of which became smaller after several months[11]. When monoclonal antibody targeting GPI-APs CD52(CAMPATH1H) was used to treat lymphoma patients, the GPI negative cells turned up and then disappeared gradually several months after the drug was discontinued.

This suggested that GPI-APs negative cells did exist in some patients[12]. Moreover, it has been confirmed that minimal clone with mutant PIG-A gene did existed in normal population[13,14,15]. All of this mentioned above indicated that inactivation of PIG-A was not enough for expansion of mutant cells but a stumbling stone for differentiation and maturation. Therefore, we killed PNH clone with combined chemotherapy, then stimulated normal clones with growth factors. Normal clone would take the place of PNH clone. The reduction of PNH clone after chemotherapy also confirmed this assumption.

Our results showed that chemotherapy with DAG or HAG regimens could reduce intravascular haemolysis, reduce or even eliminates transfusion, diminish PNH clone and improve anemia in patients with PNH. The data supported DAG or HAG chemotherapy was an effective and promising treatment for PNH patients. But prophylactic procedures should be taken to control the adverse events during bone marrow depression.

Authorship

XD,RF and HW did the treatment, statistics and writing, ZS designed the regime and treatment, DW,LYL,WQ,YL,YW,GW,HL,JS,XW,LX,JG,ER,JW, LJL participate the treatment.

Acknowledgements

This work was supported by grants from National Natural Science Foundation of China (No. 30971286), Natural Science Foundation of Tianjin (09JCYBJC11200, 08JCYBJC07800), Specialized Research Fund for the Doctoral Program of Higher Education (200800620004).

References

1. *Takeda J, Miyata T, Kawagoe K, et al. Deficiency of the GPI anchor caused by a somatic mutation of the PIG-A gene in paroxysmal nocturnal hemoglobinuria. Cell. 1993; 73: 703-11.*

2. *Bessler M, Mason PJ, Hillmen P, et al. Paroxysmal nocturnal haemoglobinuria-(PNH) is caused by somatic mutations in the PIG-A gene. EMBOJ. 1994; 13: 110-7.*

3. *Rother RP, Bell L, Hillmen P, et al. The clinical sequelae of intravascular hemolysis and extracellular plasma hemoglobin: a novel mechanism of human disease. JAMA. 2005; 293: 1653-1662.*

4. *De Latour RP, Mary JY, Salanoubat C, et al. Paroxysmal nocturnal hemoglobinuria: natural history of disease subcategories. Blood. 2008; 112: 3099-3106.*

5. *Brodsky RA. How I treat paroxysmal nocturnal hemoglobinuria. Blood. 2009; 113(26): 6522-7.*

6. *Hillmen P, Young NS, Schubert J, et al. The complement inhibitor eculizumab in paroxysmal nocturnal hemoglobinuria. N Engl J Med. 2006; 355(12): 1233-43.*

7. *Antin JH, Ginsburg D, Smith BR,et al. Bone marrow transplantation for paroxysmal nocturnal hemoglobinuria: eradication of the PNH clone and documentation of complete lymphohematopoietic engraftment. Blood. 1985; 66(6): 1247-50.*

8. *Zhao M, Shao Z, Li K, et al. Clinical analysis of 78 cases of paroxysmal nocturnal hemoglobinuria diagnosed in the past ten years. Chin Med J (Engl). 2002; 115(3): 398-401.*

9. *Savage WJ, Brodsky RA. New insights into paroxysmal nocturnal hemoglobinuria. Hematology. 2007; 12(5): 371-6.*

10. *Hegenbart U, Niederwieser D, Forman S, et al. Hematopoietic cell transplantation from related and unrelated donors after minimal conditioning as a curative treatment modality for severe paroxysmal nocturnal hemoglobinuria. Biol Blood Marrow Transplant. 2003; 9(11): 689-97.*

11. *Rosti V, Tremml G, Soares V, et al. Murine embryonic stem cells without pig-a gene activity are competent for hematopoiesis with the PNH phenotype but not for clonal expansion. J Clin Invest. 1997; 100(5): 1028-36.*

12. *Taylor VC, Sims M, Brett S, et al. Antibody selection against CD52 produces a paroxysmal nocturnal haemoglobinuria phenotype in human lymphocytes by a novel mechanism. Biochem J. 1997; 322 (Pt 3): 919-25.*

13. *Araten DJ, Nafa K, Pakdeesuwan K, et al. Clonal populations of hematopoietic cells with paroxysmal nocturnal hemoglobinuria genotype and phenotype are present in normal individuals. Proc Natl Acad Sci U S A. 1999; 96(9): 5209-14.*

14. *Nazir T, Rehman H, Omar O, et al. Neutropenia induction by vinorelbine alone and in combination with doxorubicin and cisplatin in cancer patients. HealthMED.2011; 5(3): 486-489.*

15. *Jiang J, Wang X, Tian J,et al.Thymosin plus cisplatin with vinorelbine or gemcitabine for non-small cell lung cancer: A systematic review and meta-analysis of randomized controlled trials.Thoracic Cancer. 2011; 2(4): 213-20.*

Corresponding author
Zong-hong Shao,
Department of Hematology,
General Hospital,
Tianjin Medical University,
Heping,
Tianjin,
People's Republic of China,
E-mail: shaozonghong@sina.com

Patients' satisfaction with primary health care in Georgia

Nato Pitskhelauri[1], Nino Chikhladze[1], Elene Pitskhelauri[2]

[1] Faculty of Medicine, Ivane Javakhishvili Tbilisi State University (TSU), Georgia,
[2] Georgian Association for Quality in Health Care (GAQHC), Georgia.

Abstract

Evaluation of patients' satisfaction with medical care has received increasing emphasis due to the possibility to measure not only an important component of care - outcomes, but to assess care from the patient's unique perspective. In Georgia the concept of patient satisfaction is relatively recent. The objective of this study is to evaluate the level of patients' satisfaction with primary health care in Georgia. International instrument of patients' evaluation of General Practice Care (EUROPEP) was used. Four hundred twenty patients invited to complete 23 items of the questionnaire. Our survey indicates that patients generally rated positively the level of primary health care in all domain of clinical behavior and organization of care. A mean of 55,33 % respondents rated level of care as excellent. Patients' opinion is an important tool in evaluation quality of medical care. The study identified that patients generally rated positively the level of general practice care, however some aspects of clinical behavior and organization of care need to be improved. Primary Health Care provider should pay more attention to their patients' opinion and introduce patients satisfaction study for quality care improvement towards achieving main goals: to protect health, rights and dignity of patients and all society.

Key words: patients' satisfaction, primary health care, quality of health care.

Introduction

Evaluation of patients' satisfaction with medical care has received increasing emphasis due to the possibility to measure not only an important component of care - outcomes, but to assess care from the patient's unique perspective (1-4). Patients' satisfaction Concept has a long history [5-8]. Various patient experience surveys focus on specific diseases (9-11), different aspects of health care services and health professionals (12-14) were carried out. Several number of measurement tools to assess health care from patients' perspective have been developed and used (15-23). Among them is EQuiP Task Force developed International instrument of patients evaluation of General Practice Care (EUROPEP), which was used not only in National studies to assess the quality of care, but also in an international comparison of care. A systematic review of the literature has found that EUROPEP questionnaire has been tested in most of the European countries, and then has been used widely in different countries (24-40).

In Central, Eastern Europe and former soviet countries the concept of patient satisfaction is relatively recent (41-49). In Georgia the literature addressing patients' satisfaction and the dates about patients' expectation are very limited (50, 51). After the collapse of the Soviet Union, Georgia restored political independence. Georgia, like many former Soviet Republics, inherited a highly centralized and inefficient model of health care. The government of Georgia has carried out several reform initiatives for building more effective and patient-centered health care system. From 1997, primary health care (PHC) service providers were incorporated under commercial law. As a result part of facilities grouped together to create one legal entity, others registered as independent legal entities. However, there are a variety of PHC service providers (polyclinics, ambulatory, hospital-polyclinic-ambulatory unions, medical centre, village ambulatories etc.) across the country. Family medicine in Georgia was recognized as a specialty in 1998. This explains the diversity of the staffing structure of PHC facilities, with a mixture of family doctors, generalist physicians and other specialists (52). PHC utilization rates in Georgia are among the lowest in the WHO European Region (53).

Ministry of Labor, Health and Social Affairs of Georgia prepared the draft of the national health policy and elaborated strategic plan for 2011-2015 years. Assuring and improving the quality of medical services were defined as one of the priorities. Key challenges for improving quality of health care services include incorporating performance and outcome measurements for improvement and accountability (54). As a part of the strategic initiatives of the Government it is envisaged the development of the Primary Health Care Sector in the country, which should radically improve the efficiency and the quality of care. In order to achieve these goals the necessity of evaluation of patients satisfaction with primary health care services become evident.

Therefore, we conducted this study for evaluation the level of patients' satisfaction with Primary Health care and the care they were delivering over the last 12-month in Georgia. The dates were collected between May and September 2011. We hypothesized that the level of satisfaction will be as highly as in Central, Eastern European and transitional countries.

Materials and Methods

A random sampling method was done. The PHC facilities were stratified according to the location and in order to involve all region of Georgia. The PHC facilities from largest city, town and villages were included in the study. The types of facilities in the sample included medical centre, ambulatory, policlinics. The study was comprised of patients with recent experience with primary health care. Every third patient coming to visit his or her physician was invited to participate in the study. 420 patients were approached and all patients' were informed about the purpose of the study, patients were assured that survey would be anonymously, the questionnaire would not be present to their physician. All Patients were informed about the possibility to refuse the participation in the study. The patients were asked to complete the questionnaire after a visit to the physician at waiting room. A total of 38 patients refused to participate in the study and a total 382 respondents were identified and selected. All patients participate on a voluntary basis. Every third patient aged 18 or over, who came in the primary health care facilities, was asked to participate in the survey.

International instrument of patients' evaluation EUROPEP questionnaire has been used (23). The questionnaire covers two internally consistent dimensions: clinical behavior (17 questions) and organization of care (6 questions). Six questions focused on doctor-patient relationship and communication, five questions on medical care, four questions on information and support, two questions on organization of care-continuity and cooperation and six questions on facilities availability and accessibility. The questionnaire also contained the questions about demographic characteristics (sex and age). A five-point Likert answering scale with the ranging from poor to excellent was used. The original version of the questionnaire into Georgian has been translated. Epi-info statistical package was used for date entry.

Ethical considerations

The Faculty Scientific Board (FSB) of the Tbilisi State University has approved the study. All questionnaires included description of the study aim.

Results

A total of 38 patients refused to participate in the study and the dates of a 382 patients were analyzed. (response rate 90,1%). The main reasons for refusal were the lack of time, patients' status (due to health status), etc. All participants were aged 18 and over. About 59,9% of the respondents were female (n=229) and 40,1% male (n=153). The mean age of the participants was 51,4 years SD 14,78, Median 57, Mode 58 (49,5 years for women SD 15,77 and 54,3 years for men SD 12,67). Demographic characteristics of the respondents are presented in Table 1. The majority of patients were satisfied with general practice care (Table 2). On average 55,33% (30,10%-84,03%) of respondents rated received level of care as excellent. On average 58,29 % (33,77%-84,03%) of respondents rated the level of doctor-patients relationship as excellent, on average 51,73% (30,89%-71,73%)- the level of medical care, on average 57,39% (30,10%-74,87%) - the level of informational support of patients, on average 50,78% (41,62%-59,95%) - the level of organization of care, on average 55,5% (42,93%-67,02%) - the level of

Table 1. Demographic characteristics of the respondents

Independent variable	n	%
Gender		
Female	229	59,9
Male	153	40,1
Age		
18-39	121	31,6
40-65	192	50,3
>65	69	18,1
Area of residence		
City	117	30,6
Town	131	34,3
Village	134	35,1

accessibility. The comparison between clinical behavior dimension (17 questions) and organization of care (6 questions) showed that organization of care was evaluated with insignificant difference (mean percentage of 55,5%) than clinical behavior (55,27%). The highest response rates with excellent evaluation had the items: „Listening to you" (84,03%), „Keeping your records and data confidential" (81,94%), „Helping you understand the importance of following his or her advice" (75,13%), „Telling you what you wanted to know about your symptoms and/or illness" (74,87%), „Physical examination of you" (71,73%). The items, which were evaluated as the best (excellent and good evaluation): „Keeping your records and data confidential" (97,91% excellent and good versus 1,57% poor and bad), „Listening to you" (97,90% excellent and good versus 2,1,% poor

Table 2. The level of satisfaction in regards to 23 items of the questionnaire

Items	Poor	Bad	Average	Good	Excellent
What is your assessment of the general practitioner over the last 12 months with respect to:					
Making you feel you have time during consultation	0,79	1,31	8,11	44,76	45,03
Showing interest in your personal situation	1,31	1,83	9,95	43,72	43,19
Making it easy for you to tell him or her about your problem	1,05	2,36	4,97	29,84	61,78
Involving you in decisions about your medical care	2,09	12,57	35,34	16,23	33,77
Listening to you	0,52	0,79	0,79	13,87	84,03
Keeping your records and data confidential	0,52	1,05	0,52	15,97	81,94
Providing quick relief of your symptoms	1,31	2,88	14,92	30,11	50,78
Helping you to feel well so that you can perform your normal daily activities	1,05	0,79	8,11	36,91	53,14
Thoroughness of the approach to your problems	2,09	1,31	5,50	39,01	52,09
Physical examination of you	1,57	2,35	7,33	17,02	71,73
Offering you services for preventing diseases (e.g. screening, health checks, immunizations)	2,09	4,97	23,04	39,01	30,89
Explaining the purpose of examinations, tests and treatments	1,31	4,45	13,87	30,89	49,48
Telling you enough about your symptoms and/or illness	1,05	2,09	2,88	19,11	74,87
Helping you deal with emotions related to your health status	5,50	14,40	25,13	29,87	30,10
Helping understand why it is important to follow the GPís advice	1,05	1,57	2,36	19,89	75,13
Knowing what has been done or told during previous contacts in the practice	1,31	2,09	5,76	30,89	59,95
Preparing you for what to expect from specialists, hospital care or other care providers	2,88	6,02	13,35	36,13	41,62
The helpfulness of the practice staff (other than the doctor) to you	1,83	8,38	17,02	29,84	42,93
Getting an appointment to suit you?	2,09	9,95	14,92	30,11	42.93
Getting through to the practice on telephone?	2,36	3,67	12,04	19,63	62,30
Being able to talk to the general practitioner on the telephone	6,02	6,02	14,92	6,02	67,02
Being able to talk to the general practitioner on the telephone	3,93	4,97	8,90	19,63	62,57
Providing quick services for urgent health problems?	2,36	3,67	4,97	33,77	55,24

and bad), ,,Helping you understand the importance of following his or her advice" (95,02% excellent and good versus 2,62% poor and bad), ,, Making it easy for you to tell him or her about your problem" (91,62% excellent and good versus 3,41% poor and bad). The items ,,Helping you deal with emotional problems related to your health status (30,10%), ,,Offering you services for preventing diseases" (30,89)",,Involving you in decisions about your medical care" (33,77) had the lowest rates. The highest satisfaction index for the patient sample was for the item ,,Listening to you" (4, 80 men points) and the lowest for the item ,,Helping you deal with emotional problems related to your health status" (3,60 mean points) out of a maximum of 5 points.

Discussion

In Georgia this is the first study evaluating Patients satisfaction by an internationally validated instrument EUROPEP. This finding is similar to the results of other researchers, showing that in most countries the level of patients' satisfaction is high (26,27,31,33,41,42,45). Our survey indicates that patients generally rated positively the level of general practice care in all domain of clinical behavior and organization of care (doctor-patient relationship, medical care, information and support, organization of care and accessibility). A mean of 55,33 % respondents rated level of care as excellent. The observed level of satisfaction reported in this study corresponds to previously reported dates by Health Utilization and Expenditure Survey (HUES07) findings in Georgia though it is comparably low (51).

Physician's clinical skills were evaluated positively, especially listening, keeping patient's records and data confidential. 84,03% of patient believed that in spite of the lack of time physician is a good listener and 81,94% of patient believed that physician keeps patient's records and data confidential. Helping the patients to deal with emotional problems related to his or her health status, offering patients services for preventing diseases and involving patients in decisions about his or her medical care are ranked in European countries highly, whereas the same items have got lower rates in our study. These aspects seem to be similar with funding in Former soviet countries, Slovenia and Turkey (41-43, 31).

This can be explained by the decades-long existing curing diseases oriented and physician centred authoritarian tradition that influenced the style of the relationship between doctor and patients and consultation of physician. There were previously no ethical or judicial mechanisms of regulation. During the Soviet era in Georgia, legal activities meant only paraphrasing the Soviet government's given rules. In 1972, the government passed a law on health care, but the rights of patients were not protected and medical ethics principles were ignored. (An exception was the right of confidentiality of patients' personal data). In that model, the patient was not the subject but the object of the system, with no right to choose either the hospital or the doctor, physicians primarily paid attention to the clinical aspects of the medical problem and not to the emotional status of the patient and/or their participation in decision-making process, and less attention to the preventive medicine. The health care system soon became more and more corporate and ultimately it became uncontrollable by society. The Soviet model left as its heritage a health care system with no experience of the legal system, having paternalistic relations with patients, and a tradition of isolating people from health care, leading to society in general being indifferent about it (55).

Nowadays the traditional physician-oriented approach in health care is shifted with a patient-oriented approach. In 2000 the Georgian parliament has passed a Law on patients rights. Bioethics Curricula is included at all level of medical education (undergraduate, postgraduate, continuing professional development). Despite the challenges in Health Care system, it seems to be a too short period for transformation of medical specialists' attitude. However, it is necessary to increase knowledge about the patients' rights and quality of health care not only for physician, other medical specialists and manager, but also public education and patients' involvement. Research in this area should be encouraged for further development of health care quality based on appropriate evidence.

Dissatisfaction with items shows an importance area for improvement the process of reformation health care services in Georgia. We expect

that if more attention is paid to the development of patients-centred care and patients' autonomy concept, the variation between Georgia and European countries will diminish.

The study had some limitation: due to the small number of respondents and facilities involved in evaluation of the level of primary health care quality, the study cannot be viewed as representative for country as a whole. Therefore, we may consider that the results of this study describe observed general tendencies of the patients participating in our survey, reveal specific key factor for improvement in primary health care and underline the importance of future research of patients satisfaction in Georgia.

Conclusion

Patients' opinions are an important tool in evaluation quality of medical care. The study identified that patients generally rated positively the level of general practice care, however some aspects of clinical behavior and organization of care need to be improved. Primary Health Care provider should pay more attention to their patients' opinion and introduce patients satisfaction study for quality care improvement towards achieving main goals: to protect health, rights and dignity of patients in order to assure high quality in Health Care.

Author's contribution

TSU contributed to study design, data collection, statistical analysis, interpretation of the data, drafted the manuscript, provided substantial input to the intellectual content of the manuscript and provided revisions of the manuscript. GAQHC contributed to data collection, drafting of manuscript and provided valuable administrative support. All authors approved the final manuscript.

Acknowledgements

We would like to thank all patients who have participated in the survey and who were willing to share their opinion. We gratefully acknowledge to the staff of the Department of Public Health at Faculty of Medicine Tbilisi State University for continuous encouragement and support.

References

1. *Donabedian A.. The quality of care. How can it be assessed? JAMA 1988; 260 (12): 1743-1748.*
2. *Wenzel RP. Assessing Quality Health Care. Perspective for clinicians. Edited by Williams &Wilkins, USA; 1992.*
3. *Wilson L, Goldschmidt P. Quality Management in Health Care. McGraw-Hill Book company Sydney; 1995.*
4. *Kravitz RL. Measuring patients' expectations and requests. Ann Intern Med. 2001; 134(9): 881-888.*
5. *Donabedian A. Capacity to Produce Services in Relation to Need and Demand. In Aspects of Medical Care Administration: Specifying Requirements for Health Care. Cambridge, MA: Harvard University Press; 1973.*
6. *Locker D, Dunt D. Theoretical and methodological issues in sociological studies of consumer satisfaction with medical care. Soc Sci Med. 1978; 12: 283–292.*
7. *Ware J. et al. The Measurement and Meaning of Patient Satisfaction. Health and Medical Care Services Review. 1978; 1(1): 2-15.*
8. *Department of Health and the Welsh Office. General practice in the National Health Service: a new contract. London: HMSO; 1989.*
9. *Hjoerleifsdottir E. et al. Satisfaction with care in oncology outpatient clinics: psychometric characteristics of the Icelandic EORTC IN-PATSAT32 version. J Clin Nurs. 2010; 19 (13-14): 1784 – 1794.*
10. *Johansson H, Eklund M. Patients' opinion on what constitutes good psychiatric care. Scand J Ca Sci. 2003; 17(4): 339-346.*
11. *Robertsson O, Dunbar M. Patient satisfaction compared with general health and disease-specific questionnaires in knee arthroplasty patients. The Journal of Arthroplasty. 2001; 16(4): 476-482.*
12. *Bjorvell H. Patients' perceptions of the health care received in an emergency department. Ann Emerg Med. 1991; 20(7): 52-56.*
13. *Young GJ, Meterko M. and Desai KR. Patient satisfaction with hospital care: effects of demographic and institutional characteristics. J Med Care. 2000; 38(3): 325-334.*
14 *Pantoja T. et al. Patients' perspective in Chilean primary care: a questionnaire validation study. Intern J Qual in Health Care. 2009; 21(1): 51 –57.*

15. *Jenkinson C, Coulter A, Bruster S. The Picker Patient Experience Questionnaire: development and validation using data from in-patient surveys in five countries. International Journal for Quality in Health Care. 2002; 14(5): 353-358.*

16. *Marshall GN, Hays RD. The Patient Satisfaction Questionnaire Short-form (PSQ-18).RAND, Santa Monica; 1994.*

17. *Special Eurobarometer. Patients Safety and Quality of Health Care. European Commission. Brussel, Belgium; 2010.*

18. *Oltedal S. et al. The NORPEQ patient experiences questionnaire: Data quality, internal consistency and validity following a Norwegian inpatient survey. Scand J Publ H. 2007; 35(5): 540-547.*

19. *White B. Measuring Patient Satisfaction: How to Do It and Why to Bother. Fam Pract Man. 1999; 6(1): 40-44.*

20. *Client Satisfaction Evaluation. WHO, Geneva; 2000.*

21. *Grogan S. et al.. Development of a questionnaire to measure patients' satisfaction with general practitioners' services. Br J Gen Pract. 1995; 45(399): 525-529.*

22. *Ramsay J. et al. The general practice assessment survey (GPAS): test of data quality and measurement properties. Fam Pract. 2000; 17(5): 372–379.*

23. *Shi L, Starfield B, Xu J. Validating the Adult Primary Care Assessment Tool. Jf Fam Pract. 2001; 50(2): 161–71.*

24. *Grol R, Michel M, Kernik J. Patients Evaluate General/Family Practice. The EUROPEP instrument. University Medical Centre; 2000.*

25. *Grol R. et al. Patients' priorities with respect to general practice care: an international comparison. Fam Pract. 1988; 16(1): 4-11.*

26. *Grol R. et al. Patients in Europe evaluate general practice care: an international comparison. Br J Gen Pract. 2000; 50(460): 882-887.*

27. *Klingenberg A. Bahrs O, Szecsenyi J. How do patients evaluate general practice? German results from the European Project on Patient Evaluation of General Practice Care (EUROPEP). Journal Arztl Fortbild Qualitatssich. 1999; 93 (6): 437-445.*

28. *Wensing M, Mainz J, Grol R. A standardised instrument for patient evaluations of general practice care in Europe. 2000; 6(3): 82-87.*

29. *Kersnik J, Svab I, Vegnuti M. Frequent attenders in general practice: quality of life, patient satisfaction, use of medical services and GP characteristics. Scand J Prim Health Care. 2001; 19(3): 174-177.*

30. *Kersnik J. Patients' recommendation of doctor as an indicator of patient satisfaction. Hong Kong Med J. 2003; 9(4): 247-250.*

31. *Dagdeviren N, Akturk Z. An Evaluation of Patient Satisfaction in Turkey with the. EUROPEP Instrument. Yionsay Med J. 2004; 45(1): 23-28.*

32. *Mourad T. Abu et al. An Evaluation of Patients' Opinions of Primary Care Physicians: the Use of EUROPEP in Gaza Strip-Palestine. J Med Syst. 2007; 31(6): 497-503.*

33. *Mainz J. et al. How do patients evaluate their general practitioners? Danish results from a European study. J. Ugeskr Laeger. 2000; 162(5): 654-658.*

34. *Marian F. et al. Patient satisfaction and side effects in primary care: An observational study comparing homeopathy and conventional medicine. BMC Complem and Altern Med. 2008; 8: 52-62.*

35. *Esch B. et al. Patient satisfaction with primary care: an observational study comparing anthroposophic and conventional care. Health and Quality of Life Outcomes. 2008; 6: 74-89.*

36. *Petek D. et al. Patients' evaluations of European general practice—revisited after 11 years. Intern J Qual Health Care. 2011; 23(6): 621-628.*

37. *Bjertnaes O. et al. The Norwegian EUROPEP questionnaire for patient evaluation of general practice: data quality, reliability and construct validity. Fam Pract. 2011; 28(3): 342-329.*

38. *Heje H. et al., 2006. A cluster-randomized trial of the significance of a reminder procedure in a patient evaluation survey in general practice. Intern J Qual Health Care.18(3): 232-237.*

39. *Milano M. et al. Validation of the Italian version of the EUROPEP instrument for patient evaluation of general practice care. Eur J Gen Pract. 2007; 13(2): 92–94.*

40. *Haggerty J. L. Measurement of Primary Healthcare Attributes from the Patient Perspective. Healthcare Policy. 2011; 7: 13-20.*

41. *Zebiene E. et al. Meeting patient's expectations in primary care consultations in Lithuania. Intern J Qual Health Care. 2004; 16(1): 83-89.*

42. *Kersnik J. An evaluation of patient satisfaction with family practice care in Slovenia. Intern J Qual Health Care. 2000; 12(2): 143-147.*

43. *Harutyunyan T. et al. Patient satisfaction with primary care in Armenia: good rating of bad services? J Health Serv Manag Res. 2010; 23(1): 12-17.*

44. *Zebiene E. et al. Agreement in patient-physician communication in primary care: a study from Central and Eastern Europe. Pat Educ Couns. 2008; 73(2): 246-250.*

45. *Calnan M. et al. Major determinants of consumer satisfaction with primary care in different health systems. Fam Pract.1994; 11(4): 468-478.*

46. *Põlluste K. et al. Primary health care system in transition: the patient's experience. Intern J Qual Health Care. 2000; 12(6): 503-509.*

47. *Marcinowiczi L. et al. The patient's view of the acceptability of the primary care in Poland. Intern J Qual Health Care. 2008; 20(4): 277-283.*

48. *Tähepőld H. et al. Patient Expectations from Consultation with Family Physician. Croat Med J. 2006; 47(1): 148–154.*

49 . *Health Care. Georgia. Statistical Yearbook. 2010. Ministry of Labour, Health and Social Affairs of Georgia, National Centre for Diseases Control and public Health. Tbilisi; 2011.*

50. *Survey on Youth Friendly Reproductive Health Services in Georgia, Tbilisi; 2007.*

51. *Georgia Health System performance assessment. WHO, Geneva; 2009.*

52. *Chanturidze T. et al. Georgia: Health system review. Health System in Transition. WHO Regional Office; 2009.*

53. *WHO Regional Office for Europe. European Health for All Database (HFA-DB) Copenhagen, WHO Regional Office for Europe; 2009.*

54. *Georgia-National Health Care Strategy 2011-2012. Access to Quality Health Care. Tbilisi; 2011.*

55. *Schildmann J, Gordon JS, Vollmann J. Clinical Ethics Consultation: Theories and Methods, Implementation, Evaluation. Ashgate; 2010.*

Corresponding Author
Nino Chikhladze,
Faculty of Medicine,
Ivane Javakhishvili Tbilisi State University,
Georgia,
E-mail: chikhladze.nino@gmail.com

Ranking the strengths of Iranian health new financial management reform with approach of experts' attitude, group hierarchical analysis and Simple Additive Weighted model

Masoud Abolhalaj[1], Ahmad Barati Marnani[2], Peivand Bastani[3], Maryam Ramezanian[4], Javad Jafari[5]

[1] Research Center for Health Services Management, Kerman University of Medical Sciences, Kerman, Iran, Faculty member of Ministry of Health and Medical Education, University of medical sciences, Tehran, Iran,
[2] School of Management and Information Sciences, Tehran University of Medical Sciences, Tehran, Iran,
[3] Student`s scientific research center,Tehran University of medical sciences, Tehran, Iran, Research Center for Health Services Management, Kerman University of Medical Sciences, Kerman,Iran,
[4] Research Center for Health Services Management, Kerman University of Medical Sciences, Kerman, Iran,
[5] Administrator of health new financial management reform, Iran.

Abstract

Background: Since Ministry of Health and Medical Education was the first Iranian governmental organization which established accrual accounting as the first phase of health financial reform, this study was conducted to set the priority of this phase of reform`s strengths in order to give scheme of this experience to the organizations with similar conditions which tend to establish accrual accounting.

Methods: This study was performed in two separate and consecutive phases on financial and budget managers of Universities of Medical Sciences and trainers of health financial new system in these universities in order to prioritize and rank the most important strengths of health new financial reform applying thematic analysis and Multi-index decision making techniques such as AHP and SAW.

Results: 30 main themes were extracted as the most important strengths of the health new financial management reform in the first phase, Final analysis applying AHP and SAW for ranking these strengths shows that "Support of the financial new system by management of Ministry of Health" was attained the first rank with 51 points and "personnel with low expectation" attained the last rank (25^{th}) with 5 points.

Conclusion: Although this study can help recognize the status quo after establishment of the first phase of reforms from authorities and users of these changes points of view, it is suggested that similar studies be done for identifying weaknesses and limitations of this phase of reform in Iranian health system to have better perspective of the future planning and execution of the next phases of reforms with a list of the most important weaknesses and strengths.

Key words: Iranian health new financial management reform, accrual accounting, strengths, Additive Weighted model

Background

Authorities regard four factors of increasing costs in health care, increasing expectations of the people, limitation of resources and increase of the public request of the governments as driving force of reforms in health sector due to weak sovereignty, powerful and inhibiting bureaucratic relations and corruption and inefficiency [1]. On the other hand, excessive focus of decision-making, weak allocated efficiency, weak technical efficiency, high financial share of the patients for enjoying health services, low quality of services and bad performance of the health personnel are regarded as the factors which forced the developing countries to do reforms in their health system [2].Since financial resources supply and distribution management is regarded as the most important concerns of health systems policymakers, even increase of financial credits is not effective on more proper and better use of these resources until suitable infrastructure is not available for

effective use of resources and money to allow efficiency, effectiveness, assessment and supervision of the financial resources [3] , So main and fundamental reforms remain necessary. These basic changes which affected different organizations in governmental sector and the health organizations in many countries within the past 20 years include movement toward accrual accounting and acceptance of financial model of private sector in governmental system [4]. Different studies show many advantages of such essential changes in governmental sector accounting which include increase of accountability , management of assets , increase of efficiency , emphasis on outputs instead of inputs, promoting quality of the information given to the managers , decision makers and allocators of budget , comparability of performances , etc [5-7].Meanwhile, health and therapeutic system of the country faced many problems before reforms. Lack of long term and integrated financial planning in the sector and insufficient governmental regulations regarding prices control and impossibility to measure responsibility of the therapeutic and health services' providers especially failure to define real tariff in health and medical education sector are regarded as main problems of inefficiency in financial resources management of health and therapeutic sector [3-8] . In addition, lack of strong and suitable relationship between information and weak decision making on the basis of this information and island human resources, logistic , financial and budget information of the available financial systems in health and therapeutic sector of the country , failure to define monetary and financial turnover , cost and productivity management , weak regulations and the related byelaws, failure to calculate unit cost, absence of financial experts with the related specialty, and lack of single coding in the country necessitated health and medical education sector financial system reform and execution of reforms in financial health management as health financial new system in this sector [9].The first phase of reform was change of cash to accrual accounting approach which started since early 2005. This project was performed as pilot method in five universities of medical sciences i.e. Shahid Beheshti, Tehran, Qazvin, Tabriz and Bandar Abbas and was put into action after study of the primary results in all universities and faculties of medical sciences. The main goals of its execution were to clarify accounts and present comprehensive financial report by calculating unit cost of services and management of costs , prepare combined financial statements of all universities of medical sciences and periodical performance report and its alternate goals were to provide opportunity for establishing comprehensive budget, supply, develop, complete and integrate applied software , create equal coding in all universities of medical sciences and the affiliates. With regard to the fact that Ministry of Health and Medical Education was the first governmental organization which established accrual accounting, we study priority of the financial experts' attitudes employed in middle and operational levels of the universities of medical sciences regarding the most important strengths of this phase of reform in order to give scheme of this experience to the organizations with similar conditions which tend to establish accrual accounting.

Method

This study was performed in two separate and consecutive phases on financial and budget managers of universities of medical sciences and trainers of health financial new system in these universities in order to prioritize and rank the most important strengths of health new financial system as follows:

In the first phase, we gathered attitudes and points of view of the authorities with qualitative method. Target population of this study included all financial managers and budget managers employed in universities of medical sciences with the trainers dealing with financial new system of the country which taught principles and fundamentals of accrual accounting to the persons as subset of their universities. On this basis, the experienced and interested persons were identified among 80 financial and budget managers of the country and 60 trainers of financial new system with convenience sampling method and they were invited for participation in this research. We tried to consider variety of their service place in terms of university typology (1/2/3) in this choice. At first, we prepared mental framework on the basis of results of the pilot study and some expert panels regarding the definitions and compensated weaknesses and its shortages in

two brainstorm sessions for the managers and trainers. In this mental framework, we tried to discuss different fields such as general principles of accrual accounting in public sector, advantages of its establishment, experiences of other countries and potential strengths which implementation of this phase had in Iranian health system.For this purpose, 15 trainers of health financial new system and 10 financial and budget managers of these universities participated in brainstorming sessions and four expert panels. All of these persons had experiences for 7 years above and at least 5 years of experience in financial or budget units of the universities, furthermore, all of them held at least bachelor's degree in one of the related fields. At the beginning of the group discussions in these sessions, goals of research were mentioned clearly and key words were defined to allow brainstorming. Open space was provided for group discussion with the least interference of the researches and maximum members participation was allowed. Concurrently with the participants' views presented, all key concepts and terms were recorded accurately. After each one of these participants were given chance of expressing their views and ideas for three times, Open questionnaire containing questions relating to the mentioned field were given to the persons and they were asked to answer the questions on the basis of the previous experiences and their understanding of the provided discussions. Discussions and views of the persons were fully recorded during sessions and two members of research team extracted the discussions and verbal codes by studying the discussions. In addition, one of the team members noted main subjects of the research at time of holding sessions. In the next phase, all concepts and evidence mentioned in intra- group discussion between the researchers and the given answers as questionnaires were analyzed as content study and the mentioned concepts were classified and coded as strengths of health financial new system. Key terms mean the terms on which interviewees emphasized by repeating that concept during the session with different terms or adding the adverbs of emphasis. Since results of the discussion were close to each other and almost all concepts which were mentioned in the results were pointed out by more than one person, it seems that the receivable answers were saturated to some extent and sample size was enough. Criterion for finding saturation level was failure to find important and effective massage at the end of the session in such a manner that the participants didn't add new facts to the research finding. In the second phase, priority of the obtained strengths was specified with use of Simple Additive Weighted as one of the simplest methods of multi-index decision-making [10-11]. After preparing a list of strengths, a session was held with the primary participants and weight and importance of each option and indices effective on each option were determined with regard to view of these persons as decision maker. In the next phase, values of decision making matrix were linearly scale free. With regard to the fact that the indices applied in this research all are positive, the following relation in order to make values of decision making scale free:

$$n_{\mathrm{ij}} = \frac{a_{ij}}{MAX\ a_{ij}}$$

Then, the options were ranked in descending manner by multiplying the scale free matrix by weights of the indices. On the other hand, the most suitable option (A*) was calculated on the basis of the calculated value by calculating weight of the indices (W):

$$A^{*}=\{A_i \mid \mathrm{Max} \sum_{j=1}^{n} n_{ij}\ \ w_j\}$$

Where a_{ij} is jth index for ith option, n_{ij} is scale free value of the jth index for ith option and w_j is importance coefficient of jth index.

At the end, preferred option was selected in such a manner that its weight was higher than that of other options with regard to the above relation.

Finding

Finding obtained from analysis of the implemented texts of experts panels with financial and budget managers and trainers of health financial new system employed in universities covered by Ministry of Health and Medical Education regarding strengths of the first phase of financial reforms in health system of the country led to presentation of 30 strengths as follows:

Table 1. Strengths of financial new system resulting from attitude of the experts in panels

Views of the experts about strengths of financial new system
Teamwork space
Creativity and innovation of managers in settlement and domestication of financial new system
Definition of new structure for financial departments and forces
Suitable and applied local bylaws and instructions
Data website
Unsuitable and timely control of financial services
Organizing financial information and equal coding
Application of theories, standards and financial new classifications
Support of financial new reform by major management of the Ministry of Health
Financial resources for execution of the plan
Suitable equipment
Cost effective training
Creating common language between management of financial affairs and board of directors of the universities
Directing the auditor to execute accrual accounting
certainty of the auditor about compliance with laws and regulations
Presence of specialized, powerful and committed employees in financial field
Personnel with low expectation in financial affairs units of universities
Synergy in activities of the personnel
Decisive and interested authorities on top of the plan
Ability of managers to use managerial levers
Suitable and continual on the job trainings for the trainers
Holding national and international conferences for synergy of the managers
Technical and specialized committees of financial and budget managers
Speed of data transfer
Reliability of information
Systematic and process information system
Integration of information system
Active and expansive informal relations
Criticism and suggestion tools in financial new system
Work and competition culture

After summarizing views and concluding them as the above table, the participants were asked to identify the most important indices which were affected by 30 options (strengths). In this phase, three indices of efficiency, clarity and control were identified and pair comparisons were made in order to determine their importance coefficient. In order to make pair comparison between indices, views of 17 participants in the research were used and finally group AHP method was used in order to combine views of these decision makers through which pair comparison matrix elements were obtained from geometrical average of each decision maker's pair comparison matrix. In addition, since comparisons incompatibility rate was smaller than 0.1 (equivalent to 0.02) with use of Expert choice software, compatibility of comparisons was achieved and weights of each index were obtained according to table 2. In the next phase, general point of each option which includes strengths of health financial system was obtained after applying the obtained weights of indices in options and performing the related calculations and options were ranked as described in table 3

Table 2. Weight of indices with use of group AHP method

	Efficiency	Clarity	Control
Weight of indices	0.307	0.362	0.331

Table 3. Ranking the strengths of financial new system on the basis of point obtained from simple additive weighted method (SAW)

Rank	Strengths of financial new system	Point
1	Support of financial new reform by major management the Ministry of Health	51
2	Decisive and interested authorities on top of the plan	49
2	Suitable and applied local bylaws and instructions	49
3	Suitable and continual on the job trainings for the trainers	47
4	Presence of specialized, powerful and committed employees in financial field	46
5	Synergy in activities of the personnel	44
6	Directing the auditor to execute accrual accounting	43
7	certainty of the auditor about compliance with laws and regulations	42
7	Integration of information system(software)	42
8	Systematic and process information system	41
9	Active and expansive informal relations	40
10	Teamwork space	39
10	Work and competition culture	39
11	Technical and specialized committees of financial and budget managers	38
12	Holding national and international conferences for synergy of the managers	37
13	Creating common language between management of financial affairs and board of directors of the universities	36
14	Creativity and innovation of managers in settlement and domestication of financial new system(pilot execution)	35
15	Cost effectiveness of training	34
15	Criticism and suggestion tools in financial new system	34
15	Speed of information transfer	34
16	Suitable equipment	33
17	Financial resources for execution of the plans	32
18	Reliability of information	31
19	Application of financial new theories, standards and classifications	26
20	Organizing financial information and equal coding in spite of complexity of health and therapeutic services	25
21	Information website	23
22	Definition of new structure for financial forces and departments	21
23	Power of the managers to use managerial levers	16
24	Suitable and timely control of financial services	16
25	Personnel with low expectation in financial affairs units of universities	5

from the highest to the lowest point. Support of the financial new system by management of Ministry of Health was attained the first rank with 51 points and personnel with low expectation attained the last rank (30^{th}) with 5 points.

Discussion

Health system department with limited resources and increasing costs requires management based on timely and reliable information, while information was produced and financial reports were prepared traditionally in this section only for the supervisory organizations and thereto was no need for intra-organizational financial information for managing the sector, therefore, the managers only relied on major budget information. In addition, cost manager governed these organizations instead of professional managers and there was no attention to necessity of income production in the organization [3]. A set of these problems required reforms of health sector financial system of the country and it started by changing accrual to cash accounting system, in the universities and faculties

of medical education.In this regard, different studies showed two main functions for establishment of accrual accounting systems in public sector: providing comprehensive and reliable information regarding public assets and providing opportunity for better and more effective financial supervision on activities of the government [12].

On the other hand, other studies indicate that familiarity of the public sector with accrual accounting depends on commitment of the managers to establish it and allocate enough time to this work and this shall be emphasized from the highest level to the low levels [13], and new investments are necessary in training of accrual accounting technical notes and learning of its related subjects in order to achieve this goal.Finding obtained from the present study emphasized on reliability of information and speed of data transfer, suitable and timely control of financial services, suitable and continual on the job training for the trainers, holding national and international conferences for consultation of the managers to use managerial levers, presence of decisive and interested authorities on top of the plan of each university, support of the financial new system by Ministry of Health as strengths of accrual accounting system in health system of the country.

On the other hand, other studies believe that application of accrual accounting is effective on increasing accountability level and realization of the goals of financial reporting [14]. In this regard, organizing financial information and equal coding was regarded as the strength of accrual accounting in health system of the country leading to clarity of the financial information.It is evident that ranking and prioritizing the strengths can help planners and policymakers of health system direct the mentioned reforms and use the strengths to remove the shortage due to diversity and dispersion of the mentioned strengths. In this regard, two multi-index decision making techniques of hierarchical analysis and simple additive weighted have been used for access to the said goal. Multi-index decision making techniques have been widely applied in different fields and the reason is simplicity and comprehensibility of these techniques for different users. In addition, these techniques are able to enter quantitative and qualitative variables concurrently in the decision making process in contrary to mathematical models of planning and decision making which don't enter qualitative variables effective on modeling [15]. Simple additive weighted model is one of the simplest multi-index decision-making methods which consider indices weights in calculation technique however, we can reduce values of other indices by increasing values of the index which has the highest weight without changing the simple additive weighted value and create the determined rank for each option [16]. In this study, support of financial new system by Ministry of Health, presence of decisive and interested authorities on top of the plan in each university, presence of suitable and applied local bylaws and instructions, suitable and continual on the job training for the trainers, presence of the specialized personnel in financial field, synergy of the personnel's activities, directing the auditor to execute the accrual accounting, certainty of the auditor about compliance with laws and regulations , integrity of the information system (software) and systematic and process information system were identified as the 10 important strengths of health new financial system in the first phase (change from cash to accrual accounting) and were included on top of the ranking table by attaining the highest rank.

As said before, this prioritization allows the policymakers and decision makers to focus on the most important options and achieve more desirable result by spending less energy, time and cost while helping the planners exploit the most important strengths of this plan and use it for reducing barriers, problems and limitations. At the end, it is necessary to note that application of accrual accounting in public sector was regarded as reaction to changes and reforms in management field of this sector like experiences of other countries. The said reform was done in order to create performance based management and result based management in which promotion of efficiency level, effectiveness and operational accountability of public sector were emphasized with increase of management's carefulness in spending the resources instead of emphasis on inputs [17]. These reforms were shown as use of accrual basis in accounting system in different countries and our country while sensitivity of these reforms in our country can be higher than that of other countries because it has been executed for the first time in subsets of Ministry of Health and Medi-

cal Education which is not comparable with any public sectors in terms of mission. With regard to high importance of the mentioned reforms in the organizations which aim at preservation and promotion of health level of society, it is evident that such studies can help recognize the status quo after establishment of the first phase of reforms from the points of view of authorities and users of these changes. In addition, it is suggested that similar studies be done for identifying weaknesses , shortages and limitations of this phase of reform in health system of the country to have better perspective of the future planning and execution of the next phases of reforms with a list of the most important weaknesses and strengths.

References

1. *Neema S. The impact of health policies and health sector reform on the readiness of health systems to respond to women's health needs. United Nations Expert Group Meeting. Bangkok, Thailand; 2005: 12.*
2. *Bodart C, Servais G, Mohamed YL, et al. The influence of health sector reform and external assistance in Burkina Faso. Health Policy Plan 2001; 16(1): 74-86.*
3. *Abolhalaj M , review of financial system in health sector , Gozideh Modiriat Periodical, Humanities Periodical, 2009 [persian]*
4. *Van Helden, G. J., Researching Public Sector Transformation: The Role of Management*
5. *Accounting, Financial Accountability & Management, 2005; 21(1) : 99-133*
6. *Skarbak, P.; Melander P. The politics of the changing forms of accounting: A field study of strategy translation in a Danish government-owned company under privatization, Accounting, auditing & Accountability Journal, 2005;17(1) :17-40*
7. *Cortes, J. P. The international situation vis-à-vis the adoption of accrual accounting. Journal of Public Budgeting, Accounting & Financial Management , 2006; 18(1):1-26*
8. *Ellwood, S., Newberry, S. Public sector accrual accounting: institutionalizing neo-liberal principles?. Accounting, Auditing & Accountability Journal, 2007; 20(4): pp. 549-573.*
9. *Barati Marnani A, SadeghifarJ, Pourmohammadi K, Mostafaie D, Abolhalaj M, Bastani P, Performance assessment indicators: How DEA and Pabon Lasso describe Iranian hospitals` performance ,HealthMED, 2012; 6(3): 791-6*
10. *Abolhalaj M, Ramezanian M, experience of Ministry of Health and Medical Education in execution of financial new reform, Eghtesad Salamat Specialized Scientific Periodical, 2010, 1(1):83-92. [persian]*
11. *Azar A, Rajabzadeh A. Applied Decicion Making. Tehran:Publications Negah Danesh; 2008. [persian]*
12. *Hwang C.L., Yoon K., "Multiple Attribute Decision Making: Methods and Applications", Berlin, Springer, 1981*
13. *Vareille, L., P. Adhémar, The Modernization of Government Accounting in France: The Current Situation, the Issues, the Outlook. Public Sector Committee, IFAC, 2003*
14. *Saint-Martin, D. Building the New Managerialist State: Consultants and the Politics of Public Sector Reform in Comparative Perspective, Oxford: Oxford University Press, 2000*
15. *Matheson A. Better Public Sector Governance : The Rationale for Budgeting and Accounting Reform in Western Nations, OECD Journal on Budgeting, 2002; 2 (1);*
16. *Chowd hury, S. , Squire, L. " Setting weights for aggregate indexes :an application to the commitment to development index and human development index". Journal of Development Studies,2006; 42 (5), 761–77*
17. *Hyde, K.M., Maier, H.R., Colby, C.B., A Distance-Based Uncertainty Analysis Approach to Multi Criteria Decision Analysis for Water Resource Decision Making, Journal for Environmental Management, 2005; 77: 278-290.*
18. *Ouda H. Basic Requirements Model for Successful Implementation of Accrual Accounting in the Public Sector, Public Fund Digest, 2004; 4 (1);*

Corresponding Author
Peivand Bastani,
Department of Health Services Management,
School of Health Management And Information Sciences,
Tehran University of Medical Sciences,
Iran,
E-mail: p-bastani@razi.tums.ac.ir

Anatomical approach to the Liver mobilization A study on cadaveric livers

Andrej Starc[1], Abdelwaheb Morjane[3], Raja Dahmane[1,2]

[1] Faculty of Health Sciences, University of Ljubljana, Slovenia
[2] Faculty of Medicine, Institute of Anatomy, University of Ljubljana, Slovenia,
[3] Department of Surgery, Faculty of Medicine, University of the Center, Monastir, Tunisia.

Abstract

Background: The reasons for the restrained popularity of the laparoscopic liver resections involve mainly technical issues derived from the difficulty in laparoscopically reproducing the basic surgical manipulations used in the traditional approaches. These manipulations include direct control of the portal triad and liver mobilization

Aim: Detailed anatomical data about the ligaments, fascia, vascular and biliary structures attaching the liver are of important significance in liver mobilization. The primary purpose of our research was to present a new approach to the description of the topographic liver anatomy by classifying these different structures.

Materials and methods: surgical dissections were carried out on 88 cadavers of both sexes. A particular attention was paid to the portal pedicle dissection, which was realized extra-fasciae and extended, to the cystic and umbilical fissure searching for the left and the right hepatic sectional pedicles. Mobilization of the left and right hemiliver and exposure of the anterior face of the hepatocaval venous junction were achieved by dividing the teres hepatis, falciform, left triangular and coronary ligaments.

Results: The dissection procedure is presented in three steps of mobilization in relation to the location and type of the dissected tissues and to the difficulty of access. Conclusions: In conclusion laparoscopic liver mobilization is not an easy procedure. It requires detailed anatomical knowledge and technical skills in both liver surgery and laparoscopy. In the current series of 88 cadaveric liver dissections, we greatly benefited from extensive experience in open liver surgery.

Key words: liver anatomy, liver mobilization, laparoscopic liver resection, hepatocaval ligament, venous ligament

Introduction

First laparoscopic liver resection (LLR) was reported in 1992 (Gagner et al., 1992). Since then, less than 3500 procedures have been performed (Lanitis et al., 2010). Even today, only few centers perform LLR systematically and the reasons for its restrained popularity involve mainly technical issues derived from the difficulty in laparoscopically reproducing the basic surgical manipulations used in the traditional approach. These manipulations include direct control of the portal triad, liver mobilization and dissection of the parenchyma (Cherqui et al., 2000; Descottes et al., 2000). The mobilization and exposure of the liver are still difficult in the absence of specific nontraumatic instruments for safe handling of such a fragile and heavy organ. The "hidden" vascular anatomy of the liver exposes it to the risk of massive bleeding, which can be difficult to control by laparoscopy (Dagher et al., 2007; Gutt et al., 2001). In addition to laparoscopic approach we detect weaknesses in anatomical (big volume of right lobe, depth of the pedicle, big diameter of vessels) and surgical terms (location of big tumor(s) on the posterior side, air embolism).In relation to the laparoscopic or open surgery hepatic approach, researches were focused on the anatomical and surgical relevance of intra- and extra-hepatic structures for a better/ safe mobilization (Morjane et al., 2008; Dahmane et al., 2009). Detailed anatomical data about the ligaments, fascia and vascular structures attaching the liver are of important significance in liver mobilization. The primary purpose of our research was to present a new step by step approach to the description of the topographic liver anatomy by classifying these different structures. Secondly, the aim of our group was consistent training/exercising for laparoscopic mobilization and elective vascular exclusion.

Materials and methods

Surgical dissections were carried out on 88 cadavers (72 men and 16 women) aged 20-70 years. For the mobilization of the right hemiliver, a sub-costal laparotomy approach was used; we extended to the right side with a sub-scapular block. A pillow was placed under the right flank and a swing at the left side. During the dissection, a particular attention was paid to the portal pedicle, which was realized extra-fasciae and extended, to the cystic and umbilical fissure searching for the right hepatic sectional pedicles. The segment of the inferior vena cava (IVC) between the liver and the diaphragm and the inflows of the hepatic veins were exposed. The hepatocaval ligament (HCL) was then carefully isolated; it was located above the middle suprarenal vein, toward the right hepatic vein (RHV). The HCL was divided and ligated; it then presented an anterior and a posterior border. The anterior border was turned left to expose the postero-lateral angle of the RHV. Then the dissector was introduced first in the postero-lateral angle of the RHV, and then in the anterior angle that had been already exposed by the dissection of the posterior angle of insertion of the falciform ligament. Mobilization of the left hemiliver and exposure of the anterior face of the hepatocaval venous junction were achieved by dividing the teres hepatis, falciform, left triangular and coronary ligaments. The left hemiliver was lifted up and pulled to the right to expose the dorsal part of the left hepatic fissure with the insertion of the lesser omentum and the venous ligament (VL) between its two layers. The VL was individualised over all its length – from the left portal branch up to its insertion on the LHV. With the release of the ventral layer of the omentum, the denudation of the extrahepatic part of the LHV from the liver parenchyma towards its inflow was achieved. The release of the dorsal layer of the omentum with simultaneous traction of the VL cranially and to the right enabled the denudation of the angle between the CT/LHV and the IVC; the procedure was facilitated by countertraction of the caudate lobe (segment 1). The terminology for liver anatomy was based on the Brisbane classification (Strasberg et al., 2000)

Results

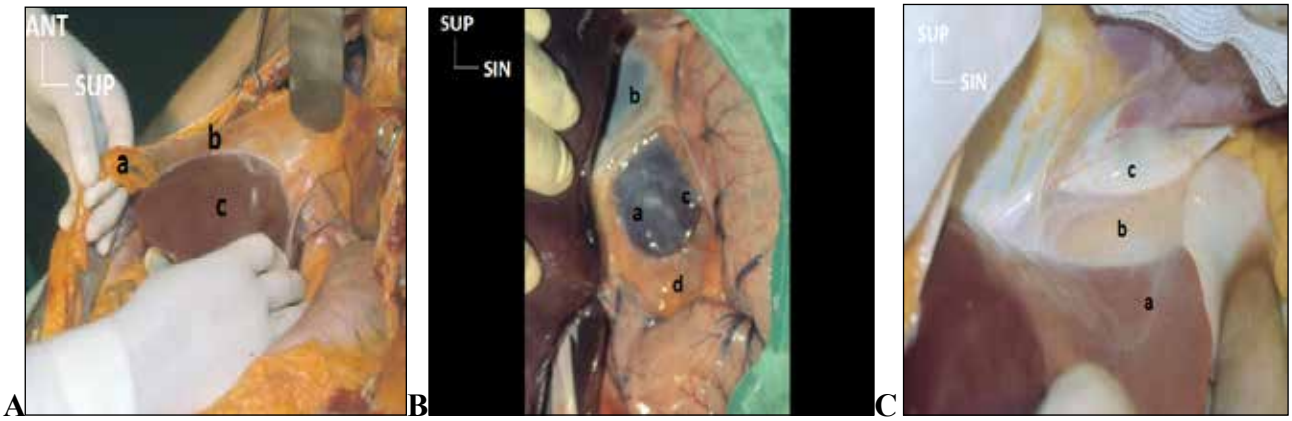
We divided the dissection procedure in three steps of mobilization in relation to the location and type of the dissected tissues and to the difficulty of access.

First step of liver mobilisation

In the first step a special attention is paid to the ligaments group and to the anterior mobilization structures. The ligament group is constituted by the adhesion of two peritoneal sheaths, lying anteriorly and of easy access. On the anterior (inferior) margin (figure 1A), we divided the ligament teres hepatis and on the superior surface the falciform ligament and the anterior portion of the coronary ligament. This led to the posterior portion of the coronary ligament. The stump of the falciform ligament was grasped for retraction. To reach the structures on the inferior surface, we lifted up the left hemiliver and pulled it to the right to expose the dorsal part of the left hepatic fissure with the insertion of the lesser omentum (pars-flaccida, pars-condensa and pars-vasculosa). The pars-vasculosa led to the intra-fascial portion of the portal pedicle (figure 1B). to reach the posterior portion of the coronary ligament the left and the right triangular ligaments were been followed (figure 1C). Discontinuation of triangular and coronary ligaments enables the second step of liver mobilization.

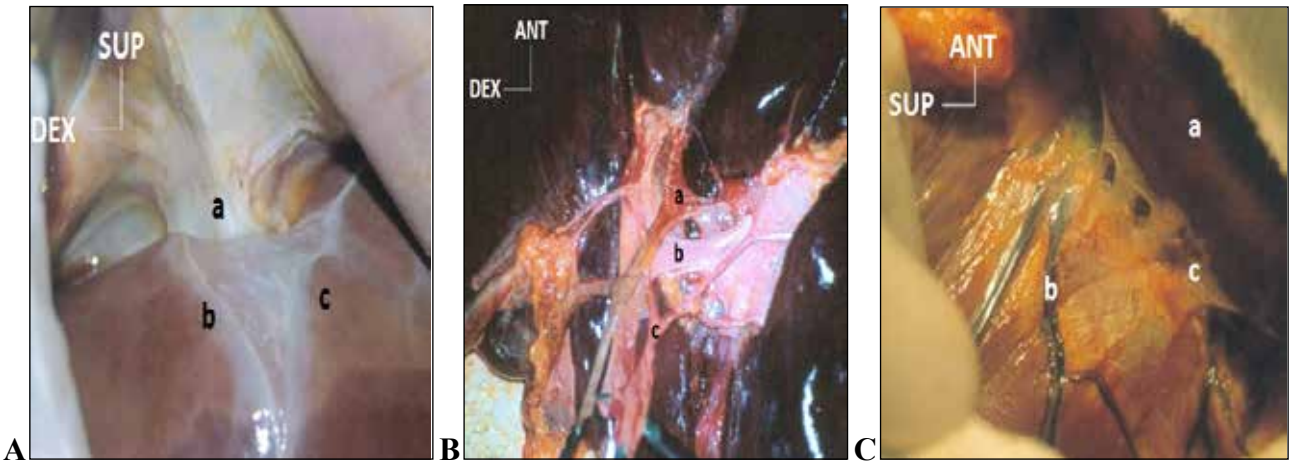
Second step of liver mobilization

In the second step of liver mobilization attention is paid to the fascias group or middle mobilization structures. It is a loose and less vascularized tissue, lying deep enough and rather difficult of access. On the superior liver surface (figure 2A), dissection of the falciform ligament was continued to the level of its triangle of posterior insertion (superior coronary fascia) and to the level of the inferior vena cava (IVC) and the inflow of the hepatic veins. On the inferior surface (figure 2B) the dissection is continued to the pre-portal intra-fascial portion of the portal pedicle, which leads to the porta hepatis. On the left side of the posterior surface (figure 2C), the left portion of the coronary ligament leads to the left edge of the IVC which is covered by the venous ligament. On the right side, the right coronary ligament leads to the right edge of the IVC, which is covered by the hepatocaval ligament. This dissection leads to the vestigial group.



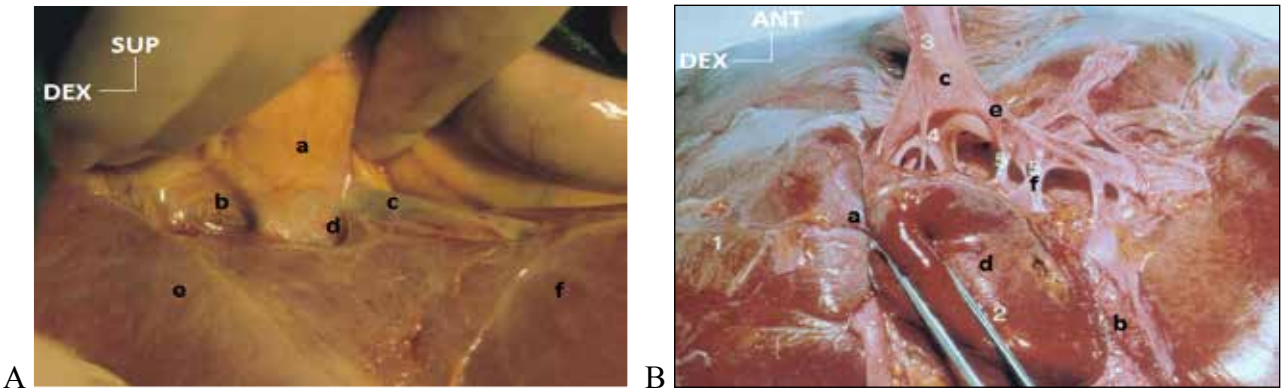
A B C

Figure 1. First step of liver mobilisation: A-superior liver surface a. teres hepatis ligament b. falciform ligament c. lobus sinister B- inferior liver surface-lesser omentum a. segment 1 b. pars condensa c. pars flaccida d. pars vasculosa C- posterior liver surface–left side a. lobus sinister b. left triangular ligament c. diaphragm



A B C

Figure 2. Second step of liver mobilization: A-superior liver surface a. inferior vena cava b. right part of the falciform ligament c. left part of the falciform ligament B-inferior liver surface, porta hepatis a. ductus hepaticus communis b. vena porta c. a. hepatica propria C- right side of the posterior liver surface, right coronary ligament a. lobus dexter b. vena diaphragmatica inferior and the diaphragm c. right coronary ligament (posterior portion)



A B

Figure 3. Third step of liver mobilisation: A-superior liver surface a. inferior vena cava b. right hepatic vein c. left hepatic vein d. middle hepatic vein e. lobus dexter f. lobus sinister B- inferior liver surface, 3 compartments a. right hepatic fissure b. left hepatic fissure c. vena portae d. segment 1 e. left portal pedicle f. sectional portal pedicle.

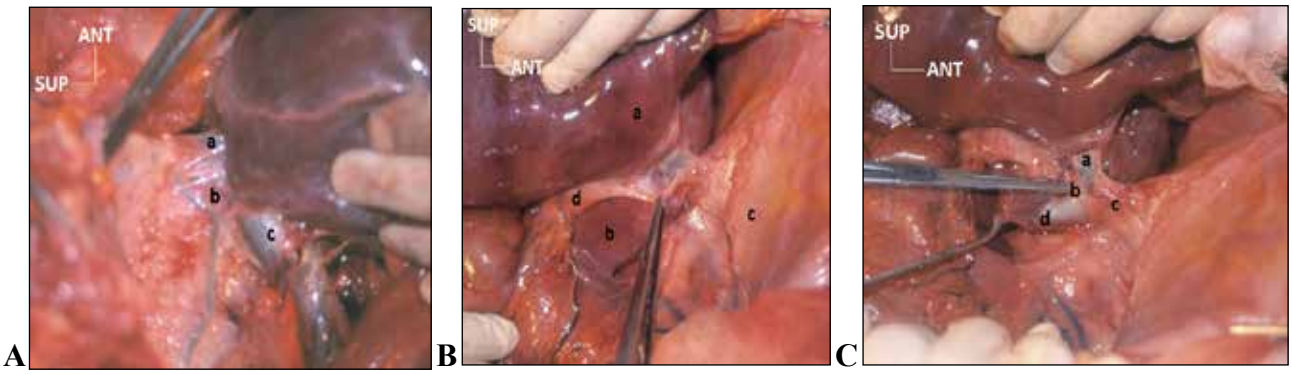


Figure 4. Third step of liver mobilisation: posterior liver surface A- right side a. right hepatic vein b. hepatocaval ligament c. inferior vena cava B- left side before the dissection of the venous ligament a. lobus sinister b. segment 1 c. diaphragm d. venous ligament C. left side after the dissection of the venous ligament a. left hepatic vein b. middle hepatic vein c. common trunk d. inferior vena cava

Third step of liver mobilization

In the third step of liver mobilization attention is paid to the vestigial group and the vascular plan. It is lying very deep in the posterior plan, and has the most difficult and deepest approach. On the superior surface (figure 3A) the sheath of the IVC and the Glisson's capsule lead to the angle of the hepatocaval inflow and to the hepatic veins. The inferior surface (figure 3B) is divided in three compartments: the central compartment or porta hepatis, the right compartment or right hepatic fissure, the left compartment or left hepatic fissure. The mobilization leads to the sectional and segmental pedicle. On the posterior surface the hepatocaval ligament leads to the inflow of the right hepatic vein (figure 4A) and the venous ligament leads to the inflow of the left hepatic vein or of the common trunk (figure 4B and 4C).

Discussion

The indications for laparoscopic liver resection (LLR) do not differ from the traditional approach. The difference lies solely in the technical feasibility which mainly depends on the lesion size and side (Dagher et al., 2007). The present anatomical study about the liver mobilization (LM) facilitates the laparoscopic as well as the open approach; totally LLR appears safe for lesions located in the anterior and lateral segments (segments 2 to 6) but is also viable for central and posterior segments. It can also prove that the laparoscopic approach should eventually replace part of the open liver surgery.

The primary determining factor of the feasibility of the laparoscopic approach is also the experience of the surgical team (Lanitis et al., 2010). Understanding hepatic anatomy is of great importance in LM. Laparoscopic liver surgery is a safe and effective approach if it is in the hands of trained surgeons with experience in hepatobiliary and laparoscopic surgery. Therefore, national and international societies should become involved in the goal of establishing training standards to ensure consistent applications and clinical outcomes. These principles have led our group to explore and mobilize about 88 cadaveric livers (88 repetitions). Exposure and mobilization of the right hemiliver remain problematic. The correct positioning of the cadaver on the dissection table with thick cushions behind the right shoulder and buttock is essential. This allow the right liver to fall toward the left hypochondrium, exposing the right triangular ligament during the first step of the dissection.Several technical and technological advances account for the increased safety, all of which aim at preventing intraoperative bleeding. These include the vascular clamping of the portal pedicle (Farges et al., 2002). Our results indicate that mobilization and clamping of the portal pedicle, which is the vascular control technique of reference, can be used safely after the second step of the liver mobilization.During the third step, the Glisson's capsule extends as a condensation of fascia around the biliary and vascular branches of the portal triad (Glissonian sheaths). Therefore, if the segmental supply branches are approached from within the liver parenchyma, ligation of a sheath will devas-

cularise the segment. Glisson's capsule structures within the hepatic substance do not need to be dissected individually; the sheath can be ligated en masse (Gagner et al., 2004). In the third step of the mobilization, we used the HCL to expose the right hepatic vein (Morjane et al., 2008) and the VL to expose the left hepatic vein and the common trunk (Dahmane et al., 2009). Several authors described "Arantius ligament" approach to the left portal pedicle. It was stated that the division of the venous ligament is a useful step to obtain quick access to the left portal pedicle (Machado et al., 2004; Sareli et al., 2009). Other authors used the VL –as we did- to expose the middle and left hepatic vein (Majno et al., 2002). We recommend that further surgical techniques will be conducted to test the applicability of our approach in practice. In conclusion liver mobilization by laparoscopy is not an easy procedure. It requires detailed anatomical knowledge and technical skills in liver surgery and laparoscopy. In the current series of 88 cadaveric liver dissections, we greatly benefited from extensive experience in open liver surgery.

Abbreviations used in this paper

CT common trunk
HCL hepatocaval ligament
IVC inferior vena cava
LHV left hepatic vein
LM liver mobilization
LLM laparoscopic liver mobilization
LLR laparoscopic liver resection
MHV middle hepatic vein
RHV right hepatic vein
VL venous ligament

References

1. *Cherqui, D., E. Husson, R. Hammoud, B. Malassagne, F. Stéphan, S. Bensaid, N. Rotman, P.L. Fagniez (2000) Laparoscopic liver resections: a feasibility study in 30 patients. Ann Surg 232 (6): 753–762.*

2. *Dagher, I., J.M. Proske, A. Carloni, H. Richa, H. Tranchart, D. Franco (2007) Laparoscopic liver resection: results for 70 patients. Surg Endosc. 21(4): 619-24.*

3. *Dahmane, R., A. Morjane, D. Ravnik, M. Hribernik (2009) Anatomy of the Ligamentum Venosum Arantii and its Contribution to the Left Hepatic Vein and Common Trunk Control. Cell Tissues Organs 5: 297-300.*

4. *Descottes, B., F. Lachachi, M. Sodji, D. Valleix, S. Durand-Fontanier, B. Pech de Laclause, D Grousseau (2000) Early experience with laparoscopic approach for solid liver tumors: initial 16 cases. Ann Surg 232 (5): 641–645.*

5. *Farges, O., P. Jagot, P. Kirstetter, J. Marty, J. Belghiti (2002) Prospective assessment of the safety and benefit of laparoscopic liver resections. J Hepatobiliary Pancreat Surg 9: 242–248.*

6. *Gagner, M., M. Rheault, J. Dubuc (1992) Laparoscopic partial hepatectomy for liver tumor. Surg Endosc Abstract 6: 99.*

7. *Gagner, M., T. Rogula, D. Selzer (2004) Laparoscopic liver resection: benefits and controversies. Surg Clin North Am 84: 451- 62.*

8. *Gutt, C.N., V. Riemer, Z.G. Kim, J. Erceg, M. Lorenz (2001) Impact of laparoscopic surgery on experimental hepatic metastases. Br J Surg 88: 371–75.*

9. *Lanitis, S., Ch. Kontovounisios, M. Korontzi, V. Zafeiriadou, Ch. Karaliotas, G. Sgourakis, C. Karaliotas (2010) Laparoscopic Liver Resection: Where Do We Stand Today? Hellenic Journal of Surgery 82(5): 318-323.*

10. *Machado M.A., P. Herman, M.C. Machado (2004) Anatomical resectionof left liver segments. Arch Surg 139 (12): 1346-1349.*

11. *Majno, P.E., G. Mentha, P. Morel, A. Sagelin, D. Azoulay, J. Oberholzer, C. LeCoultre, J. Fazel (2002) Arantius' ligament approach to the left hepatic vein and to the common trunk. J Am Coll Surg 195: 737-739.*

12. *Morjane, A., R. Dahmane, D. Ravnik, M. Hribernik (2008) Anatomy and Surgical Relevance of the Hepatocaval Ligament. Cell Tissues Organs 187: 243-246.*

13. *Sareli, M., I. Chanukvadze, A. Valeanu, D.B. Zippel, R. Shapiro, M.Z. Papa (2009) The posterior intrahepatic approach to the left portal pedicle using the ligamentum venosum: anatomical basis. Surg Radiol Ant 31: 809-813.*

14. *Strasberg, S.M., J. Belghiti, P.A. Clavien, E. Gadžijev, J.O. Garden, W.Y Lau, M. Makuuchi, R.W. Strong (2000) The Brisbane 2000 terminology of liver anatomy and resections. HPB 2: 333-339.*

Corresponding Author
Raja Dahmane,
University of Ljubljana,
Faculty of Health Sciences,
Ljubljana,
Slovenia,
E-mail: raja.dahmane@guest.arnes.si

Fertility in Curitiba, Brazil: levels, trends and differentials

Vania Muniz Nequer Soares[1], Neia Schor[2], Carlos Mendes Tavares[3], Maria Graciela Gonzalez de Morell[4]

[1] Nucleo de Saúde Coletiva do Programa de Mestrado e Doutorado em Disturbios da Comunicacao/Universidade Tuiuti do Parana, e Secretaria Estadual de Saúde do Parana, Brazil,
[2] Departamento de Saude Materno Infantil. Faculdade de Saúde Publica da USP, Brazil
[3] Departamento de Saude Coletiva, Universidade Federal do Acre. Campus Universitario, Rio Branco, AC, Brazil.
[4] Universidade Federal de Sao Paulo, Campus Baixada Santista, Departamento de Saude, Educacao e Sociedade, Brazil.

Abstract

Objectives: To identify levels, tendency and recent differentials in fertility in Curitiba, Brazil.

Methods: It is a quantitative and temporal series study, in which the birth rates, general and total fertility indicators, for the period of 1995-2007, were calculated and analyzed in Curitiba, Brazil, as well as the proportion of women with high fertility in 2005-2007, compared to the state of Parana. In order to evaluate inner regional differences in the city of Curitiba the same rates were calculated for each one of the administrative districts in the capital.

Results: It was noticed a tendency of decline in fertility rates in Curitiba. The total fertility rate in 2007 was 1.49 children per woman and 1.66 in Parana state. The proportion of women with high fertility in the interior of Parana was 1.8 times higher than in the capital. The analysis of fertility rates by districts in Curitiba pointed out important differences: only 10 out of 75 districts had total fertility rates higher than 2.1 children per woman, and 9 districts concentrated 59.6% of women with high fertility.

Conclusions: Curitiba showed a quick and sharp reduction in fertility rates. However, the inner regional differences in the city suggests the need to devise actions of reproductive health and social measures, directed to specific groups of population.

Keywords: Family planning. Fertility. Health reproductive.

Introduction

Brazil is undergoing a profound and rapid demographic change, with significant changes in its age structure. The main variable responsible for these changes is fertility, which has shown steady reduction. As a result of a fertility situated at very low levels there is currently progressive decrease in the absolute volume of the juvenile quota. Thus, expanding the opportunities for the improvement of policies for this population segment, however, at the same time the elderly population over 60 years and their demands are rapidly growing [1].

Fertility is, therefore, a key indicator to be considered by health professionals and managers, since they can support and guide public policies and actions targeting different population groups in the coming decades in Brazil [1].

On the other hand, the Pan American Health Organization (PAHO, 2007) indicates that while the total fertility rate in Latin America has also reached relatively low levels, around 2.6 children per woman, the social, economic and inequities in the provision of contraceptive methods would determe the fertility differentials between states and municipalities, which are disturbing and should be considered in policy making in general and health, in particular, in each country [2-5].

Estimates of the Population Reference Bureau [6] in 2009 indicate growth of the global population of 1.2% per year. The most developed countries grow 0.2% per year and less developed countries grow around 1.4% per year. These differences in population growth are related to fertility rates in developed countries that would be close to 1.7 children / woman while in developing countries it remains at 4.6 children per woman. The global fertility rate was 2.6 children / woman in the same year [6].

The estimated world population for 2009 was 6.8 billion people. Brazil, with approximately 191 million people would be in 15th place among the most populous countries in the world, behind China, India, USA and Indonesia. However, estimates

indicate that in 2050, due to low fertility rates and population growth today, Brazil would be the 8th place, behind India, China, United States, Indonesia, Pakistan, Nigeria and Bangladesh [6].The trend of Brazilian fertility to decline began in the 1960s when the average number of children per woman, which stood at around six in the period, underwent a sharp fall in the following decades, reaching a rate of 2.4 children per woman in 2000 [7]. In 2003, the total fertility rate was 2.1 children per woman in the country, reaching the level of population replacement. Nonetheless, there were still significant differences between regions.In 2006 the country reached a birthrate of 1.8 children per woman, with a reduction in spreads between regions [8, 9]. There is, hence, a tendency toward equalization of fertility rates at low levels throughout the country, although differences remain to be identified from the breakdown of the regional and municipal analysis [10]. Thus, despite the improvement of indicators in Brazil, the existence of quotas for women with high fertility, usually those in a state of social need, can not be ignored [10].According to Berquo and Cavenaghi [10], the percentage of women aged 15 to 49 years old with five or more children in Brazil fell 11.1% in 1991, it decreased 6.6% in 2000 and reduced 4.1% in 2004. In absolute terms, they estimated at approximately four million women of reproductive age with five or more children in 1991, three million in 2000 and two million in 2004. Education and income of these women were still negatively correlated with high levels of fertility [10]. Thus, despite the decline in the proportion of women with high fertility, it is necessary to identify such populations, in order to reduce social inequalities [10].Therefore, we aimed to identify the levels, trends and differentials in fertility in Curitiba city, capital of Parana state, Brazil.

Methods

This study is part of a larger study that investigated the reproductive behavior of women with high fertility in Curitiba city [11]. This is a quantitative study based on data from the Information System Ministry of Health (SINASC), census data, 1991, 2000, from the Brazilian Institute of Geography and Statistics (IBGE). This study was also based on population estimates for the periods between censuses, conducted by the Instituto Paranaense de Desenvolvimento (IPARDES). In addition, we also considered population data by age and sex and neighborhoods, provided by the Institute for Urban Research and Planning of Curitiba (IPPUC).We carried out the calculation of birth rates and general fertility, specific and total period of 1995-2007, and calculating the proportion of women with high fertility in the period 2005-2007, the city of Curitiba and the rest of the state of Parana (Table 1).To identify the differences between regions in Curitiba, fertility rates were calculated by neighborhoods. Population data by age, by sex and districts were obtained from the IPPUC-Research Institute of Urban Planning of Curitiba [12, 13], which has estimated and provided data. The study was approved

Table 1. Definition of annual indicators used in the analyzes

Indicator	Description
Birth rate (BR)	Total number of resident live births / SINASC / MS divided by the total resident population / IPARDES or IBGE, per 1000 habitants [9].
General fertility rate (GFR)	Total number of live births of residents / SINASC / MS divided by female population 14-49 years of age living / IBGE or IPARDES expressed per 1000 women 15-49 years [9].
Specific Fertility Rates (SFR)	Number of live births to mothers living in a certain age / SINASC / MS divided by the total female population residing in this age group / IBGE or IPARDES or IPPUC [9].
Total Fertility Rate (TFR)	Sum of specific fertility rates for women 15-49 years old living, multiplying by 5, which corresponds to the interval between age groups (15-19, 20-24, 25-29, 30-34, 35 - 39, 40-44, 45-49) [9].
Proportion of women with high fertility rates	Number of mothers with five or more live births residents / SINASC / MS in relation to total live births x 100.

Source: RIPSA, 2002 [9].

by the Ethics Committee of the Faculty of Public Health, University of Sao Paulo.

Results

In Curitiba city, the Total Fertility Rate (TFR), which was 2.1 children per woman in 1995, dropped to 1.49 children in 2007, representing a reduction of 29.7% in the city, with a consequent drop in birth rates and general fertility. We also observed a negative growth of around 37% in that period. For the state of Parana, including the capital, the total fertility rate was estimated at 1.66 children per woman in 2007 (Table 2).In Curitiba city, 3.0% of women had high fertility rates (≥ 5 live births) in 2005, this percentage decreased to 2.7% in 2007. In the interior of Parana (excluding other capital cities) the proportion of women with high fertility was 5.5% in 2005 and it rose to 4.9% in 2007 (Table 3).Figure 1 presents the specific fertility rates by age in Curitiba, it appears that the cusp curve of fertility changed in the age group 20-24 years, from 1995 to 2000, for the age of 25 -29 years from 2001.

We identified significant reduction of fertility rates at 15 to 19 years old, 77 per thousand women in 1995 to 44.9 per thousand women in 2007, resulting in a reduction of 41.7%. In the age group range of 20-24 years old this rate decreased from 118.4 to 64.44 per thousand women between 1995 and 2007, a decrease of 45.6%. The reduction was less pronounced at 45-49 years old, followed by the 25-29 and 34-39 years old range. In the range of 35-39 and 40-44 years old there was a small increase in specific rates of fertility, approximately 4% during the same period (Figure 1).

By analyzing the total fertility rates and specific women aged between 15 and 19 years old, and the number and percentage of women with high fertility, according to Curitiba, it was observed that the neighborhood of Campo Santana, Parolin, Prado old, Riviera, Tatuquara and Umbara were those who exhibited the highest specific fertility rates from 15 to 19 years old (Table 4). A total of nine districts in descending order, the Industrial City, Ranch Fence, Uberaba, Cajuru, Tatuquara, Parolin, Boqueirao, Xaxim, Pinheirinho, presented the highest percentages of women with high fertility, representing 59.6% of women with high fertility five (or more children) (Table 4).

Seventeen districts did not present mothers with five or more live births in 2005 (22% of the 75

Table 2. Birth rate, fertility rate and general fertility rate in Curitiba and Parana, from 1995 to 2007. BR-birth rate, GFR-General fertility rate, TFT-Total fertility rate

Year	BR (Per 1,000 hab)		GFR (Per 1,000 women from 15 to 49 years old)		TFR (N of children per women from 15 to 49 years old)	
	Curitiba	Parana	Curitiba	Parana	Curitiba	Parana
1995	21.52	22.4	69.76	80.55	2.12	2.39
1996	20.19	21.70	68.14	79.24	2.10	2.37
1997	19.68	21.38	66.57	77.83	2.08	2.37
1998	18.72	19.99	63.18	72.32	1.99	2.22
1999	18.88	19.85	62.84	71.29	1.99	2.21
2000	18.50	18.73	60.70	67.12	1.95	2.11
2001	16.71	17.22	54.98	61.87	1.77	1.96
2002	16.02	16.82	52.47	60.31	1.71	1.92
2003	14.86	15.85	48.48	56.71	1.59	1.82
2004	14.89	15.89	48.17	56.73	1.59	1.84
2005	13.95	15.58	45.98	56.23	1.53	1.83
2006	13.82	14.77	45.42	53.19	1.53	1.74
2007	13.39	13.95	44.08	50.28	1.49	1.66
Variation % 95-07	-37.8	-37.7	-36.8	-37.6	-29.7	-30.5

Based on SINASC/MS, IBGE e IPARDES.

Table 3. Number and percentage of live births per woman in Curitiba, Parana state and Interior in 2005, 2006, 2007.

Live births	2005		2006		2007	
	N	%	N	%	N	%
Curitiba						
One	11.942	48,7	12.276	49,7	12.189	50,1
Two	7.573	30,9	7.635	30,9	7.603	31,2
Three	3.108	12,7	3.054	12,4	2.966	12,2
Four	1.152	4,7	1.034	4,2	923	3,8
> Five	**736**	**3,0**	**708**	**2,9**	**662**	**2,7**
Ignored	4	0,0	2	0,0	6	0,0
Not informed	3	0,0	6	0,0	4	0,0
Total	**24.518**	**100,0**	**24.715**	**100,0**	**24.353**	**100,0**
Interior do Paraná						
One	57.117	42.2	56.231	43.6	53.815	44.0
Two	41.418	30.6	38.854	30.1	37.196	30.4
Three	20.245	15.0	18.693	14.5	17.556	14.3
Four	8.553	6.3	7.922	6.1	7.275	5.9
> Five	**7.479**	**5.5**	**6.708**	**5.2**	**6.027**	**4.9**
Ignored	97	0.1	50	0.0	32	0.0
Not informed	482	0.4	464	0.4	513	0.4
Total	**135.391**	**100.0**	**128.922**	**100.0**	**122.414**	**100.0**
Paraná						
One	69.059	43.2	68.507	44.6	66.004	45.0
Two	48.991	30.6	46.489	30.3	44.799	30.5
Three	23.353	14.6	21.747	14.2	20.522	14.0
Four	9.705	6.1	8.956	5.8	8.198	5.6
> Five	**8.215**	**5.1**	**7.416**	**4.8**	**6.689**	**4.6**
Ignored	101	0.1	52	0.0	38	0.0
Not informed	485	0.3	470	0.3	517	0.4
Total	**159.909**	**100.0**	**153.637**	**100.0**	**146.767**	**100.0**

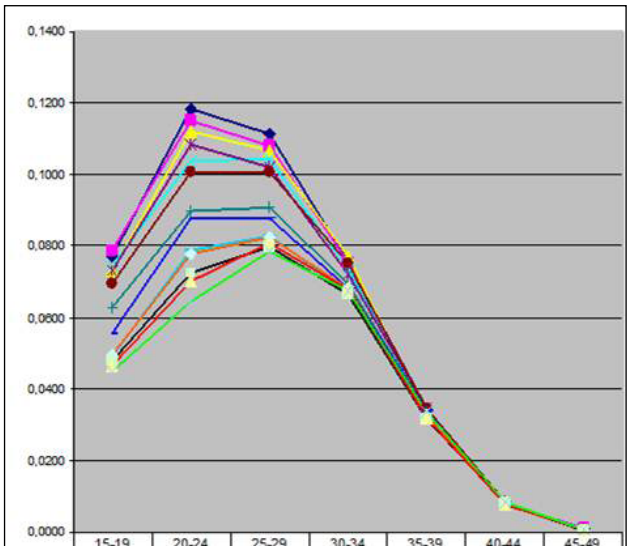
Based on SINASC/MS.

city districts), which included Ahu, Alto da Gloria, Bom Retiro, Bacacheri, Cascatinha, Fanny, Hugo Lange, Social Garden, Juvevê, Lamenha Small, Mercy, Mossunge, Riviera, Seminar, San Miguel, Taboao and Vila Isabel (Table 4). Figure 2 shows the distribution of total fertility rates according to neighborhoods in Curitiba city. The neighborhoods with the highest fertility rates were located in the south, while the central and surrounding neighborhoods presented the lowest rates.

Discussion

The study showed that in Curitiba there was a rapid and sharp drop in fertility rates during the study period. The current rate of 1.49 children per woman, found in Curitiba, is similar to European countries and other developed countries, experiencing the known post-demographic transition, or the second demographic transition, when rates reached levels below the level of population replacement (2.1) [6, 14].

According to Bongaarts [14], past and future trends in fertility in rich / developed countries are influenced by socioeconomic, psychosocial and cultural development attributes of these countries and the low fertility of the difficulties of women in contemporary industrialized societies, in reconciling the care of children with career as well as the increase of individualism and consumerism. It states that this process would determine a "second demographic transition". This new transition wo-



	15-19	20-24	25-29	30-34	35-39	40-44	45-49
1995	0,0770	0,1184	0,1113	0,0756	0,0324	0,0079	0,0008
1996	0,0788	0,1150	0,1080	0,0756	0,0334	0,0081	0,0009
1997	0,073	0,1121	0,1069	0,0772	0,0327	0,0077	0,0007
1998	0,0744	0,1037	0,1043	0,0734	0,0332	0,0084	0,0006
1999	0,0733	0,1084	0,1022	0,0722	0,0346	0,0075	0,0008
2000	0,0695	0,1006	0,1008	0,0751	0,0345	0,0082	0,0006
2001	0,0629	0,0897	0,0906	0,0694	0,0335	0,0083	0,0005
2002	0,0557	0,0879	0,0878	0,0682	0,0338	0,0080	0,0004
2003	0,0491	0,0787	0,0829	0,0674	0,0321	0,0082	0,0003
2004	0,0495	0,0779	0,0824	0,0681	0,0327	0,0079	0,0004
2005	0,0480	0,0725	0,0798	0,0665	0,0315	0,0079	0,0004
2006	0,0466	0,0701	0,0808	0,0678	0,0318	0,0076	0,0006
2007	0,0449	0,0644	0,0786	0,0674	0,0337	0,0082	0,0005

Figure 1. Specific fertility rate by age group. Curitiba,1995 to 2007. Based om SINASC/MS, IBGE e IPARDES.

uld bring the spread of changes in attitudes and behaviors related to sexuality, contraception, cohabitation, marriage, divorce, which act on fertility, extending its decline.

The study also showed that the total fertility rate estimated for Parana (1.66), was very close to the rate of 1.69 children per woman, estimated to southern Brazil, which showed low fertility rates in different Brazilian regions [9]. According to the DHS-2006, the lowest fertility rate was observed in the southern region (1.66 children per woman) and the highest in the North (2.28 children per woman), which was followed by the Midwest region, with 2.05 children per woman, the Northeast region, with 1.75 children per woman, and the southeastern region with 1.72 [9].

In this context, it would suggest to the rulers, and new studies, to identify reasons that would determine the low fertility rates in Curitiba city and Parana state. Moreover, studies to find risk groups which do not have access to reproductive health services are also recommended.

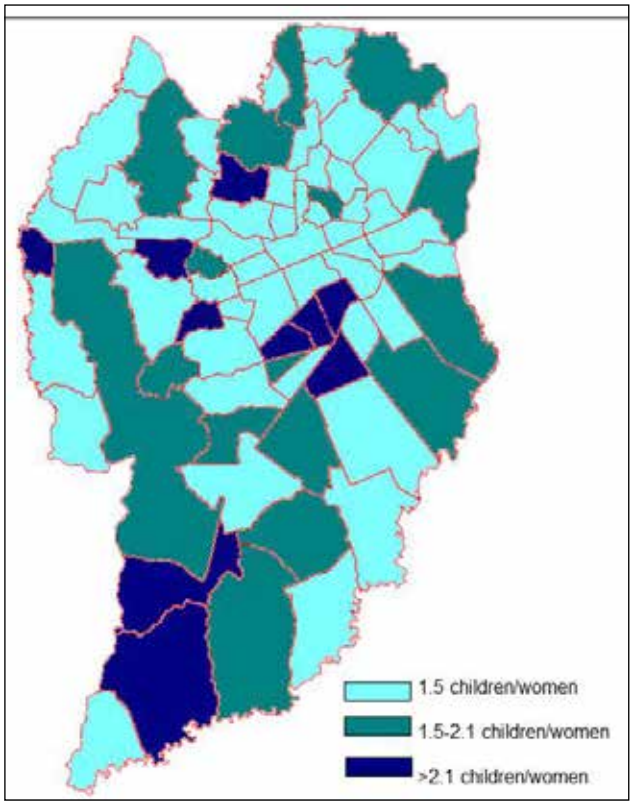


Figure 2. Total fertility rate by district, Curitiba, 2005

In Spain, which has one of the lowest fertility rates in the world, 1.24 children per woman, one study found that a significant portion of the female population of childbearing age (7.2%) was exposed to the risk of an unintended pregnancy, which caused the increase in abortion rates in the country (7 per 1,000 women) [15]. In China, a country with the world's largest population, the TFR was 1.6 children per woman, according to estimates of the PRB in 2009. According to Cao et al. [16], the reduction of the population in China was previously considered to be favorable, because of possible environmental and social risks related to overcrowding. More recently, it was found that the reduction in population size may lead to other problems due to aging population. They claimed that survey in 19 provinces in China in 2005 indicated that the increase of income, schooling, and urbanization, and the provision of better jobs, reduced the desire of young women to have children. This fertility reduction was intensified by the family planning policy of "one child". Thus, it is considered that the population policies in this country should encourage women to have more than one child [16].

Table 4. Number and percentage of women with high fertility (five or more children), specific fertility rate (SFR) of women aged 15 to 19 years old, total fertility rate (TFR), by neighborhood of Curitiba, 2005.

Neighborhood	N of women with high fertilify	% of women with high fertility*	TFR 15-19 years olds**	TFR
Cidade Industrial	89	12.2	66.03	1.66
Sitio Cercado	70	9.6	69.81	1.83
Uberaba	60	8.2	47.06	1.64
Cajuru	56	7.7	53.08	1.61
Tatuquara	51	7.0	121.64	2.29
Parolin	29	4.0	107.16	2.45
Boqueirão	27	3.7	36.95	1.25
Xaxim	26	3.6	57.97	1.89
Pinheirinho	26	3.6	47.72	1.47
Bairro Alto	22	3.0	42.40	1.62
Alto Boqueirão	22	3.0	41.25	1.33
Capão Raso	20	2.7	58.57	1.90
Barreirinha	17	2.3	46.02	1.46
Santa Cândida	15	2.1	61.65	1.77
Umbará	14	1.9	84.48	1.98
Fazendinha	13	1.8	65.08	2.02
São Braz	13	1.8	38.53	1.43
Portão	12	1.6	26.66	1.05
Abranches	11	1.5	45.07	1.71
Pilarzinho	10	1.4	44.03	1.52
Santa Felicidade	8	1.1	46.85	1.97
Campo Comprido	8	1.1	37.81	1.37
Campo de Santana	7	1.0	88.26	2.77
Prado Velho	7	1.0	109.21	2.13
Lindoia	7	1.0	55.60	2.02
Ganchinho	7	1.0	51.00	0.94
Santa Quitéria	6	0.8	58.15	3.10
Hauer	5	0.7	53.04	2.53
Boa Vista	5	0.7	26.54	1.27
Tingui	5	0.7	26.61	1.13
Novo Mundo	5	0.7	26.13	1.05
Guaira	4	0.5	56.87	2.56
Guabirotuba	4	0.5	26.10	1.25
Capão da Imbuia	4	0.5	31.50	1.04
Jardim Botânico	4	0.5	34.25	1.03
Centro	4	0.5	17.14	1.00
Vista Alegre	3	0.4	40.00	2.65

Bairros	N of women with high fertility	% of women with high fertility*	TFR 15-19 years olds**	TFR
Campina do Siqueira	3	0.4	63.14	1.58
Augusta	3	0.4	37.62	1.28
Orleans	3	0.4	21.12	1.25
Caximba	3	0.4	54.18	1.24
Santo Inácio	3	0.4	25.48	1.16
Rebouças	3	0.4	11.38	0.85
Cabral	2	0.3	9.07	1.10
Butiatuvinha	2	0.3	24.14	0.83
Tarumã	1	0.1	39.47	1.46
Centro Cívico	1	0.1	4.43	1.39
São Lourenço	1	0.1	30.10	1.24
Cristo Rei	1	0.1	8.13	1.14
Jardim das Américas	1	0.1	11.51	1.12
Batel	1	0.1	7.41	1.09
São Francisco	1	0.1	6.84	1.09
Cachoeira	1	0.1	30.10	0.95
Atuba	1	0.1	22.97	0.91
Bigorrilho	1	0.1	4.78	0.76
São João	1	0.1	13.09	0.69
Água Verde	1	0.1	2.61	0.41
Alto da XV	1	0.1	10.23	0.17
Riviera	0	0.0	150.49	3.68
Mossunguê	0	0.0	43.59	2.27
Juvevê	0	0.0	6.78	1.70
Bacacheri	0	0.0	14.07	1.19
Alto da Glória	0	0.0	7.46	1.11
Ahú	0	0.0	8.49	1.01
Cascatinha	0	0.0	8.94	0.97
Mercês	0	0.0	8.44	0.91
Bom Retiro	0	0.0	33.14	0.85
Hugo Lange	0	0.0	7.99	0.85
Seminário	0	0.0	7.30	0.85
Lamenha Pequena	0	0.0	0.00	0.82
Jardim Social	0	0.0	6.87	0.79
Fanny	0	0.0	9.26	0.27
Vila Izabel	0	0.0	0.00	0.21
São Miguel	0	0.0	0.00	0.00
Taboão	0	0.0	20.22	1.11
Curitiba	731	3%	48	1.53

Based on IPPUC, 2005/ IBGE.

** Percentage of women with high total fertility rate (731 in which there was information in the neighborhood)***

We also reported a differentiation in the composition of the fecundity of Curitiba from the rest of the state. We observed that the proportion of women with five or more children was 1.8 times higher in the rest of the Parana state, which may be related to gaps in access to information and / or contraceptive methods.The analysis of specific fertility rates by age, in Curitiba showed a pattern of dilated fertility [9], in which most women would have children in the 25-29 years old range group. This pattern is consistent with very low fertility rates in the population and distinct from the national standard, which is still at the age of 20 and 24 years old identified in the PNDS 2006 [9, 10]. The postponement of childbearing women is a typical phenomenon of populations that are in the latter stages of the demographic transition [1, 14]. This situation observed in Curitiba, which is expected to reach Brazil in the coming years, may lead to increased risk of pregnancies and new demands to be met. Therefore, in terms of health services, and quality adjustment it should occur in the provision of maternity care for this population group, since the coverage is practically universal [1].The specific fertility rate, aged 15 to 19 years old in Curitiba decreased from 77.0 per thousand in 1995 to 44.9 per thousand in 2007. This rate is below the national rate of 77.1 per thousand in 2006, identified by the PNDS [9]. Among the possible factors related to this reduction in Curitiba we may include the implementation of reproductive health programs, especially the development of educational activities targeted at adolescents in recent years.

In Brazil, even in large urban centers like São Paulo, the fertility differentials persist as a consequence of inequalities in access to better education, income and goods and services, as demonstrated by studies of Martins and Almeida [17] and Yazaki [18], and it is a reality identified by this study, in Curitiba. Goldani [19] states that these differences are related to social inequalities, and, therefore, could affect the life trajectories of men and women, determined primarily by the process of social exclusion suffered by the popular classes. Thus, the expected trajectories of education, work, promotion and security of person and family, did not materialize for a portion of the population. These factors certainly interfere in setting the desired number of children.On the other hand, we must consider that the final fertility is often the result of a number of unexpected individual events, such as failure of contraception, sterility, fetal loss, long waiting time to conception, a combination of unwanted children by sex, divorce, widowhood or death of a child, remarriage, or it is the result of a series of events and experiences that may influence multi related fertility trends [20].

The future demographic and social policies are essential to ensure women and couples the ideal conditions for the free decision of procreation and child rearing.The intention to not have children in Brazil, as shown by data PNDS [9], was expressed by one in ten women, growing to 42.7% among those who already have one or two children. Also, according to PNDS [9], comparing the number with the ideal number of alive children, it was found that children from three women presented more children than desired, even the difference of 2 to 3 children.Even though random variations may occur in the analysis of indicators by districts of Curitiba, due to the relatively small numbers of such groups, it can be stated that the neighborhoods that had the highest fertility rates in Curitiba, are located in the south of the capital, most populous, settled recently, with large areas of invasion or slums. In part, the maintenance of a group of women with high fertility, even in large urban centers, would be determined by social inequalities and the difficulty of access to contraception, because of remittances, not always regular contraceptive methods sent by the Ministry of health, which are most dependent on states and cities, including Curitiba and Parana state. This is because, in practice, according to Osis et al [21], the family planning program occupies the second place among health actions, not valued or understood as an essential component of primary care and it is still prioritized the mother and child actions.Thus, the differences in fertility in Curitiba showed that the neighborhoods identified in the study deserve attention directed by the municipal government aimed to assess possible gaps in health care and social protection, especially for women who remain in a regime of high fertility as well as the interior of Parana state.The study indicated a trend of declining fertility rates, suggesting that reductions may continue to occur

in the coming years, in Curitiba, Parana, Brazil. In order to remain fertility rates closer to replacement level, governments will need to articulate the economic support and maternity protection. The challenge for governments is to protect women who want children, guaranteeing employment, adequate health care and security for raising children, including the quality and humanized birth, the construction of kindergartens, schools and access to housing [15].Finally, we concluded that the programs of primary health care should include among its lines of action, the increase in quantity and quality, offering reproductive health care including contraception, reducing inequalities still present, regarding such shares in Brazil, and because of changes in age structure, the government must prepare itself to meet the demands of the elderly growing population [1].

Acknolewdgements

This study received financial support from FAPESP.

References

1. *RIPSA Rede Interagencial de Informações para Saúde. Demografia e saúde: contribuição para análise de situação e tendências / Rede Interagencial de Informações para Saúde. – Brasília: Organização Pan-Americana da Saúde, 2009*

2. *Godinjak Z, Huki M. Sex determination of the Bosnian population based on discriminant function analysis. HealthMED J, 2012;6:694-698.*

3. *Vertamatti MAF, Abreu LC, Otsuka CF, Costa PRF, Drezett J, Tavares C, Santos ME, Barbosa CP. Factors Associated to Time of Arrival at the Health Service after Sexual Violence. HealthMED J, 2012;6:37-41.*

4. *Torigoshi MF, Valenti VE, Siqueira AAF, Reis AOA, Leone C, Abreu LC. Outcomes of newborns admitted in the intensive care unit at a public hospital. HealthMED J, 2011;5:295-300.*

5. *Abreu LC, Valenti VE, Oliveira AG, Leone C, Siqueira AAF, Gallo PR, Fonseca FLA, Nascimento VG, Saldiva PHN. Effects of physiotherapy on hemodynamic variables in newborns with acute respiratory distress syndrome. HealthMED J, 2011; 5:528-534.*

6. *OPAS. Organização Pan-americana de Saúde. Salud en las Américas. 2007. Disponível em URL: http://www.paho.org. [2008 out 8]*

7. *PRB. Population Reference Bureau 2008. World population data sheet. USAID. Washington. DC. USA. 2009. Disponível em URL: http://www.prb.org/pdf09/09wpds_sp.pdf. [2010 dez 20]*

8. *Brasil. Ministério da Saúde. Saúde Brasil 2004: uma análise da situação de saúde. Brasília: Ministério da Saúde; 2004.*

9. *IPEA. Instituto de Pesquisa Econômica Aplicada. PNAD 2007. Primeiras análises Demografia e Gênero. Brasília. 2008. Disponível em URL: http://www.ipea.gov.br. [2008 nov 30].*

10. *Brasil. Ministério da Saúde. Pesquisa Nacional de Demografia e Saúde da Criança e da Mulher: PNDS 2006. Brasília: Ministério da Saúde; 2008.*

11. *Berquó E, Cavenaghi S. Fecundidade em declínio: breve nota sobre a redução no número médio de filhos por mulher no Brasil1. Novos Estudos, 2006; 3: 74-81.*

12. *Soares VMN. Intenções e comportamento reprodutivos de mulheres que vivenciam alta fecundidade em um grande centro urbano. [tese doutorado] São Paulo: Faculdade de Saúde Pública, Universidade de São Paulo; 2009. Disponível em URL: http://www.teses.usp.br. [2010 dez 20]*

13. *RIPSA. Rede Interagencial de Informações para a Saúde. Indicadores básicos de saúde no Brasil: conceitos e aplicações. Brasília: Ministério da Saúde; 2002.*

14. *Instituto de Pesquisa Planejamento Urbano de Curitiba. Bairros Curitiba 2007. Maxigráfica. Curitiba: IPPUC; 2007.*

15. *Bongaarts J. The end of the fertility transition in developing world. Population and Development Rewiew, 2002;28:419-443.*

16. *Lete I, Martinez-Etayo M. La salud reproductiva: datos y reflexiones. Gac Sanit, 2004;18:170-4.*

17. *Cao S, Tian T, Qi F, Ma L, Wang G. An investigation of women's attitudes towards fertility and China's family planning policy. J Biosoc Sci, 2010; 42: 359-75.*

18. *Martins CM, Almeida MF. Fecundidade e diferenciais intra-urbanos de desenvolvimento humano. Rev Saúde Pública. 2001;35.*

19. *Yazaki LM. A fecundidade no município de São Paulo e em suas subprefeituras: algumas características do padrão reprodutivo. In: XIV Encontro Nacional de Estudos Populacionais, 2004. Disponível em URL: www.abep.org.br. [2010 dez 12]*

20. *Goldani AM. O regime demofigura brasileiro nos anos 90: desigualdades, restrições e oportunidades demográficas. In: Saúde sexual e reprodutiva no Brasil. São Paulo: Hucitec/Population Council; 1999.*

21. *Camarano AA. A hipotóse de convergêngia dos níveis de fecundidade nas projeções populacionais. São Paulo: Perspectiva. 1996; 10(2).*

22. *Osis MJD, Fagundes A, Makuch MY, Mello MB, Sousa MH, Araújo MJO. Atenção ao planejamento familiar no Brasil hoje: reflexões sobre os resultados de uma pesquisa. Cad Saúde Pública. 2006; 22(11):2481-2490.*

Corresponding Author
Vania Muniz Nequer Soares,
Nucleo de Saúde Coletiva do Programa de Mestrado e Doutorado em Disturbios da Comunicacao,
Universidade Tuiuti do Parana,
e Secretaria Estadual de Saúde do Parana,
Brazil,
E-mail: vaniam@onda.com.br

Autism and current approaches to nursing

H. Demet Cabar, Gul Sultan Ozeren

School of Health, Sinop University, Sinop, Turkey

Abstract

In social and communication areas due to identification of life-long difficulties, autism, according to the criteria proposed by the American Psychiatric Association in 1994, pervasive developmental disorders are discussed under the main title (1).As in every case, the starting point for a child with autism and his family from the moment of birth is the development stage of each child's place and role of the nurse can not be ignored. The nurses, in every period of life, authenticating of health risks and making plans for improving health, enhance the development of personal growth and health of individuals and societies (2). For this reason, a child with autism and their families should be planned approaches to current nursing.

Autism and pervasive developmental disorders are complex disorders (3). Navigating the deterioration in multiple fields and to deal with these disorders with certain forms could be difficult and misleading. Because generally other disorders may associated with autism (4, 5, 6). For this reason, a wide perspective of nursing approaches determining may have to be multi-dimensional planning. Nursing on the basis of assessment, the child's communication, social, sensory, behavioral skills and the strategies for adaptation should succeed (7). For this reason, ın this study aimed to provide information on autism current nursing approaches.

Key words: Autism, Children, Nursing Approaches, Nursing Diagnoses

Introduction

As a first in 1943, eleven cases described by an American child psychiatrist Leo Kanner and definition of autism used by specifying of difference between those cases and schizophrenia. These children emphasized such as obsession, echolalia, repetitive movements features during definitions, and so these cases are used as criteria for today features to autism. Kanner, these children for being insist on maintaining the sameness and also he mentioned which they couldn't make a proper communications by using appropriate pronouns in making of sentences(8).

In social and communication areas due to identification of life-long difficulties, autism, according to the criteria proposed by the American Psychiatric Association in 1994, pervasive developmental disorders are discussed under the main title (1). As in every case, the starting point for a child with autism and his family from the moment of birth is the development stage of each child's place and role of the nurse can not be ignored. For this reason, ın this study aimed to provide information on autism current nursing approaches.

General Information

Pervasive developmental disorders; social development, cognitive development and communication areas latency with unique deviations are deterministic. An effective group of neuropsychiatric disorders at every stage of life and early-onset (9). The best-known and most studied disorder is indicated into pervasive developmental disorders of autism (10). Disorders in these three areas are regarded as key features of autism:

1. Deterioration in social relations,
2. Deterioration in verbal and nonverbal communication,
3. Obsessive, repetitive behaviors, restricted interests areas have been reported (11, 12).

Autism in DSM-IV, under the name of Pervasive Developmental Disorders Rett Syndrome, Childhood Disintegrative Disorder, Asperger Syndrome and Not Otherwise Specified (CTA Computerized Tomography Arthrography) is in conjunction with Pervasive Developmental Disorders (13,14,9).

The most commonly used diagnostic criteria of autism, the DSM IV (American Psychiatric Association), ICD (International Classification of Disease) and criteria has been accepted by WHO

(World health Organization) and these criteria are adopted by experts associated with autism research. According to the DSM-IV, these criteria are;

A. At least two of them (1). From substance and each of one (2). And (3). Including of substances (1), (2) and (3). A total of six substances (or more) presence of substance:

(1) Presence of at least two of the following and qualitative impaired in social interaction manifesting itself:

(a) To provide social interaction with the hand-arm movements, the body position, the attitude of facial expression, being a significant deterioration as eye contact and more with non-verbal behavior.
(b) Not to develop the appropriate relationships with coevals to the level of developmental.
(c) Having fun with other people, there interests or achievements not to be in search of self to share (ex, not to show, bring or specify their interested objects).
(d) Not to provide social or emotional responses.

(2) Manifested itself by the presence of at least one of the following qualitative impairment in communication:

(a) Being delay in the development of spoken language or never being development (hand, arm or other communication routes, such as facial movements are not to associate the initiative of substitute).
(b) Individuals with adequate speech, a significant impairment when they start talking with others or sustain.
(c) Stereotyped, repetitive or using a special language.
(d) Appropriate level of development of various, imaginary or self to play games base on the counterfeits of social.

(3) Manifesting itself by the presence of at least one of the following behaviors, limited interests and activities, to be repetitive and stereotyped patterns:

(a) Dealing level or focusing on unusual of one or more stereotyped and limited interest within framework of patterns to remain closed.
(b) Specific, non-functional, as usual in everyday tasks or without showing any flexibility to comply with strict to the ritualistic forms of behavior.
(c) Stereotyped and repetitive motor mannerisms (ex, finger snap, hand flapping or twisting or complex whole body movements).
(d) Continuously struggling with pieces of merchandise

B. At least one of the following fields, delays before 3 years of age or extraordinary of one functioning.

(1) Social interaction,
(2) The language used in social communication, or
(3) Symbolic or imaginative game

C. This disorders can not described better with Rett`s Disorder or Childhood Disintegrative disorders (13).

Epidemiology

In prevalence of autism in recent years the whether increase to addressed study, this disorder concluded much prevalent than expected (15). The prevalence of all autism spectrum disorders has reported the number of case which reached in 6.7 per 1000 children (16). Autism Spectrum Disorders, showing widespread with studies of epidemiological indicated as well the frequency of diagnosis of autism debate continues about the causes of increase (17). Known Eric Fombonne with studies on epidemiology of autism, mentioned the 13/10000 frequency of autism in the study of his research between 1996-2004 (18). Frequency of the autism of United States, according to 2007 data provided by the Ministry of Health throughout the country 1/150 the frequency reaches have been reported (19). Also today, one of every 110 children at risk of autism and the condition of about 2.5 million people with first-degree relatives, social and economic life has effects on the participation and integration into society (20).The most current information on the situation in our country;

The world scale, considering of a child has taken 185.000 diagnosis of autism in the primary school (19).

The systematic research and lack of healthy data in the field of autism, both diagnostic stage and diagnostic separation stems to limitations of used methods. Increase in the incidence of autism appears mostly due to the use of different methods mentioned studies. Sample sizes; definition of autism made in limited or such as particularly not otherwise specified Pervasive Developmental Disorders (PDD), PDD to be included in the study of other disorders; educators, parents, and increasing awareness among doctors disorders and particularly mild cases are often known for being reported of important method among the difference.

Possible causes of autism disorder

Neurobiological Basis

Neurobiological basis of autism can be summarized under the following headings;

- Genetic disorders that cause autism,
- Often encountered immune system disorders in autism,
- Development of autism depending on actual diseases such as encephalitis,
- Autopsy brains of autistic children to be detected by neuroimaging or neuroanatomical abnormalities,
- Determination of neurochemical abnormalities in the blood and body fluids of autistic children,
- Electrophysiological studies (EEG) abnormality determination,
- Being of a connection between autism and epilepsy,
- The deficiencies encountered in neurological examination revealed,
- Detection of specific detection in neuropsychological testing,

Familial and Psychodynamic Factors

Generally in autism children mother`s parents are obsessive properties, cultural and socio-economic level is high, widespread belief that people are unable to sufficiently emotional relationship with their children. However, many studies indicated whether the child's life experiences are as descriptive for this disorder (12). Study examined the relationship between ethnicity and mother immigration autism (21) of the relationship between ethnicity and immigration, concluded that the increased risk of autism.

Genetic Factors

Autism is 3-4 times more frequent in males than females, suggesting a genetic basis. According to various studies in the twin autistics, the identical twins from fraternal twins are significantly higher percentage of the genetic basis of autism seen defending the researchers support the idea (11). The genetic of autism is originated, however the exact mechanism of this inheritance is unknown (22, 23). First-degree relatives of individuals with subclinical symptoms of autism mostly encountered with autism are known since the 1950s (10). A comprehensive study addressing the risk factors in autism, genetic transition might be related to advance maternal age specifying the results of the study no shows of increased risk to advanced maternal age has been reported (24). Best of genetic studies are performed on identical twins with autism. However, these genetic studies are difficult to make due to lack of a sufficient number of twins autism cases (11).

Immunological Factors

Between the mother and the fetus has an effort to cause of immune impropriety autism. Mother's antibodies reacted with lymphocytes of some autistic patients and that reason also supports the relationship between autisma, given the damage after the birth (14).

Perinatal and Familial Factors

Breech position, a low Apgar score, 35 weeks premature birth and such as familial psychiatric history risk factors in study are dealt with, familial psychiatric history as the most important variable was associated with autism (24)

Environmental Factors

In literature the autism are not only related to genetic factors but also connected with environmental causes, for example, genetically very similar to each other and expressed not even 70% chance of having twins with autism. An effective in disorders of the immune system such as viruses has reported. Changes of intrauterine blood flow, blood biochemistry, and used drugs with radiation among the environmental factors must be indicated (11)

Some autistic individuals were identified the adversely affected to the symptoms autism of milk and grain consumption. Vaccines in the etiology of autism and mercury poisoning, although the causes were serious discussions on these subjects made research and concluded that there was insufficient evidence on the accuracy (10).

Some Neurological Diseases Associated with Autism

Mental retardation is often accompanied by autism. In addition, children with Fragile X syndrome with presence of autism also have been reported in 2 to 5% (10). Attention deficit hyperactivity disorder in autism, usually accompanied by tuberous sclerosis (TS) for behavioral and psychiatric disorders such as anxiety and aggression. % 1-4 TS are diagnosed with autistic children (25).

Approaches in autism and nursing

As in every case, the starting point for a child with autism and his family from the moment of birth is the development stage of each child's place and role of the nurse can not be ignored. The nurses, in every period of life, authenticating of health risks and making plans for improving health, enhance the development of personal growth and health of individuals and societies (2). For this reason, a child with autism and their families should be planned approaches to current nursing.

Autism and pervasive developmental disorders are complex disorders (3). Navigating the deterioration in multiple fields and to deal with these disorders with certain forms could be difficult and misleading. Because generally other disorders may associated with autism (4, 5, 6). For this reason, a wide perspective of nursing approaches determining may have to be multi-dimensional planning. Nursing on the basis of assessment, the child's communication, social, sensory, behavioral skills and the strategies for adaptation should succeed (7). The nurse in nursing approach to autism; care planning for children and adults, health promotion, nutrition, excretion, activity / rest, cognitive-perceptual space, self-perception, role relationships, sexuality, coping-stress tolerance, and such as security-protection activities of daily living, should take into account that contains the fields. When a nurse planning the maintenance, may have to collect the data, identify nursing diagnoses, identify nursing interventions, apply, to evaluate and keep records.

For excellence in education and application, scientific competence, perceptual awareness and sensitivity is required. This unique synthesis of art and science, nursing and other professions in health areas are among the distinctive features of each other (26). North American Nursing Diagnosis Association (NANDA) - according to Functional Health Patterns will be dealt with by the nursing diagnoses. Children with autism spectrum disorder, in a study of investigating health-related quality of life, evaluates of 286 healthy quality of life according to the child's healthy population was found to be significantly lower (27). This result and the literature with autism baby / children, social relationships, communication, behavioral, and cognitive delay, and deviation may suggest an ineffectiveness diagnosis in sustaining health (28).

Accordingly, the nurses; continuation of the growth and development should aim to ensure an optimum level. To achieve this goal, especially making careful follow-up in primary health care facility is important to keep careful records. To support parents with having infants with suspected autism, the diagnosis of autism, the first stage is placed to the family especially the mother`s intense anxiety reduction and to prevent deviation from care giving role the nurse has a very effective place. A functional approach should not be forgotten that may be able to dress and fed by self (29). In addition, nurse the baby / child and attempts to steer his family centers should be accurate and reliable. Baby's / child's grasp of the family-owned properties to keep expectations achievable and realistic limits is very significant place in the field of health maintenance.

The planning of nursing interventions, parents and the child's social, communication and in behavior areas should be priority to identify strengths and weaknesses (7). Studies related to the eating habits of children with autism; the reasons of more food selection, eating rejection and the development of dysphagia have reported (30). Gastro-intestinal system of children diagnosed with autism related to diarrhea, constipation, esopha-

geal reflux, vomiting, gas pains, and also more symptoms exhibited such as abdominal swelling and discomfort has been proposed. (31,32). 124 children diagnosed with autism constipation, eating habits / food selection in complaints reported to be the difference between the groups are compared with the control group in terms of gastrointestinal symptoms in a study, and emphasized that many behavioral reasons reported much more GIS symptoms in children with autism due to GIS organic source (31). Reviewing of treatment practices in autism related to the gastrointestinal tract gluten and / or casein diet lacking, secretin, ketogenic diet, diet, probiotics / antifungal agents / yeast-deprived diet, specific carbohydrate diet, digestive enzymes, vancomycin, and with famotidine applications encountered. If they also called popular at different times but not enough found with proving of valid scientific data (32).

Food selection and changes in eating habits due to changes in the gastrointestinal tract; dietary imbalance and nutritional risk, less need for the body may occur. Therefore nurse, health sustaining, growth and development should aim for ensuring the provision of adequate-balanced and regular diet. However, in light of this information in the field of discharge, constipation and diarrhea comes to mind (28). Consistency of provision and the normal frequency to these, if you have sustaining the elimination of discomfort and pain may include the intended goals of nursing.

Autistic baby / child should endeavor to know the special features of its own. Feeding and excretory habits need to do regular follow-up to find out. During follow-up recording of the data obtained, digestive system problems such as constipation and diarrhea, not in instant but it may provide long-term detectable benefit. Family, particularly first-degree caregivers (in our society this person is identical with mother however for some reason instead of mother the father or grandmother, aunt, caregivers should not be ignored) is important to ensure cooperation. Health team to emphasize the importance of providing accurate and continuous flow of information with confirming the role of caregiver must be encouraged. Each autistic infant / child is important to consider within their own properties.Some of the diet devoid of gluten and casein on autistic symptoms or behavioral problems has been found helpful information, but this practice banned in foods in the milk, dairy products, almost all grains other than rice, pasta, apples, grapes and other nutrients are very important. This may be difficult to return after getting used to the diet, heavy financial burden to the family may cause conflict between parents and children with them (33). Nurses considering this topic, age / stage of development should be followed according to the state planned to be taken of all foods.

In a study that monitored in terms of special education and autistic symptoms of children with autistic disorder who use drug and evaluated in terms of additional diagnostic features (34) found that attention deficit and hyperactivity problems are high in autistic disorder. It is reported that while some children with autism can be extremely active, some of them can be sluggish, or the same child's extremely active period can be followed by extremely passive extremely period. Meanwhile, frequent sleep disturbance in children with autism is reported. It is mentioned that emergence of sleep disorders such as frequent awakening, crying spells after waking up, getting up early while sleeping late can be seen (5). In autistic children, lack of perception of self and the environment, due to incomplete development of attention control, discomfort in the energy field, deterioration in sleep pattern and risk of activity intolerance in activity-rest field can occur (28). In children with autism, while carrying out daily living activities, nurse should aim provision of the protection of energy field, enough-regular sleep and rest.It should be noted that organizing the leisure activities of autistic children will not be easy. Knowing that they are persistent in doing the same things, drawing their attention to various obfuscations should be proceeded. Audible, bright, animated toys may be preferred. In order to make them get in contact with people rather than objects, hand in hand games, close contact games may be preferred. For the maintenance of healthy eating and training activities, keeping short the periods, removal of distracting objects should be provided. In addition, it is mentioned that nurses are expected to have the knowledge to implement play therapy, behavioral therapy and music on autistic children who has interest (35).

Autistic children's responses to auditory, visual stimuli, pain, hot or cold reactions are indicated

to be deviated from normal according to various sources (4). Children with autism often live disorders in the sensory stimulus. In other words, over-reaction or no reaction to stimuli can be seen. There could be extreme sensitivity to touch problems. Many children can not tolerate to bandages, dressings, arm boards, and blood pressure cuffs. Some noises and smells can trigger inappropriate behavior (7).In autistic infant/child, related to the disruption of sensory responses distortion of sensory perception, distortion in processes of thinking, distortion in the communication and distortion in interpretation of the environment syndrome can be seen in cognitive-perceptual field (28). In cognitive-perceptual process, infant/child's becoming better in their own condition should be aimed in this field in terms of nursing. Adopted therapy, in general, is cognitive behavioral methods and special education (12). With this approach, while maintaining the infant/child from isolation, albeit limited, socializing, spending their leisure time effectively and gaining some self-care skills such as washing their face can be considered as objective to be achieved (28).Behavioral problems are among the most challenging and stressful issues towards effort to provide educational programs for schools and parents of children with autism (and other children) (36). In adolescents with autism, in addition to compulsive behavior and stereotypes movements, tendency to anxiety, concern, and phobias are observed (6). Parents of children with autistic features have mentioned that their children show off various behaviors that they can not understand such us getting under the bed, cuddling in blankets, self-compressing in narrow spaces. The author addressing the subject of autism has invented a special compression machine for himself/herself and stated that he/she had many benefit from it. Parents of children, who have tantrums due to sensory reasons, have stated that dressing the children with soft cloths that covers most of the body may prevent this problem (37). It is expressed that generally autistic children learn skills in very limited way and show their capacity in very concrete and specific environments, thus, the importance of providing the improvement and usage of skills in different environments is emphasized (38).

Due to significant deterioration in social interaction, discomfort in the concept of individuality, discomfort in body image, deterioration in the definition of individual identity and risk of loneliness can be seen in autistic infants/children (28). For these, nurses should aim to protect the integrity of ego to receive a lifetime health protection. For this purpose, whether parents' expectations are realistic or not can be discussed. Realistic alternatives can be examined. Encouraging parents to ask questions, trying to make the parents, whom baby or child has diagnosed with autism, accept the nursing behavior can be considered among the basic nursing approaches.Quoted from the book that the author is an autistic individual and "expresses the autism from inside": It used the expression "The studies performed in many laboratories in different parts of the world, have showed abnormal results in brain stem function tests of individuals with autism characteristics; and clearly showed the worst results in severely disabled and individuals with non-verbal expression. However, feeling and compassion circuits in the babies who are deprived from the comforting touch may completely dry out" (37). This expression may provide an important insight into the potential of sensory deprivation of autistic infants/children.Usually involvement of a new member in the family causes large changes in the habits and living conditions of the family (39). Care of children with autism is considered to be a challenging experience for families; however, it is indicated that the sources of the problems and their relationship with autistic symptoms is not yet clear (40). Having a handicapped child is very effective on mental health of the parents. To be in a continuous dependence with the child, the requirement of the child to special care and education with constantly worrying about the future are the important dimensions of stress (41). Coping attitudes of mothers of the children with autism, in a study evaluating the relationship between depression and anxiety levels; depression and anxiety symptom levels of these mothers, are determined to be higher than healthy controls. In the same way, depressive symptom levels of mothers are found to be higher compared to mother of the children with Pervasive Developmental Disorders and Other Unspecified Disorders (40). It is reported that autistic children do not connect with parents and they do not need to communicate with other people. In infancy they do not cry like most normal babies and are defined as calm and

good-natured babies. It is stated that they can overreact to cradling, kissing, loving as they can be indifferent, they have no or limited eye contact (42). It is mentioned that families with autistic children live in panic, guilt and suffering, and depending on these have difficulty to fulfill their roles (43).

In families with autistic infant/child, deterioration in role relationship depending on family process change, strain in the role of nursing, degradation in the processes of the continuity of family, deterioration in devotion of parent/child and deterioration in social interaction can be seen (28). Aiming to ensure the achievement of saturation in nursing parent and being cared infant/child by developing positive relationships between autistic infant/child and his/her family, nurse could provide a functional structure that family members support continuous care. Assisting the assessment of family situation and approval of the strengths can also be considered as nursing approaches (28). It is important not to accusatory attitude towards family. By showing the positive aspects of the child, willingness to work with the children can be increased in the family; appropriate level of hope for the future should be considered (35). It is stated that the parents, which have a child diagnosed with autism, usually use the approach of avoidance method to get through the stress (44). The stress that arises from having an autistic baby/ or a child occurs as chronicle loss of being right-minded and the anxiety of the incapability of coping with the autism, incapability of coping with the parental responsibilities and chronicle mental anguish(28). The aim to overcome aforementioned stress can be stated as to provide the techniques of getting through the problems and prepare the parents to the situations that induce the sadness. The encouragement for sharing the feelings, the lost hope and dreams through the stress can be provided to the parents. The parents should be reinforced in the developmental duration of intensified loss of rightmindness such as the times that the children with the same age with their child starts to school and sports activities. The parents should also be reinforced to join the support groups that the other parents with having autistic children also attend. It can be useful to make a proper explanation about the sadness that can be passed completely but the parent will have fluctuations in their feeling among the years (28).Autistic child, inability to tolerate frustration, ups and downs in mood, develops of carelessness and agitation in result of being easily excitable. Excessive anger and self wounding also can be seen in behavior disorders (7). Hyperactivity and attention deficit hyperactivity can be seen in many children with autism. Especially in being of very obvious children around the age of two, some of the major problems whether to continue for a long time has become one of the listed (5). Some autistic children and adults that are insensitive to pain severe, which means pain, can be extremely durable. When there is inability to recognize cold to some of them and when there is an increased sensitivity can be seen to cry with the cold water when washing their hands (4).Autistic child, not to be aware of the dangers connected with the deterioration in security-protection may occur trauma / injury risk in detection process (28). Nurses should avoid harming of herself or others in this field of autistic infant / child. For this reason, infants / children which required monitored continuously have to be explained to parents. To teach basic skills such as the Heimlich maneuver to parents can be thought in basic nursing intervention (28). In addition, effective aerobic exercises in the literature showing features of autistic adults with developmental disabilities, for report of reduce aggression and self-harm also may be encouraged to exercise for the later period (45).It may not be easy to provide nursing care to children with autistic disorder. May be performed support to the pair of imitation-role models. Auxiliary temperature measurement on a toy example; first of all measuring of the non-hazardous an object such as a pencil, then the parent after then asked the same to do more from children. Then the thermometer probe of child first used on toy then on his own. The following steps should be praise or reward. The next method, the first order of the nurse, “my turn”, and then the child order “your turn” is carried out in the order form. Children, for example, when it has fulfilled the required product during physical exercise such as “open your mouth”, will be rewarded with an award such as the “well done” verbal. All possible options should be presented to child in every time. For example, “which one of your arm you want me to measure your tension?” Or “which color of cuff you like?”

Option offered in the form. when it need to divert attention, family, school, pets, hobbies, when asking questions about hobbies or favorite toy it may draw attention to another direction, it will be asked to sing everyone`s known song and how to end it (7). He is also an author of autistic scientist T. Grandin; educational and behavioral studies, almost that would be useful in all of individuals with autistic features and states the increase functionality. A good early intervention program, nearly half of children with autistic features normally refer to an elementary school will provide first-class continuation (37). Autistic children, the difference from normal adolescents in the processes of sexual development of adolescents, they also seems in changes of brought lives such as peers. However, during this period perception, comprehension and reasoning skills may be a difference because of slowing down has been reported (46). In a study of 89 autistic individual, stated that frequent sexual behavior problem is masturbation (47). When examined the sexuality of autistics, different from normal individuals, changing, hugging, kissing, or could exhibiting of random behavior, printing and may be subject to penalties (46). Nurse encounters with autistic children, if child has the mental barrier especially about neglect and abuse should be observer and evaluation. Demonstrate the child's privacy due diligence in making this evaluation (48).As result, affects of all life is very large topic to autism as stated earlier. For every period of life for individuals with autism and their families need for a functional nursing approach, requiring of the first step is to understand the world of autism and autistics are different. The next phase in this area is a follower of the social and scientific developments in this area, this knowledge and resources of our skill can professionally move to our areas.

References

1. *Bodur Ş, Soysal A.Ş. Otizmin Erken Tanısı ve Önemi. Sted. Dergisi 2004;13:10,394-98.*
2. *Sayan A. Durat G. Risk Tanılaması Yoluyla Otizmin Erken Teşhisi: Hemşirenin Rolü. Atatürk Üniversitesi Hemşirelik Yüksekokulu Dergisi 2007;10:4,105-113.*
3. *Muhle R, Trentacoste, SV, Rapin I. The Genetics of Autism. Pediatrics 2004;113:5,472-486.*
4. *Korkmaz, B. Otizm: Başlıca Davranış Sorunları ve Pratik Yaklaşım. Yeni Symposium 2001;39:1,26-34.*
5. *http://www.todev.org/otizm/otizme-eslik-eden-durumlar/ Erişim tarihi: Şubat-2012.*
6. *Bradley EA, Ames CS, Bolton PF. Psychiatric Conditions and behavioural Problems in Adolescents With Intellectual Disabilities: Correlates With Autism. The Canadian Journal of Psychiatry 2011;56:2,102-109.*
7. *Souders MC, Freeman KG, DePaul D, Levy SE. Caring for Children and Adolescents With Autism Who Require Challenging Procedures. Pediatric Nursing. November- December, 2000;28:6,555-562.*
8. *Kanner L. Autistic disturbances of affective contact. Nervous Child 1943; 2:217-250.*
9. *Öztürk O, Uluşahin A. Ruh Sağlığı ve Bozuklukları- 2, Yenilenmiş 11. Baskı 2008;744.*
10. *Ulay HT, Çengel Kültür SE. Otizm. Clinic Pediatri 2010;5:6,33-43.*
11. *Korkmaz B. Bir sendrom, bir belirti, bir hastalık: Otizm. Nörobiyolojik temelleri ve nörofonksiyonel mekanizmalar. Sendrom Dergisi 2000;12:4,43-58.*
12. *Şenol S. Çocuk ve Gençlik Ruh Sağlığı. HYB Yayıncılık, 2006. 216-227.*
13. *Amerikan Psikiyatri Birliği. Psikiyatride Hastalıkların Tanımlanması ve Sınıflandırılması Elkitabı, Yeniden Gözden Geçirilmiş Dördüncü Baskı (DSM-IV-TR) Amerikan Psikiyatri Birliği, Washington DC, 2000'den çeviren Köroğlu E, Hekimler Yayın Birliği, 2001.50-52.*
14. *Kaplan HI, Sadock BJ. Klinik Psikiyatri, Çev. Editörü: Ercan Abay, I. Baskı, Nobel Tıp Kitapevleri, 2004. 511-515.*
15. *Gillberg C, Wing L. Autism: not an extremely rare disorder. Acta Psychiatrica Scandınavıca, 1999; 6: 399-406.*
16. *Bertrand J, Mars A, Boyle C, Bove F, Yeargin-Allsopp M, Decoufle, P. Prevalence of autism in a United States population: the Brick Township, New Jersey, investigation. Pediatrics 2001; 108: 1155-1161.*
17. *Volkmar FR, Lord C, Bailey A, Schultz RT, Klin A. Autism and pervasive developmental disorders. Journal of Child Psychology and Psychiatry 2004;45:1,135–170.*
18. *Fombonne E. The Changing Epidemiology of Autism. Journal of Applied Research in Intellectual Disabilities 2005;18: 281–294.*
19. *http://www.otizmplatformu.org/index.php/2011/04/basin-bulteni/. Erişim tarihi: Ocak-2012.*
20. *http://www.tohumotizm.org.tr/Resim/04042011154605.pdf Erişim tarihi: Şubat -2012.*
21. *Keen DV, Reid FD, Arnone D. Autism, ethnicity and maternal immigration. The British Journal of Psychiatry 2010;196:274–281.*

22. *Folstein SE, Bisson E, Santengelo SL, Piven J. Finding spesific genes that cause autism: a combination of approaches will be needed to maximize power. J Autism Dev Disord 1998;28: 439-445.*
23. *Abrahams BS, Geschwind DH. Advances in autism genetics: on the threshold of a new neurobiology. Nat Rev Genet 2008;9:5,341–355.*
24. *Larsson HJ, Eaton WW, Madsen KM, et al. Risk factors for autism: Perinatal Factors, Parental Psychiatric History, and Socioeconomic Status. American Journal of Epidemiology 2005;161:10,916–925.*
25. *Smalley SL. Autism and Tuberous Sclerosis. J Autism Dev Disord 1998;28: 407-415.*
26. *Erdemir F. Hemşirenin Rol ve İşlevleri ve Hemşirelik Eğitiminin Felsefesi. Cumhuriyet Üniversitesi Hemşirelik Yüksek Okulu Dergisi 1998;2:1,59-63.*
27. *Kuhlthau K, Orlish F, Hall TA, Sikora D, Kovasc EA, Delahaye J, et al. Health-Related Quality of Life in Children with Autism Spectrum Disorders: Results from the Autism Treatment Network. Journal of Autism and Developmental Disorder 2010;40:6,721-729.*
28. *Carpenito L. Hemşirelik Tanıları El Kitabı, Erdemir, F. (Çvr. Ed.) Nobel Tıp Kitabevleri, İstanbul. (2005).*
29. *Friedlander AH, Yagiela JA, Paterno VI, Mahler ME. The neuropathology, medical management and dental implications of autism. The Journal of the American Dental Association (JADA) 2006;137:11,1517-1527.*
30. *Field D, Garland M, Wiiliams K. Correlates of spesific childhood feding problems. J. Paediatr Child. Health 2003;39:4,299-304.*
31. *İbrahim SH, Voigt RG, Katusic SK, Weaver AL, Barbaresi WJ. Incidence of gastrointestinal symptoms in children with autism: a populationbased study. Pediatrics 2009;124:2,680-686.*
32. *Şişmanlar ŞG, Karakaya I, Yıldız Öç Ö. Otistik Bozuklukta Yeni Tedavi Arayışları: Gastrointestinal Sistem. Çocuk ve Gençlik Ruh Sağlığı Dergisi 2010;17:1,51-58.*
33. *Bilgiç A, Cöngöloğlu A. Otizm Spektrum Bozukluklarında Biyolojik temelli Tamamlayıcı ve Alternatif Tıp Uygulamaları. Çocuk ve Gençlik Ruh Sağlığı Dergisi 2009;16:3,153-164.*
34. *Akbaş S, Karabekiroğlu K, Pazvantoğlu O, Böke Ö. Özel eğitim ve ilaç alan otistik bozukluklu çocukların otistik belirtiler açısından sekiz haftalık izlemi ve ek tanı özellikleri. Klinik Psikiyatri 2009;12:134-140.*
35. *http://server.karaelmas.edu.tr/saglik/ayse2.htm Erişim tarihi: Şubat -2012.*
36. *Educating Children with Autism. (Catherine Lord and James P. McGee, Ed.) Committee on Educational Inverventions for Children with Autism National Research Council Staff. National Academies Press. 2001:323. Erişim http://site.ebrary.com/lib/bilim/Doc?id= 10032464&ppg=119. Erişim tarihi: 10.12.2011*
37. *Grandin T. Resimlerle Düşünmek, Otizmin İçerden Anlatımı. (Çev: Mehmet Celil İftar). 3. Baskı. TOHUM Otizm Vakfı, Sistem Yayıncılık, İstanbul. 2011. (59-63-76-77-83).*
38. *Psikiyatri Temel Kitabı (2007). Ed. Köroğlu E., Güleç C., HYB Basım Yayın, Ankara. 798-808.*
39. *Brown TE. Dikkat Eksikliği Bozukluğu. Çocuklarda ve Yetişkinlerde Odaklanamayan Zihin. ODTU Yayıncılık. 2010:153.*
40. *Durukan İ, Erdem M, Tufan AE, Tükbay T. Otistik Spektrum Bozukluğu Olan Çocukların Annelerindeki Baş Etme Tutumları ve Depresyon ile Anksiyete Düzeyleriyle İlişkisi. Çocuk ve Gençlik Ruh Sağlığı Dergisi 2010;17:2,75-82.*
41. *Akkök F, Askar P, Karancı N. Özürlü Bir Çocuğa Sahip Anne Babalardaki Stresin Yordanması. Özel Eğitim Dergisi 1992;1:2,8-12.*
42. *Özusta S. Otizim: Tanı ve Ayırıcı Tanı. Eksi, A.(Ed.). Ben Hasta Değilim. İstanbul: Nobel Tıp Kitapevi. 1999. 259-267.*
43. *Üstüner Top F. Otistik Çocuğa Sahip Ailelerin Yaşadıkları Sorunlar ile Ruhsal Durumlarının Değerlendirilmesi: Niteliksel Araştırma. Çocuk Dergisi 2009; 9:1, 34-42.*
44. *Özyıldız S, Gürkan A, Yıldırım S. Otistik Bozukluk Tanısı Almış Çocukların Ebeveynlerinin Stresle Başa Çıkma Stratejileri Ve Etkileyen Faktörler. IV. Ulusal Psikiyatri Hemşireliği Kongresi Özet Kitabı 2010:144.*
45. *Elliott RO, Dobbin AR, Rose GD, Soper HV. Vigorous, aerobic exercise versus general motor training activities: Effects on maladaptive and stereotypic behaviors of adults with both autism and mental retardation. Journal of Autism and Developmental Disorders 1994; 24: 5,565-576.*
46. *Küçük L, Buzlu S. Otistik Çocuklarda Ergenlik ve Cinsel Eğitim. Androloji Bülteni, Haziran, Sayı 25, İstanbul. 2006. 93-94.*
47. *Van Bourgondien ME, Reichle NC, Palmer A. Sexual behavior in adults with autism. J. Autism Dev. Disord. 1997;27:2,113-125.*
48. *Gönener HD. Zihinsel Engelli Çocuklarda İhmal-İstismar ve Hemşirelik Bakımı. Journal of Experimental and Clinical Medicine 2010; 27:137-143.*

Corresponding Author
Gul Sultan Ozeren,
School of Health,
Sinop University,
Sinop,
Turkey,
E-mail: qulsultan@gmail.com
gonener@hotmail.com

Diagnostics and treatment of liver injuries in polytrauma

Goran Vukovic[1], Zeljko Lausevic[1,2]

[1] Clinical Center of Serbia, Clinic for Emergency Surgery, Serbia,
[2] University of Belgrade, Faculty of Medicine; Serbia.

Abstract

Trauma is one of the most serious and most expensive health problems and most common cause of death in youth. In last decade, non operative treatment is the standard treatment strategy in blunt liver injuries in haemodynamic stable patients.

Methods: restrospective study included patients with liver injury admitted between May 2005 and May 2012. in the Center for Emergency Surgery of the Clinical Center of Serbia. Total number of patients was 224.

Results: Out of 224 patients with liver injuries, 183 had blunt injury, and only 41 had penetrant injury. Isolated injury was found in 25.9% of patients, and 74.1% had multiple injuries. Average Injury Severity Score (ISS) was 22.48 (SD=12.16). Patients underwent intraoperative classification according to Moore. In 2% of patients who were haemodynimically instable we used "damage control surgery". Out of 224 patients, 89,7% were successfully treated, 2,7% died as „mors in tabula", or within first 24 hours, and 7.6% died during hospitalization.

Conclusion: Modern diagnostic procedures provided a much more precise verification of liver injuries associated with polytrauma and reduced mortality. Higher percentage of patients with non-operative treatment was among patients with ISS lower than 10, and among those with injuries grades I and II.

Key words: polytrauma, liver injury, ISS, diagnostic procedure

Introduction

Liver injuries are, even today, object of many studies which aim to improve diagnosis as a mean for better injury treatment [1,2]. In the last decade, it lead to a significant decrease in mortality, especially in patients with liver injuries grade III and IV, mostly due to improved sensitivity and specificity of certain diagnostic procedures in early detection of isolated as well as concomitant liver injuries[3,4,5].

Pringle manouever significantly improved surgeons' ability to assure hemostasis. Perihepatic packing and planned re-exploration are part of the concept of „damage control" when the operation must be terminated in conditions of hemodynamic instability and coagulopathy. Today, possibilities to treat juxtahepatic vein injuries with or without intracaval shunts, are available[6,7]. Certainly, in patients with injuries of lower grade (I, II or III) emphasis is on non-operative treatment which requires all available diagnoistic procedures as well as continuous monitoring of injured patient[8].

Aim

The aim of the study was to perform clinical assessment of certain diagnostic methods and procedures in early detection of liver injuries, as well as their significance in making decision for adequate treatment. The objective was to assess senzitivity, specificity and prognostic value of various procedures and methods which are used in detection of liver injuries associated with blunt abdominal injury. The objective was also, to compare patients with conservative and those with operative treatment, and patients with isolated and concomitant injuries, as well as to estimate the proportion of patients with non-operative treatment.

Methods

For those purposes, a retrospective study design using data collected in the Center for Emergency Surgery of the Clinical Center of Serbia was used. All patients with isolated or concomitant liver injury addmitted from May 2005 until May 2012 were included, total of 224 patients. Patients underwent following diagnostic procedures:

peritoneal lavage, biochemical analysis, X ray of thorax and CT of abdomen, as well as ultrasonography. In order to provide as objective as possible assessment of severity of the injuries, we calculate ISS for all patients. Diagnostic procedures such as peritoneal lavage, echotomography, computerised tomography and laparoscopy diagnostic procedures were analysed[9,10,11,12]. Their sensitivity, specificity, positive and negative predictive value were calculated in order to demostrate how those diagnostic procedures can detect and assess severity of isolated and concomitant liver injuries[3,4,5,13,14].

The sensitivity of a test is the proportion of patients who had positive operative finding who tested positive for it (Echo, CT, PL): Se= A/ (A+C)

The specificity of a test is defined as the proportion of patients who did not have positive operative finding who would test negative for it. Sp= D/ (B=D)

Positive predictive value is defined as the proportion of those with a positive test result who actually had positive operative finding: PPV = A/ (A+B)

Negative predictive value is defined as the proportion of those with a negative test result who did not have positive operative finding: NPV = D/ (C+D)

Prevalence is number of cases with positive operative finding: P = (A+C) / (A+B+C+D)

Results

Patients' distribution by sex and age showed that there was a higher proportion of male patients, 156 (69.9%) comparing to female, 68 (30.4%). The youngest patient was 14 year old, and the eldest was 78. Average age was 33.75 years with standard deviation of 7.2 years. Traffic accidents were the most common cause of both isolated and concomitant liver injuries. Out of 224 patients, 132 (58.9%) were injured in traffic accidents (as drivers or passangers, or as pedestrians). Blunt injuries were found in 183 (81.7%) of patients, and penetrant injuries were found in 41 (18.3%).

Isolated liver injuries were found in only 58 patients (25.9%), and concomitant were diagnosed in 166 (74.1%) of patients (Chart 1).

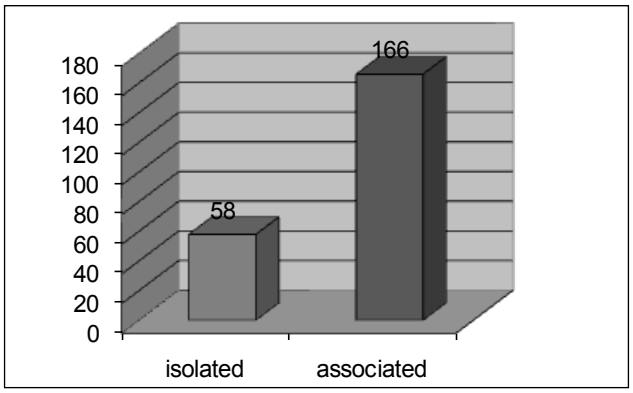


Chart 1. Number of patients with isolated and concomitant liver injuries

Operative findings according to Moore were distributed as follows: 23 (10.0%) as grade I, 72 (32.14%) as grade II, 70 (31.25%) as grade III, 43 (19.2%) as grade IV, 14 (6.25%) as grade V, and 2 (0.9%) as grade VI according to Moore's classification (Chart 2).

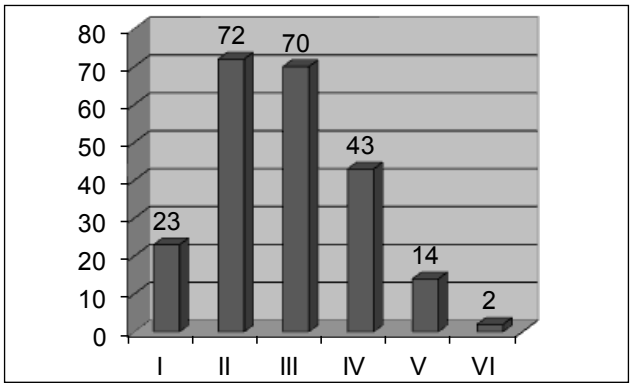


Chart 2. Distribution of cases by injury severity (Moore's classification)

In order to quantify injury severity in patients, ISS was calculated. Value range was between 3 and 75 (which is the hughest possible value). Average value of ISS in our patients was 24.06 with standard deviation of 14.26. Most patients had score 27, namely 55 (24.55%) of them. Among our patients, 54 (22.1%) had ISS over 29, which are considered to be very severe injuries with possible lethal outcome. ISS value less than 29 was found in 170 patients (75.89 %) (Chart 3).

Multiple linear regression was used to obtain the model of operative finding according to Moore. As independant variables: sex, penetrant liver injury, associate liver injury, duration of golden hour and ISS, were used. Analises showed that ISS was highly significant and concomitant liver was significantly associate with operative finding. Higher ISS was associated with higher value of operative finding acoording to Moore classification. Also, isolated liver injury was associated with higher grade injury according to Moore's classification (Table 1). Analysis of average ISS by outcome, occurence of surgical and non-surgical complications, concomitant injuries, type of operation, re-intervention, type of injury and treatment showed that average ISS was significantly different between patients who died and those who were successfully treated, between those who had and those who didn't have surgical complications, between those who had and those who didn't have concomitant injuries, as well as between those who underwent operative and those who underwent non-operative treatment.

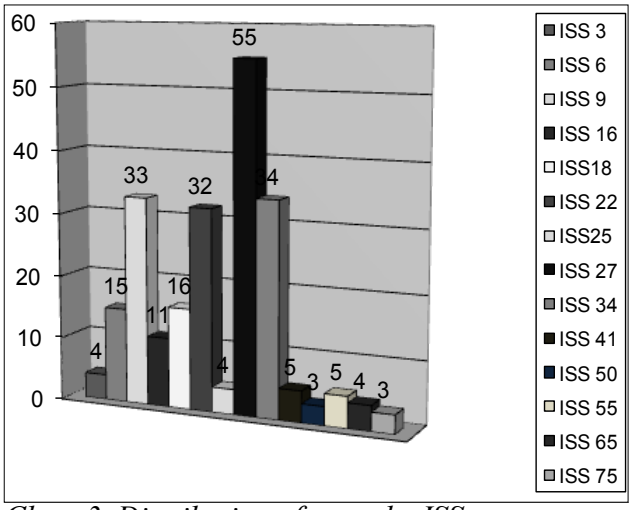


Chart 3. Distribution of cases by ISS

Significantly higher ISS was found in patients with complications, concomitant injuries, those who underwent operative treatment and those who died. In patients who underwent operative treatment, most frequent type of operation was suture of the heaptic parenhyma, and it was performed in 72.76% of cases. Resectional debridement was performend in 11% of cases. In only a few cases (3%), left or right lobectomy was necessary. In even fewer cases, only 2% of them, tamponade (prehepatic packaging) was needed in order to establish hemostasis.

Out of 224 patients 201 (89.7%) were successfully treated, and 23 died. Among those who died, 6 (2.7%) died as »mors in tabula«, and 17 (7.6%) died in the post-operative period. Of those who underwent non-operative treatment, there were no lethal outcomes (Table 2).Statistical analysis showed that ISS was significatnly correlated to the

Table 1. Average ISS by outcome, complication, concomitant injuries and treatment

Variables		N	Average	SD	T test	p
Outcome	Exitus	23	39.21	17.14	-3.078	0,002**
	Successfully treated	201	23.29	13.64		
Surgical complications	No	181	24.65	13,95	-1.64	0,101
	Yes	26	37.95	14.02		
Non-surgical complications	No	203	21,40	13.16	-3.120	0,002**
	Yes	21	41.38	19.40		
Concomitant injuries	No	64	12.66	12.69	12.34	0,000**
	Yes	160	28.39	12.32		
Type of operation	Sutura plus	44	36.59	14.33	-3.267	0,01
	Only sutura	163	22,10	12.82		
Re-intervention	No	190	24.62	13,75	-2.22	0,027
	Yes	17	40.10	15.76		
Type of injury	Blunt	170	23.59	14.13	-1.55	0.12
	Penetrant	54	26.25	14.73		
Treatment	Operative	207	25.05	13.98	-6.750	0.000**
	Non-operative	17	6.12	2.37		

outcome (with was logical finding), presence of concomitant injuries, type of treatment and complications. Spearman test showed highly significant correlation of ISS and operative finding as well as duration of treatment (Table 3). Surgical complication that were found in our patients were reccurent bleeding, absces, biliary fistulae, dehiscences and sepsa. Multiple logistic regression showed that penetrant injuries were highly significant predictors of surgical complications (Table 4).

Number of blood units administered ranged from 0 to 9 with average of 4.51 per patient. The number of units per patient was relatively high, although it should be taken into account that none of the liquid blood which was found during operation was used. Statistical analysis showed that CT diagnostics is by far the best one for diagnostics of liver injuries grade II. PPV was 100%, sensitivity 94%, specificity 100% and NPV was 97%. Then, we found high validity of CT diagnostics for injuries grade I, III and IV. For liver injuries grade V and VI, CT diagnostics showed high specificity and NPV (23).

Peritoneal lavage showed high sensitivity for liver injuries grade II and higher. For injuries grade I sensitivity was only 67%. For injuries grade II, sensitivity of PL was 94%, and for injuries grade III, IV, V and VI it was 100%. NPV was 100% for injuries grade III, IV, V and VI, however it was only 67% and 33% for injuries grade I and II, respectively.

Today laparoscopy diagnostics is a routine diagnostic procedure in assessing liver injuries. We found that sensitivity of laparoscopy diagnostic was 100% as well as negative predictive value, specificity was 92%, and positive predictive value

Table 2. Average age by outcome, occurence or non-occurence of surgical and non-surgical complicaitons, concomitant injuries, type of operation and re-intervention

Variables		**Age**				
		n	**average**	**SD**	**T test**	**p**
Outcome	Died	23	27,29	6,24	-2,476	0,035*
	Successfully treated	201	33,74	7,32		
Surgical complications	No	181	33,20	7,54	0,988	0,357
	Yes	26	30,17	7,00		
Non-surgical complications	No	203	33,81	7,34	-2,402	0,049*
	Yes	21	27,41	6,19		
Concomitant injuries	No	64	33,57	6,80	0,455	0,653
	Yes	160	32,56	7,79		
Type of operation	Suture plus	64	30,75	6,63	-0,949	0,363
	Only suture	163	33,24	7,63		
Re-intervention	No	190	33,07	7,47	0,674	0,543
	Yes	17	30,25	8,06		

** < 0.05*

Table 3. Spearman coefficient of correlation between operative finding, age, duration of treatment, ISS and duration of golden hour

	Operative finding	Age	**Duration of treatment**	**ISS**	Duration of golden hour
Operative finding	1,000	-0,125	0,277*	0,583**	0,030
Age	-0,125	1,000	-0,089	-0,324*	0,127
Duration of treatment	0,277	-0,089	1,000	0,202	-0,167
ISS	0,583**	-0,324*	0,202	1,000	-0,151

* *p<0,05*
** *p<0,01*

Table 4. Multiple logistic regression model of the occurence of surgical complications

Variables	B	SE	Wald	df	p	RR	Confidence interval
ISS	0,015	0,018	0.77	1	0,77	1,052	0,987-1,123
Duration of golden hour	0,009	0,018	0,411	1	0,45	1,007	0,976-1,040
Penetrant injury	**-4.96**	**0.554**	**8.018**	**1**	**0,000**	**12,295**	**1,258-12,199**
Sex	0,13	0.466	0,78	1	0,779	2,694	0,183-39,579
Isolated injury	0,256	0.570	0,201	1	0,654	1,182	0,64-21,961
constant	-2.430	0.570	6,182	1	0,007		

was 92.5%. Analysis showed that only 17 (7.6%) of patients underwent non-operative treatment, and 207 (92.4%) underwent operative treatment. Higher proportion of those with non-operative treatment was among those with ISS lower than 10 (52 patients in our study, 23.2%).

Discussion

Our objective was to analyse certain diagnostic methods and procedures in early detection of liver injuries, as well as their significance in making decision for non-operative treatment. Most of our patients with liver injuries were traffic accident victims, which is in according with other authors who showed that road traffic injuries are globally rising[15]. Analysis has showed a statistically significant difference in average age of patients who survived and those who died, and between those with and without non-surgical complications. This finding was expected as younger patients are more likely to survive after injury or surgical intervention than the older ones, and they are less prone to non-surgical complications.

When liver injury had been found, the next step was to assess the severity of the injury. Almost all large international studies, which investigated liver injuries and possibilities of quantifying liver injury severity, concluded that ISS was the most valid measure for the assessment[7,16]. Therefore, we too in our study assessed severity of injuries by calculating ISS. Values took range between 3 and 75, with average of 24.06. Taking into account that liver injuries with ISS above 29 (according to American Trauma Society) are considered to be very severe with possible lethal outcome, we can conclude that the average value in our patients was close to the limit for very severe injuries. Our findings confirmed ISS scoring system as valid in quantifying severity of liver injury, which is in accordance with all large international studies [1, 2, 17,18]. Better coordination with transfusion sevice along with better necessary equipment would make it possible to use significant proportion of blood found intraperitonelaly, and therefore reduce number of blood units that must be administered after the operation. We can found that echotomography proved to be extremly sensitive diagnostic procedure in liver injuries grade II, and somewhat less sensitive in liver injuries grade I, III and IV. It has shown high specificity and NPV in injuries grade V and VI. On the other hand, in case that other diagnostic procedures are unavailable, PL could verify liver injuries of grade II and higher, but in case of injury grade I, a false negative result is possible. As laparoscopy diagnostic is practically an operative intervention (as it offers possibility of hemostasis) it can not be performed in patients with non-operative treatment.

Fast and adequate transportation of the injured to a specialized surgical unit along with providing adequate first aid are very important in the management of injured patients[19].

Conclusion

Liver injuries are very frequent in cases of polytrauma. In penetrant abdominal injuries proportion of those with liver injury is 37%, and in cases of blunt abdominal trauma that proportion is 15%. After admittance in specialized surgical unit, which is appropriately equipped for care of polytraumatized patients, it is necessary to start resuscitation until patient is hemodinamically stable.

If it is impossible to stabilise patient, due to massive hemorrhage, it is indicated to perform surgical intervention instantly, and perform surgical hemostasis and achieve hemodynamic stability. Advancement in diagnostics made it possible to raise the proportion of patients with liver injuries that undergo non-operative treatment up to 40-60 %. It is mostly achieved through development of echotomography, CT diagnostics and intoducing laparoscopy diagnostic. Golden diagnostic standard for patients suspected for liver injury is to perform CT diagnostic initially as well as during contol check ups, if non-operative treatment was applied.

References

1. *Cogbill TH, Moore EE, Jurkovich GJ, et al. Severe hepatic trauma: A multi-center experience with 1 335 liver injuries. Journal of Trauma 1988; 28:1433.*
2. *Feliciano DV, Mattox KL, Jordan GL Jr, et al. Management of 1 000 consecuive cases of hepatic trauma (1979-1984). Annales of surgery 1986; 204:438.*
3. *Udobi KF, Rodriguez a, Chiu WC, Scalea TM. Role of ultrasonography in penetrating abdominal trauma: a prospective clinical study. Journal of trauma 2001; 3:475-79.*
4. *Richards JR, McGahan JP, Pali MJ, Bohnen PA. Sonographic detection of blunt hepatic trauma: hemoperitoneum and parenchymal patterns of injury. Journal of Trauma 1999; 6:1092-97.*
5. *Poletti PA, Mirvis SE, Shanmugathan K, Killeen KL, Coldwell D. CT criteria for management of blunt liver trauma: correletion with angiographic and surgical findings. Radiology 2000; 2:418-27.*
6. *Pachter HL, Hofstetter SR. The current status of nonoperative management of adult blunt hepatic injuries. American Journal of surgery 1995; 169:442.*
7. *Moore EE, Cogbill TH, Jurkovich GJ, et al. Orgaan injury scaling-spleen and liver (1994 revision). Journal of Trauma 1995;38:323.*
8. *Richardson J, Franklin GA, Lukan JK, et al. Evolution in the management of hepatic trauma: a 25-year perspective. Annals of Surgery 2000; 3:324-30.*
9. *Cuff RF, Cogbill TH, Lambert PJ. Nonoperative management of blunt liver trauma: the value of follow-up abdominal computed tomography scans. American Surgeon 2000; 4:332-36.*
10. *Chen RJ, Fang JF, Chen MF. Intra-abdominal pressure monitoring as a guideline in the nonoperative management of blunt hepatic trauma. Journal of Trauma 2001; 1:44-50.*
11. *Henderson SO, sung J, Mandavia D. Serial abdominal ultrasound in the setting of trauma. Journal of emergency Medicine 2000; 1:79-81.*
12. *Gonzales RP, Dziurzynski K, Maunu M. Emergent extra-abdominal trauma surgery: is abdominal screening necessary? Journal of Trauma 2000; 2:195-98.*
13. *Udobi KF, Rodriguez a, Chiu WC, Scalea TM. Role of ultrasonography in penetrating abdominal trauma: a prospective clinical study. Journal of trauma 2001; 3:475-79.*
14. *Gonzales RP, Dziurzynski K, Maunu M. Emergent extra-abdominal trauma surgery: is abdominal screening necessary? Journal of Trauma 2000; 2:195-98.*
15. *Wang AM, Dalal K. Road Traffic Injuries in Shanghai, China. HealthMed 2012; 1:74-80.*
16. *Moore EE, Shackford SR, Pachter HL, et al. Organ inury scaling-spleen, liver, and kidney. Journal of Trauma 1989; 29:1664.*
17. *Pachter HL, Spencer FC, Hofstetter SR. Experience with the finger fracture technique to achieve intrahepatic hemostasis in 75 patients with severe injuries to the liver. Annales of Surgery 1983; 197:771.*
18. *Pachter HL, Spencer FC, Hofstetter SR, et al. Significant trneds in the treatment of hepatic trauma: Experience with 411 injuries. Annales of Surgery 1992; 215:492.*
19. *Gavrilovic S, Gvozdenovic Lj, Kolarski M, Milic S, Gavrilovic S, AlibegovicJ, Dujmovic F. Transportation of heavily exsanguinated patients – a personal experience. HealthMed 2011;4:873-878.*

Corresponding Author
Goran Vukovic,
Clinical Center of Serbia,
Emergency center,
Serbia,
E-mail: gvuko@eunet.rs

Epidemiological, clinical and diagnostic characteristics of Lyme disease with patients in Vojvodina, Serbia

Jovan Vukadinov[1], Aleksandar Potkonjak[2], Grozdana Canak[1], Dusan Rnjak[1], Radoslava Doder[1], Bjanka Lako[3], Nadica Kovacevic[1], Sinica Sevic[1]

[1] Clinical Centre of Vojvodina, Clinic of Infectuous Diseases, Novi Sad, Serbia,
[2] University of Novi Sad, Faculty of Agriculture, Department of Veterinary Medicine, Novi Sad, Serbia,
[3] Blood Transfusion Institute of Serbia, Belgrade, Serbia.

Abstract

Lyme disease is a multisystemic infection with zoonotic character, caused by bacteria *Borrelia burgdorferi*. In Europe, Lyme disease is spread via ticks from *Ixodes* genus. Variations have been noticed in the number of the newly registered cases, as in the clinical manifestation of this infection in relation to genospecies of the agent. Apart from that, there are significant differences in diagnosing and interpreting the laboratory findings. The aim of this work is to present epidemiological, clinical and diagnostic features of Lyme disease with people in Vojvodina, Serbia.

Altogether 132 patients bitten by a tick were included in the research. Clinical, epidemiological and laboratory tests were performed on them in accordance with the existing defined criteria. For the serological diagnostics ELISA and immunoblot tests were used. In order to prove the existence of *B. burgdorferi* in ticks, using a dark field microscopy, a total of 152 ticks removed from the patients' bodies were examined. The research was conducted during 2011. year.

During the observed period Lyme disease was diagnosed with 58 patients bitten by a tick. With most of them ticks were removed by a professional (91) and completely (111). For most patients (70%) conditions were met for the transmission of the agent of Lyme disease, since ticks had spent more than 3 days in their skin. With one seronegative patient *Borrelia burdgorferi* was isolated from a skin bioptate from the rim of erythema migrans. A rate of ticks infection with *B. burgdorferi* of 19.7% was found. Based on the results of the research one can conclude that Lyme disease is endemically present with people in Vojvodina, and that the observed characteristics of this infection correspond to the reports of other European authors.

Key words: *Borrelia burgdoferi*, Lyme disease, erythema migrans, infection, Vojvodina

Introduction

Lyme borreliosis is an infectious disease caused by a spirochete belonging to the genus *Borrelia burgdorferi* sensu lato, which is predominantly transmitted via ticks from the *Ixodes genus* [1]. In this complex, one can find genospecies of *B. burgdorferi* sensu stricto, *B. garinii*, *B. afzelii*, which are important for the infection of people and animals in Europe [1, 2]. Recently, a new genospecies was discovered, marked as *B. spielmanii*, which can cause disease with people [3, 4].

The Lyme disease is for the most part a registered tick-borne disease in the countries of moderate climate in Eurasia and Northern America, where it is especially important for the public health of people [1]. According to our previous research work, we have confirmed the presence of the causative agent to the Lyme Disease with 22.1% ticks of the *Ixodes ricinus* species, collected from the natural environment in Vojvodina [5]. Hrnjakovic Cvetkovic et al. report that in Vojvodina, as well as in all of Serbia, there was a growing trend of registered cases and incidence of Lyme disease within the period from 2005. to 2009. year. The same authors present data about the number of the reported cases that grew from 164 in 2005, to 294 in 2009, as well as the values of the incidence of Lyme disease varying from 8.07 in 2005, to 14.85 cases per 100,000 inhabitants in Vojvodina in 2009 [6].

The infection with people is characterized through dermatological, neurological and cardiologic

manifestations, as well as problems with the muscular and joint systems. Most clinical signs and/or symptoms are similar around the world, but there are certain variations in the symptoms that are related to the geographical region and genospecies of *B. burgdorferi* which are the agents of the infection [7]. In the clinical picture of the Lyme borreliosis, three stages of the disease have been identified. The first stage is the localized infection in the form of skin manifestations and lasts from a couple of days to a couple of weeks. In the second stage, *Borrelia burgdorferi* is beginning to spread through the bloodstream, and for months and years later, a persistent infection is registered, which is typical of the third stage of the infection [2].

As various genospecies of *Borrelia burgdorferi* cause Lyme disease, and as there are significant variations in the appearance of their clinical onset, diagnosing this infection is rather complicated. For a number of years now efforts have been made to design algorithms and set up standard criteria to diagnose Lyme disease [2]. There are different direct methods to prove the presence of borrelia and they are: direct laboratory microscopic proof the presence of the agent, cultivation and proving the existence of proteins and/or nucleic acid of *Borrelia burgdorferi*. To prove the anti-*Borrelia burgdoferi* antibodies, serological techniques are used with different antigens of the agent, such as indirect immunofluorescence tests, immunoenzyme assay and immunoblot test. A complete antigen structure and the existence of significant variations in the antigen, which are the consequence of the evolutionary adaptation of the agent, make it notably more difficult to perform a serological diagnostics of Lyme disease [7]. A special problem in diagnosing Lyme disease is a possible co-infection with other agents such as anaplasmas, ehrlichias and babesias, which are also transferred by ticks [8-10].The aim of this research is to point to the epidemiological, clinical and diagnostic characteristics of Lyme disease with patients in Vojvodina, considering the fact that this naturally seated infection is endemically distributed and constantly present with people and animals in this region, and bearing in mind that there are significant differences in relation to the diseases and diagnostics of this infection in various regions.

Methods

During the period from January to December 2011., of all the patients who were forwarded to see an infectologist with doubts of Lyme disease, 132 patients bitten by a tick were involved in this research. The research was conducted at the Clinic for Infectious Diseases of the Clinical Centre of Vojvodina.

Before the clinical examination an epidemiological questionnaire was filled in with questions about the time of the first visit to the infectologist, age and sex of the patient, place of residence and activities of the patient when bitten by a tick, time of the tick's stay in the patient's skin, localization of the tick on the patient's body, patient's visit to countries abroad, if the patient was vaccinated against Lyme disease and whether the patient was pregnant. Afterwards, a physical examination was performed as well as the basic laboratory diagnostics. When it was necessary for differential diagnostics, other diagnostic methods were involved (patohistological examination of skin bioptates (stained HE, PAS, Giemsa, Gomory), cytochemical examination of cerebrospinal fluid, EEG, CT, MR, US, ECG and other).

With all the patients we performed the initial serological diagnostics to Lyme disease by applying the immunoenzyme assay and immunoblot test in order to prove the presence of anti-*Borrelia burgdorferi* antibodies of M and G classes in the patients' blood serums. The acute serum was processed immediately after the first visit to the infectologist, while the covalescent serum was analysed 4 to 6 weeks later. In the commercial ELISA test (Virion/Serion GmbH), antigens (OspC, VIsE and p100) were used of the *Borrelia garinii* (Pko) genospecies isolated in Europe. Apart from these proteins of *Borrelia garinii*, in order to increase the sensitivity of the test we have introduced the recombinant VIsE protein. Also, to increase the sensitivity of the ELISA test, in the buffer for the dilution of the patient's serum a lysate of treponema was added to absorb possibly present cross-reactive anti-treponema antibodies. In the commercial immunoblot test (Mikrogen GmbH) recombinant, highly specific and immunodominant proteins of *Borrelia burdgorferi* sensu lato genus were used. They were the following

proteins p100 (*B. afzelii*), VlsE (various genospecies *Borrelia burdgorferi*), p41 (*B. burgdorferi* sensu stricto), p39 (*B. afzelii*), OspA (*B. afzelii*), OspC (*B. burgdorferi* sensu stricto, *B. afzelii*, *B. garinii*, various genospecies), p41/i (*B. afzelii*, *B. garinii*) and protein p18 (*B. afzelii*). In order to avoid possibly false positive serological results and the cross-reactivity of antibodies to antigens of borrelia and treponema, VDRL test, ASTO, RF latex and WR were performed. The parameters of the used ELISA test in this work were calculated in relation to the affirmative immunoblot test with recombinant proteins of *B. burgdorferi* sensu lato, upon a construction of 2x2 table according to the formulas a/(a+c) for sensitivity, d/(b+d) for specificity, (a+d)/n for accuracy, a/(a+b) for positive predictive value and d/(c+d) for negative predictive value. In the presented calculations a relates to the number of true positive blood serums, b to false positives, c to false negatives and d to the number of true negative patients' blood serums. These data are presented in Table 2.

Of the direct methods to prove *Borrelia burgdorferi*, a direct dark field microscopy proving of the pathogen within ticks removed from the patients, as well as the cultivation of the agents from the skin bioptates and the removed ticks. A total of 152 microscopic examinations were performed by Kovalevsky method [26]. To isolation borrelia we used Barbour-Stoenner-Kelly (BSK-H) medium (Sigma-Aldrich Inc.).

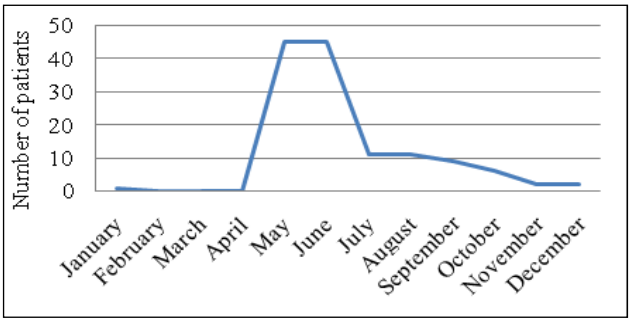
The diagnosis of Lyme disease with patients included in this research was confirmed based on the simultaneous interpretation of epidemiologic, clinical and laboratory results according to the standards that define clinical cases of Lyme disease and the laboratory diagnostics of this infection on the continent of Europe [11, 12].

Table 2. 2 x 2 construction table for the calculation of parameters of the used ELISA test

		Immunoblot test		
		Positive	**Negative**	**Total**
ELISA test	Positive	48 (a)	32 (b)	80
	Negative	10 (c)	42 (d)	52
	Total	58	74	132

Results

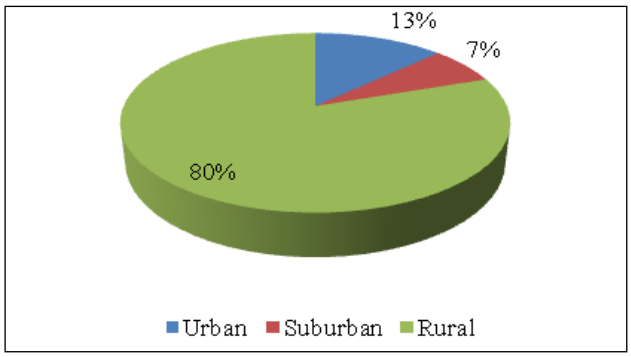
The data gathered from the questionnaire showed that most of the patients included in this investigation, who had been bitten by a tick, went to the Clinic for Infectious Diseases of the Clinical Centre of Vojvodina with suspects of Lyme disease in May and June of 2011. year. The seasonal distribution of the first visit of the patients to the infectologist was shown in Graph 1.



Graph 1. Seasonal distribution of the first visit of the patients to the infectologist

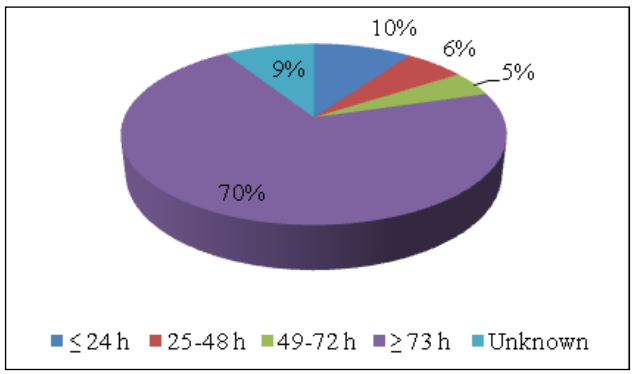
Majority of the 132 patients who were bitten by a tick and were included in this research were older than 60 (36.6%). 46 patients belonged to the age group of people between 20 and 60 years of age, while only 39 patients bitten by a tick were younger than 20. The gender structure of the patients included in this research, women went to see the doctor more often (58.3%). Information on the age and gender structure of the patients are shown in Table 1. From the results of the conducted epidemiological questionnaire one can see that most patients reported that they had noticed the bite after being outside in the country. These data are presented in Graph 2.

Most patients, 88 of them noticed the presence of ticks and their bite after a walk in the country. Significantly less people reported a tick during their professional activities (27.2%) or hobby (6%). With 70% of the patients the tick was present in the skin longer than 3 days, while only with 13 patients the tick was removed within the 24 hours after the bite. The epidemiological survey showed that 12 people did not know anything about the time span from the moment they were bitten to when it was removed. The data about the time span the tick spent on the patient's body from the moment he or she was bitten to its removal are shown in Graph 3.



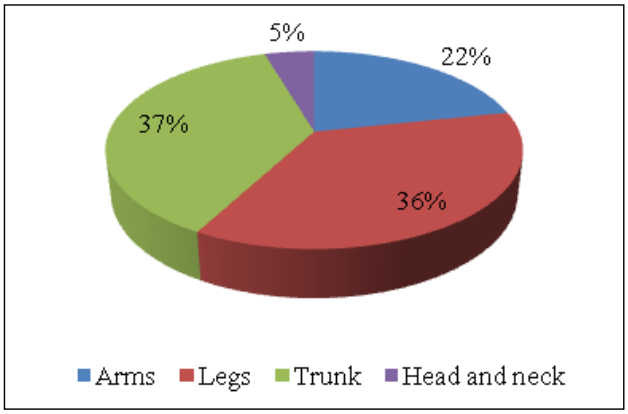
Graph 2. Geographic location of patients before the tick bite

Ticks were professionally removed from 91 patients, while 41 of them were not removed by a professional. Considering the success of removing the ticks, with most people (111/132) ticks were completely removed, while with 21 patients bits of ticks remained in the skin. The data about the manner and success of removing the tick are shown in Table 1.



Graph 3. Data about the time span ticks spent on the patients' bodies

Most people who came to the Clinic for Infectious Diseases of the Clinical Centre of Vojvodina, suspecting Lyme disease, had been in contact with ticks for the first time (91.6%), while only 11 patients reported a repeated contact with ticks. Most people had only one tick on them (93.1%). One patient had ten ticks on him. The ticks on patients' bodies were found on their torso and legs. The presence of ticks on bodies of patients who came to see the infectologist suspecting Lyme disease is shown in Graph 4. The epidemiological questionnaire reports only 6 patients going abroad. No patients were pregnant. None of the patients who were bitten by a tick and reported to the Clinic for Infectious Diseases of the Clinical Centre of Vojvodina and were suspected of Lyme disease were vaccinated against *Borrelia burgdorferi*.



Graph 4. Locations on patients' bodies where ticks were found

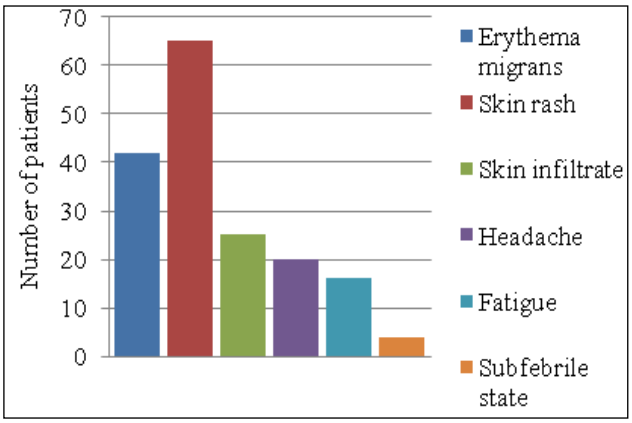
By applying the described methods of researching Lyme disease was confirmed with 58 out of overall 132 patients who were epidemiologically, clinically and laboratory observed. With all the patients Lyme disease was found to be in the first stage of the disease. The second stage (disseminated infection) and the third stage of Lyme disease characterised with chronic neuroborreliosis, chronic atrophic acrodermatitis and chronic arthritis was not confirmed during this research. The average period of incubation was 10.2 days (1-23). Of the clinical symptoms and/or signs, erythema migrans was registered with 42 patients, skin rash with 65 patients, skin infiltrate with 25 patients, headache with 20 patients, fatigue with 16 patients and subfebrile state with 4 patients. The data that refer to the registered clinical signs and/or symptoms of

Table 1. Age and gender structure and the manner and success in removing the ticks

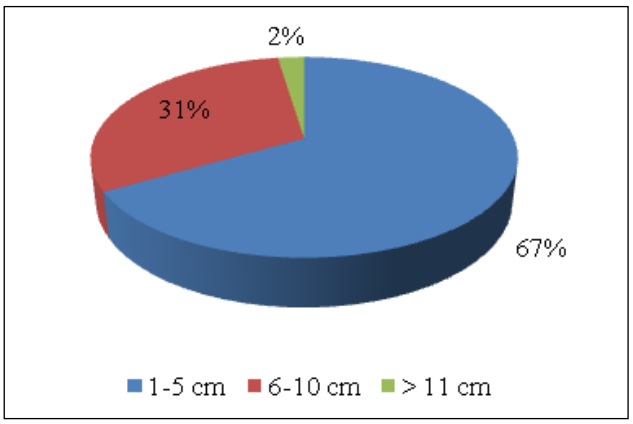
Age structure		**Gender structure Parameter n**		**Manner in which ticks were removed**			
				Parameter	**n**		
Years	n	Gender	n	Successfully	111	Professionally	91
0-20	39						
21-60	46	Men	55	Unsuccessfully	21	Unprofessionally	41
> 60	47	Women	77				

the infection with the agent being *Borrelia burgdorferi* are presented in Graph 5.

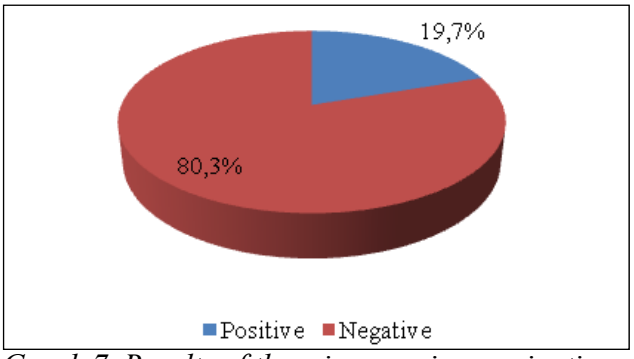
The presence of erythema migrans of 1 to 5 cm in diameter was noticed with most patients (28/42), while this dermatological change of over 11 cm in diameter was registered with only one patient. In Graph 6, one can see the diameters of erythema migrans with patients who had a confirmed Lyme disease. Apart from the general infectious syndrome and dermatological changes, rheumatologic, cardiologic and neurological manifestations have not been registered with the observed patients. Other patients (74) who had been bitten by a tick and were included in this research had no clinical signs other than the local allergic reaction to the bite. These patients were not diagnosed with Lyme disease.



Graph 5. Registered clinical signs and/or symptoms of Lyme disease



Graph 6. Diameter of erythema migrans



Graph 7. Results of the microscopic examination of ticks for the presence of Lyme disease agents

By applying the ELISA test for the detection of anti-*Borrelia burgdorferi* antibodies, classes M and G, 80 reactive serums were confirmed, while in 52 serums no antibodies to antigens, agents of Lyme disease were confirmed. With epidemiological calculations described in the research methods, sensitivity of ELISA test was calculated of 82%, specificity of 58%, accuracy of 68%, positive predictive value of 60% and negative predictive value of 80%. Data for these epidemiological calculations are shown in Table 2., which was drawn upon the 2 x 2 principle.

By applying the immunoblot technique with recombinant proteins as the "golden standard" in serological diagnostics of Lyme disease, presence of IgM and IgG was registered with 58 patients diagnosed with Lyme disease. By applying the same Western blot test in blood serums 74 patients bitten by a tick and were forwarded to an infectologist due to suspicion to Lyme disease, no antibodies were confirmed to the agent of this infection. With two seronegative (ELISA and WB) patients a positive result of ASTO and WR tests was confirmed. With one seronegative (ELISA and WB) patient, we isolated *Borrelia burgdorferi* from a skin bioptate taken from the rim of the erythema migrans. The patohistological examination of the skin bioptate spoke in favour of the chronic active dermatitis.The microscopic dark field examination of ticks removed from people who were forwarded to the infectologist because of a possible Lyme disease, the presence of the agent of Lyme disease was proven with 30 examined ticks (30/152). The results of the microscopic dark-field examination of ticks removed from patients' bodies included in this research, for the presence of *Borrelia burgdoferi* are shown in Graph 7.

Discussion

Recent outbreaks of zoonoses all over the world, but also regionally within certain countries point to the fact that the health of people and ani-

mals is closely connected. The greatest risk factor for the outbreak and spreading of the agents of zoonoses is the existence of inadequate equipment of the diagnostics service laboratories and the level of public information, as well as the lack of properly coordinated and efficient global mechanisms of epidemiological surveillance [13].

During the past two decades numerous epidemiological and clinical research of Lyme disease have been conducted all over the world. In this research, during 2011, 132 patients bitten by a tick were processed and 58 of them had a confirmed diagnosis of Lyme disease. These data correspond to the previous referral values of incidence of this infection in our midst (14.85 cases to 100.000 inhabitants in 2009), obtained by Hrnjakovic Cvijetkovic et al. [6]. Hristea reports data for seroprevalence of Lyme disease with people in Romania. In this seroepidemiological research work, referral values of seroprevalence to antigens – agents of Lyme disease with blood donors was 4.3%, while the values were higher (9.3%) among persons professionally more exposed to tick bites [14]. Christova et al. from Bulgaria processed both clinically and in laboratory 1257 patients during the period from 1999 to 2002 [15]. In review paper, Santino reports data on the prevalence of Lyme disease with people in Sweden (19%), Estonia (2.7%), Holland (28%), Switzerland (26%) and Poland (15%) [16]. In 2005, Lipozencic reports that Lyme disease is endemically distributed in Croatia [17], which corresponds to the outbreak of Lyme disease in Vojvodina.The epidemiological survey identified the greatest number of patients to be older than 60, of female gender. The researchers in Bosnia and Herzegovina reported that Lyme disease was most common with working population, and that the greatest number of infections caused by *B. burgdorferi* had been registered in the month of June [18]. A similar seasonal distribution was found in this research. Contrary to our research, authors in Bulgaria have registered the biggest number of Lyme disease cases with the youngest patients [15]. The same authors report that the greatest number of patients spent time in the rural area, which corresponds to our findings. We found out that the biggest number of ticks was removed by professionals and completely. The same data was provided previously by Mladenovic et al. in 2010 [19]. We also found out that in most cases, ticks spent more than 3 days in the skin of our patients, which, according to the reports in the literature is a condition enough for the infection with the Lyme disease agent to take place. It is said that the period of hematofagous diet of certain sorts of ticks from *Ixodes* genus, should be longer than 36 hours for the successful transmission of the agents of Lyme disease to take place [1]. Experiments with animals proved the successful transmission of *B. afzelii* during a 17-hour period after the bite of tick *I. ricinus* [20].

We found erithema migrans to be the most common clinical manifestation (72.4%) which was in most cases lesser than 5 cm in diameter. According to the diagnostics criteria for Lyme disease, identifying this dermatological change, together with positive data about the presence of a tick in patient's skin for a period longer than two days, was sufficient to make a confirming diagnosis [1, 11]. Most other authors also claim that erithema migrans is the most common clinical manifestation, while other clinical signs and/or symptoms are far rarer [1]. Christova et al. registered the presence of erithema migrans with 69.1%, average diameter being from 11 cm onwards[15], while Dautovic Krkic et al. also noted this clinical manifestation as the most common with 39 patients [18]. According to our previous research we had established also that the first stage of Lyme disease is dominantly present in the clinical manifestation of this infection in our geographical area [21].With all of the patients diagnosed with Lyme disease, we proved anti-*Borrelia burgdorferi* antibodies of classes M and G, by applying ELISA and WB tests. The initial serological diagnostics was performed according to the standards for laboratory diagnostics and is related to the application of ELISA test in the first stage, and to retesting by applying the confirmatory WB test with recombinant antigens of genus present in a certain geographical area. In the ELISA test we established a lower value of particularity (58%) which is due to the selection of antigens used in this commercial test. That is why the recommendations for serological diagnostics relate to the application of a confirmatory immunoblot test. With one seronegative patient, the agent of Lyme disease was isolated, which is explained with seroconversion [1].

In the research we registered the rate of infected ticks removed from patients' bodies to be 19.7%, which is in accord with the previous research work done in Serbia and Europe. For our geographical area, Rajkovic et al. report the prevalence of the ticks infected with *B. burgdorferi* to be from 27% to 31.7% [23]. Cekanac et al. report a similar average prevalence of *B. burgdorferi* tick infection of 21.9% for the Belgrade area [23]. For Germany, Strube et al. report a similar prevalence of the tick infected with *Borrelia burgdoferi* sensu lato of 26.6% [25].

Conculsion

This research confirms the fact that Lyme disease has constantly and endemically been present among people in Vojvodina. Based on the data about the way and success of removing ticks, one can conclude that patients recognize the risk for their health after being bitten by a tick and react adequately. With all the patients processed epidemiologically, clinically and in laboratory the diagnosis was confirmed in the first stage of the disease. As the most common clinical manifestation we registered erythema migrans. This is probably due to a relatively short period of patients' follow up, since Lyme disease takes place in a subacute and/ or chronic flow, with prolonged seropositivity, and that certain amount of time must pass (months or years) for certain symptoms of the second or third stage of the infection to take place.

Further research is necessary in the territory of entire Serbia in order to harmonise clinical and laboratory standards of diagnostics, and to systematically follow up epidemiological data and trends of registering new cases and clinical manifestations, since there are significant variations.

Acknowledgements

This research was financed by the Provincial Secretariat for Science and Technological Development of AP of Vojvodina (the name of the project: Research of Lyme Disease and Other Vector-borne Zoonoses in Vojvodina; Project number: 114-451-1892/2011)

References

1. *Stanek G, Wormser GP, Gray J, Strle F: Lyme borreliosis. Lancet 2012, 379(9814): 461-473.*

2. *Steere AC, Coburn J, Glickstein L: The emergence of Lyme disease. J Clin Invest 2004, 113(8): 1093-1101.*

3. *Richter D, Schlee DB, Allgower R, Matuschka FR: Relationships of a novel Lyme disease spirochete, Borrelia spielmani sp. nov., with its hosts in Central Europe. Appl Environ Microbiol 2004, 70(11): 6414-6419.*

4. *Maraspin V, Ruzic-Sabljic E, Strle F: Lyme borreliosis and Borrelia spielmanii. Emerg Infect Dis 2006, 12(7): 1177.*

5. *Savic S, Vidic B, Lazic S, Lako B, Potkonjak A, Lepsanovic Z: Borrelia burgdorferi in ticks and dogs in the province of Vojvodina, Serbia. Parasite 2010, 17(4): 357-361.*

6. *Hrnjaković-Cvjetković I, Milošević V, Jerant-Patić V, Stefan-Mikić S, Cvjetković D, Radovanov J, G. K: Najčešće bakterijske zoonoze u ljudi u Vojvodini u periodu 2005-2009. Arhiv veterinarske medicine 2011, 4(1): 11-18.*

7. *Aguero-Rosenfeld ME, Wang G, Schwartz I, Wormser GP: Diagnosis of lyme borreliosis. Clin Microbiol Rev 2005, 18(3): 484-509.*

8. *Swanson SJ, Neitzel D, Reed KD, Belongia EA: Coinfections acquired from ixodes ticks. Clin Microbiol Rev 2006, 19(4): 708-727.*

9. *Christova I, Schouls L, van De Pol I, Park J, Panayotov S, Lefterova V, Kantardjiev T, Dumler JS: High prevalence of granulocytic Ehrlichiae and Borrelia burgdorferi sensu lato in Ixodes ricinus ticks from Bulgaria. J Clin Microbiol 2001, 39(11): 4172-4174.*

10. *De Martino SJ, Carlyon JA, Fikrig E: Coinfection with Borrelia burgdorferi and the agent of human granulocytic ehrlichiosis. N Engl J Med 2001, 345(2): 150-151.*

11. *Stanek G, Fingerle V, Hunfeld KP, Jaulhac B, Kaiser R, Krause A, Kristoferitsch W, O'Connell S, Ornstein K, Strle F et al: Lyme borreliosis: clinical case definitions for diagnosis and management in Europe. Clin Microbiol Infect 2011, 17(1): 69-79.*

12. *Brouqui P, Bacellar F, Baranton G, Birtles RJ, Bjoersdorff A, Blanco JR, Caruso G, Cinco M, Fournier PE, Francavilla E et al: Guidelines for the diagnosis of tick-borne bacterial diseases in Europe. Clin Microbiol Infect 2004, 10(12): 1108-1132.*

13. *Cavaljuga S, Seric-Haracic S, Vasilj I, Scharninghausen J, Faulde M, Fejzic N: Development of communicable diseases surveillance infrastructure for zoonoses in Bosnia and herzegovina - a common approach? HealthMED 2009, 3(2):183-189.*

14. *Hristea A, Hristescu S, Ciufecu C, Vasile A: Seroprevalence of Borrelia burgdorferi in Romania. Eur J Epidemiol 2001, 17(9): 891-896.*

15. *Christova I, Komitova R: Clinical and epidemiological features of Lyme borreliosis in Bulgaria. Wien Klin Wochenschr 2004, 116(1-2): 42-46.*

16. *Santino I, Dastoli F, Sessa R, Del Piano M: Geographical incidence of infection with Borrelia burgdorferi in Europe. Panminerva Med 1997, 39(3): 208-214.*

17. *Lipozencic J, Marinovic B: What should be known about the activity of the Reference Center of the Ministry of Health and Social Welfare of the Republic of Croatia for Diagnosis of Lyme Disease. Acta Dermatovenerol Croat 2005, 13(2): 81-84.*

18. *Dautovic-Krkic S, Cavaljuga S, Ferhatovic M, Mostarac N, Gojak R, Hadzovic M, Hadzic A: [Lyme borreliosis in Bosnia and Herzegovina--clinical, laboratory and epidemiological research]. Med Arh 2008, 62(2): 107-110.*

19. *Mladenovic J, Cekanac R, Stajkovic N, Krstic M: Risk of Lyme disease development after a tick bite. Vojnosanit Pregl 2010, 67(5):369-374.*

20. *Kahl O, Janetzki-Mittmann C, Gray JS, Jonas R, Stein J, de Boer R: Risk of infection with Borrelia burgdorferi sensu lato for a host in relation to the duration of nymphal Ixodes ricinus feeding and the method of tick removal. Zentralbl Bakteriol 1998, 287(1-2): 41-52.*

21. *Vukadinov J, Canak G, Brkic S, Samardzija NM, Aleksic-Dordevic M, Turkulov V, Cik-Nad E, Lalosevic V: Clinico-epidemiologic characteristics of Lyme disease treated at the Infectious Disease in Novi Sad 1993-1998. Med Pregl 2001, 54(9-10): 470-475.*

22. *Rajkovic DV, Jurisic A: Ixodes ricinus as vector and reservoir of Borrelia burgdorferi in an urban environment. Archives of Biological Sciences 2005, 57(3): 253-254.*

23. *Stajkovic N, Drndarevic D, Lako B, Dmitrovic R, Obradovic M, Djerkovic V, Cekanac R, Djordjevic D: Vectors of Borrelia burgdorferi. Glas Srp Akad Nauka Med 1993(43): 45-56.*

24. *Cekanac R, Pavlovic N, Gledovic Z, Grgurevic A, Stajkovic N, Lepsanovic Z, Ristanovic E: Prevalence of Borrelia burgdorferi in Ixodes ricinus ticks in Belgrade area. Vector Borne Zoonotic Dis 2010, 10(5): 447-452.*

25. *Strube C, Schicht S, Schnieder T: Borrelia burgdorferi sensu lato and Rickettsia spp. infections in hard ticks (Ixodes ricinus) in the region of Hanover (Germany). Berl Munch Tierarztl Wochenschr 2011, 124(11-12): 512-517.*

26. *Kovalevsky YV, Korenberg YI, Kutlina GV, Ustinova OA: Standards for screening of a ixodid tick nymphal preparation by dark-field microscopy in the foci of borrelioses. Med Parazitol (Mosk) 1996(4): 18-21.*

Corresponding authors
Aleksandar Potkonjak,
Faculty of Agriculture,
University of Novi Sad,
Department of Veterinary Medicine,
Novi Sad,
Serbia,
E-mail: ale@polj.uns.ac.rs

The influence of autogenic training on state anxiety reduction among community pharmacists in Serbia

Dragana Jocic[1,2], Dusanka Krajnovic[2,3]

[1] Pharmacy ″Kumodraz II″, Belgrade, Serbia,
[2] Department of Social Pharmacy and Pharmaceutical Legislation, University of Belgrade, Faculty of Pharmacy, Belgrade, Serbia,
[3] Serbian Unit of the International Network of the UNESCO Chair in Bioethics, Serbia.

Abstract

Background: There is growing evidence that better coping with job-related anxiety among healthcare workers is important because may affect their ability to practice effectively and may put patients at risk.

Objective: to investigate the effects of autogenic training (AT) to reduce state anxiety in community pharmacists.

Materials and Methods: Fulltime employed community pharmacists with state anxiety assigned to experimental group practiced the AT daily at home for 8 weeks, with one group session each week. State Anxiety was self-assessed in both group by the Burns Anxiety Inventory (BAI) at baseline, 4 weeks and 8 weeks.

Results: Altogether, 40 pharmacists were self assessed by BAI and experimental group showed decrease of state anxiety degree after 4 weeks and 8 weeks of AT intervention. The level of state anxiety was lower in the experimental group after 8 weeks of AT intervention (99% significance level; mean of experimental group of 2.3000 and 3.7500 for the control group). ***Conclusions:*** AT is associated with significant reduction in state anxiety in pharmacists and can be used as an easily applied technique for reducing state anxiety in community healthcare professions settings.

Key words: Autogenic training, Community pharmacists, State of anxiety, Burns Anxiety Inventory (BAI)

Introduction

There can be many work-related stressors in providing health care at primary level, often resulting from environmental tensions, conflicts and workforce pressure (in general work overload, working long hours, insufficient time, skills and/or social support at work, new roles, limited resources available to meet the level of changing demands from the public) (1-4). High levels of work overload and job demands connected with stress and state anxiety, are also resulting in poor-communication and decision making, lower morale and poorer work performance (5-7). As an unavoidable part of every jobs` and individual's working life, occupational stress has the potential to cause direct or indirect harm on cognitive processes (e.g., communication, memory, decision making) safety-relevant behavior (e.g., procedural violations, error reporting), and individual outcomes. In the health care professions occupational stress may affect patients, besides having a profound effects of an individual health professional's well-being (8,9-13). Additionally, it may have effects on individuals` mental health and it can also have an impact on the quality of patient care provided (3,5,8,14,15). These ultimately may affect patient safety.

It is widely investigated in the health professions that work-related anxiety which is highly prevalent by person–directed interventions and person-work interface interventions (16-19) has an impact on the delivery of healthcare services and the experience of patients in the receipt of care (20). It is acknowledged that community pharmacists are the most accessible primary healthcare providers (21,22) which make them more affected than other healthcare workers. However, limited evidence is available regarding pharmacists and state anxiety, reporting an increased level of state anxiety at workplace, patient safety and overall

accuracy were strongly related with state anxiety (21,23-25).

Anxiety as a state

Anxiety is fear for no apparent external cause and can be estimated as a personality trait (genetic predisposition) and as a state, which is temporary condition in response to threatening stimuli of environment that is specific to the situation (26,27). At working environment this is the tendency to perceive certain situations as threatening (28,29). Different techniques could be applied in reducing state anxiety. Relaxation techniques used by healthy people are more and more applied to achieve better concentration and willingness to work (30). AT is a relaxation technique essentially based on autosuggestion. It is a cognitive-behavioral form of relaxing that a healthy individual can perform through passive concentration with certain combinations of psychophysiologically adapted stimuli (31). The AT technique, developed by Schultz, consist of six standard exercises. The first exercise aims at muscular relaxation, which is achieved mainly by repeating a verbal formula to encourage feelings of heaviness. Subsequently, the concentration is focussed passively on feeling warm, then calming cardiac activity, slowed respiration, warmth in the abdominal region and coolness in the head (32-34).

AT advantage over other relaxation techniques is that it is easy to learn and use, and shows a series of favorable effects in relation to the progressive muscle relaxation technique (that requires a lot of time and has far-reaching impact) (32). Compared to some other psychological techniques applied to reduce occupational anxiety AT proved to be more efficient (35,36).

The objective of this study was to examine the effectiveness of AT as relaxation technique in reducing the occupational state of anxiety among pharmacists employed in community pharmacies.

Methods

Study design

An open controlled trial was conducted among community pharmacists in Serbia during 2011. A thorough literature review was undertaken in order to (I) identify any published paper which addressed the AT itself (II) AT as possible person-directed intervention in reducing occupational state anxiety and (III) AT impact when applied to healthcare workers and pharmacists in particular. There is no existing published research on the influence of the AT and pharmacy practice, but few resarchrs on other health pracice which have been useful to provide the background to the present study (18,19,32,37).

Sample

Official permission was taken from the Pharmaceutical Chamber of Serbia (38) and informed consent of the particiants were obtained at the initial phase of the survey. Belgrade University School of Pharmacy Ethics Committeee for Clinical Research approved the study as well (39).

This study was based on Belgrade region (the capital of Serbia) and included 40 fulltime employed pharmacists from state and privately owned community pharmacies (a flowchart of the procedures is shown in the Figure 1). Because of the interventions planned and limited research grants only those from Belgrade region as the most saturated region in health-care pharmacy settings with 78 hospital and 1690 community pharmacists of 4475, were included. The research was announced at few pharmacy meetings during the spring 2011. Pharmacists who expressed willingness to participate were contacted for detailed explanations by phone, and only those who confirmed wish to participate were sent an information sheet and consent form by post with a one week to decide. Participants who returned consent forms were contacted to arrange further procedures. State of anxiety was initailly test with Burns Anxiety Inventory (BAI) and only those with BAI score more then zero were included to the study (40, 41). A formal sample-size calculation was not undertaken, but the sampling was by convenience including a pretesting interview(42), and every effort was made to divide a sample (n=40) into two groups of 20 participants as balanced as possible in the terms of important variables that maight modify the effects of the AT (such as gender, length of experience and age) (42-46). All participants were provided with information about the importance of completing all of the BAI items and explained all statements and questions at the initial testing. After receiving

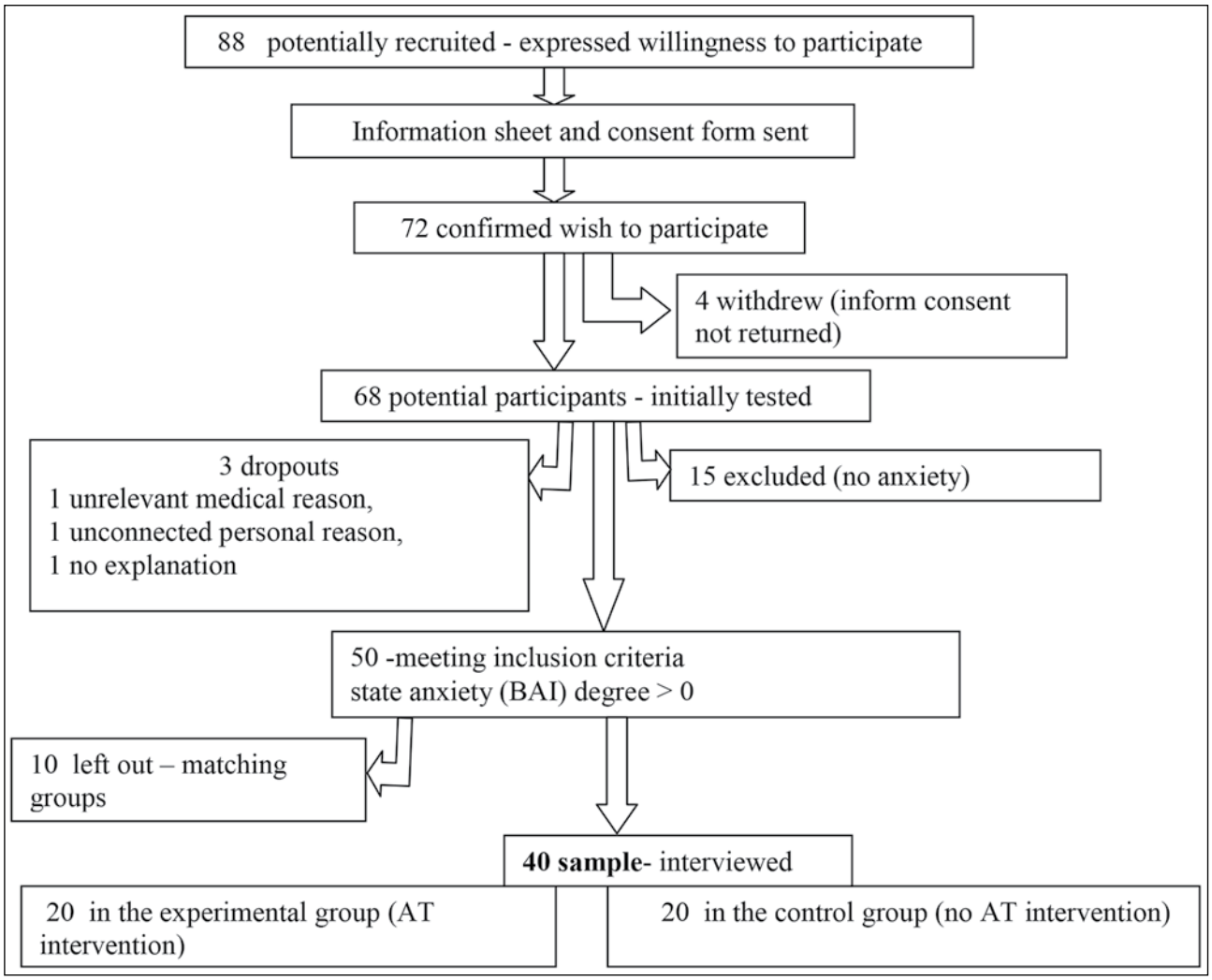


Figure 1. Flowchart describing procedures of the sample formation (values are numbers of participants)

the BAI, the researcher checked the instrument on site to determine whether any missing items exit, and the pharmacists made a refill in the case of the missing part existence.

Statistical analyses

Data were analyzed using descriptive statistics, and the ANOVA and t-test are performed. Statistical analysis was performed using the SPSS program (SPSS 18.0 for Windows, Inc., Chicago, IL, USA).

Procedure

The main part of the research, including AT interventions was conducted by the researcher DJ (registred pharmacist of eight years experience working at community settings who holds a master degree in psychology and has an AT licence).

The researcher DJ had no previous professional contact with any of the study participants. The experimental group was taught the technique of AT in a total of eight sessions lasting from 30 to 60 minutes. During the 8-week training period pharmacists were expected to practice regularly three times daily and to keep a personal diary to record their experiences of AT (40). The researcher DJ worked very closely with each study participant during group sessions, weekly and kept a field notes. Experimental group was trained in two subgroups as recomended when applying behavioral relaxation training techniques in group sessions. For consistent daily home practice which is believed to be important for mastering the technique, an email remainder was sent to all participants daily.

State anxiety was measured by the BAI prior to exposure to AT, four weeks after applying AT and eight weeks after applying AT. The control group was not exposed to AT, but state anxiety was also measured by BAI at baseline, after four weeks and after eight weeks. All AT practicing participants

were interviewed after the State anxiety measurement. Field notes recorded during group sessions and records collected from the participants` diary will not be reported in this paper, these qualitative data will be reported elsewhere.

BAI is one of the most common and very accessible instrument, and it can be self-administered as well. It is a checklist of thirty-three symptoms related to state anxiety. They are broken down into three categories: anxious feelings, anxious thoughts, and physical symptoms (emotional, cognitive and somatic state anxiety). Emotional state of anxiety accompanied by feelings such as fear, sudden and unexpected waves of panic, anxiety, feeling of coming horror, a sense of tension and pressure. Cognitive state anxiety is the mental component of state anxiety caused by something such as fear of negative social evaluation, fear of failure and loss of self-esteem. Somatic state anxiety is a natural component of anxiety and reflects the perception of physiological reactions such as rapid heartbeat, rapid breathing and muscle tension. A person taking the assessment ranks each item on a scale from zero, "not at all," to three, "a lot." To assess the level of state anxiety indicated on the checklist, every item is added up numerically. A score of zero to four indicates minimal or no anxiety, five to 10 means borderline anxiety, a score between 11 to 20 signifies mild anxiety, 21 to 30 is moderate anxiety, 31 to 50 means severe anxiety, and a score of 51 to 99 indicates extreme anxiety or panic (39,40).

Results

From the initially interested community pharmacists at Belgrade region 72 (82 %) confirmed their wish to participate after detailed explanation of study design and interventions planed, and 68 (77.2%) returned the information sheet and consent form (figure 1). After initial assessemet for state anxiety 18 (26.5 %) participants dropped out either because of zero level of state anxiety (15 pharmacists) or because of rejecting to participate after initially anxiety testing (3 pharmacists). Due to sampling method and group maching a total of 40 participants enrolled and during the 8 week intervention period there were no dropouts. Data were obtained mostly from female pharmacists (70.0%) with 6 to 10 years of working experience (65.0%). Fewer than half of the participants (37.5%), were employees from small chain pharmacy and about half (57.5 %) worked at private health care sector.

Table 1 summarises the demographic profile of the study participants. At the 4 and 8 weeks of autogenic training application State anxiety scores in experimental group showed a statistically significant fall (table 2).

Descriptive statistics revels that participants in the experimental group showed reduction in the

Table 1. Demographic characteristic of participants

Variables	frequency	percentage
Gender		
Male	12	30.0
Female	28	70.0
Age range =28-59 (Mean age=38.55)		
to 30	7	17.5
from 31 to 40	25	62.5
from 41 to 50	5	12.5
from 51 to 60	0	0
over 60	3	7.5
Years in pharmacy practice range=4-26 (Mean = 9.53)		
to 5 years	9	22.5
from 6 to 10 years	26	65.0
from 11 to 20 years	3	7.5
over 20 years	2	5.0
Ownership		
state	17	42.5
private	23	57.5
Type of pharmacy		
large chain pharmacy small chain pharmacy	8 15	20.0 37.5
independent pharmacy	13	32.5
medium chain pharmacy	4	10.0
Employment status of pharmacist		
employee	30	75.0
employer	10	25.0
Total	40	100.0

Large chain pharmacy, 25 or more pharmacies
Medium chain pharmacy, 11-24 pharmacies
Small chain pharmacy, 2-10 pharmacies
Independent, 1 pharmacy

degree of state anxiety after 4 and 8 weeks of autogenic training application. In the control group there is no reduction in the degree of state anxiety. The results of state anxiety (BAI) degree in research group and control group were presented at table 3.

Table 2. State anxiety (BAI) scores of the experimental and control groups

Time point	Experimental group	Control group
Baseline	17.5 (9.6)	18.9 (10.22)
4 weeks	14.6 (9.6)	19.0 (6.0)
8 weeks	10.9 (9.5)	20.4 (6.2)

Values are mean (SD)

ANOVA was performed in the experimental and control group to study the effect of AT to the level of state anxiety. The results (table 2) indicate that the level of state anxiety is significantly lower in the experimental group after 8 weeks of AT intervention (99% significance level; mean of experimental group of 2.3000 and 3.7500 for the control group). Similarly, autogenic training group showed decrease of state anxiety degree after 4 weeks of AT intervention.

In the experimental group ANOVA was used to assess the relationship between degree of anxiety and demographic variables (gender, age, years in pharmacy practice, employment status of pharmacist, type of pharmacy, ownership).There is statistically significant difference between the degree of reduction in state anxiety and some demographic variables within the experimental group. At both assessment periods a statistical significance was obtained between state anxiety reduction and some demographic variables. After 4-week application period of AT the gender (man) has the most impact of state anxiety reduction (F=0.043, df=3, P<0.988) and after 8-week of AT the most significant impact on state anxiety reduction occurred in the group from 6 to 10 years of community pharmacy service (F=0.0398, df=3, P<0.756).

In the experimental and control group ANOVA was used to assess the relationship between degree of anxiety and demographic variables (gender, age, years in pharmacy practice, employment status of pharmacist, type of pharmacy, ownership). There is statistically significant difference between the degree of reduction in state anxiety and the demographic variables within the experimental and control group. At both assessment periods a statistical significance was obtained between state anxiety reduction and demographic variables – type of pharmacy. After 4-week application period of AT the type of pharmacy (state) has the most impact of state anxiety reduction (F=0.352, df=4, P<0.841).

In the experimental group t-test was performed, to study the statistical significance between the test results of state anxiety before and after applying AT. Results indicate that participants in the experimental group had significantly less expressed degree of state anxiety after exposition to AT (99% significance level; mean pre-test AT is 3.1500, and post/ test AT is 2.3000).

Discussion

To the best of our knowledge this study is the first one designed to provide some insights into the impact of AT aplication of state anxiety at pharmacists

Table 3. State anxiety (BAI) degrees of the experimental group before exposure to AT, 4 weeks after exposure to AT, and 8 weeks after exposure to AT and at similar time points in the control group

Time point	Experimental group			Control group		
	Baseline	4 weeks	8 weeks	Baseline	4 weeks	8 weeks
Degree of state anxiety	Frequency (Percent)					
Minimal Anxiety	1 (5.0)	4 (20.0)	7 (35.0)	2 (10.0)	0 (0)	1 (5.0)
Borderline Anxiety	5 (25.0)	6 (30.0)	6 (30.0)	3 (15.0)	4 (20.0)	2 (10.0)
Mild Anxiety	6 (30.0)	6 (30.0)	4 (20.0)	6 (30.0)	8 (40.0)	3 (15.0)
Moderate Anxiety	6 (30.0)	0 (0)	0 (0)	6 (30.0)	5 (25.0)	9 (45.0)
Severe Anxiety	2 (10.0)	4 (20)	3 (15)	3 (15.0)	3 (15.0)	5 (25.0)
Extreme Anxiety or Panic	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
20 (100)	20 (100)	20 (100)	20 (100)	20 (100)	20 (100)	20 (100)

Values in parenthesis are percentages

population. Community pharmacists in Serbia tend to experience the state of anxiety at work and think that they have an insufficienct knowledge of how to cope with the job-related anxiety, which may affect their ability to practice effectively and may put patients at risk.The results give some evidence that an AT technique performed over a period of 8-weeks has an impact on the level of State Anxiety reduction among pharmacists from community settings. This is also the first study in Serbia to address the AT aplication among healthcare workers in general, and in particular in relation to reducing state anxiety and job related stress at healthcare sector. It is conducted as a sub-study of the comprehensive investigation of the Behavioral–psychological characteristics pertaining to pharmacy practice and their impacts on professional behavior.

The significance of this study is that it provides some evidence that AT is associated with significant reduction in state anxiety in pharmacists. AT is taught relatively easily and could be applied continually after the initial treining. As many participants stated AT is applicable at workplace settings and could be incorporated into daily practice without difficulties, both at work and at home. Pharmacists need to be motivated to use AT as any other technique that they can apply to reduce anxiety at work.

Many studies support a good, consistent and significant efficacy of relaxation training in reducing anxiety in non-clinical sample (community population) i.e. healthy population (35,47-49) and some clinical trials have shown a positive impact of AT on stress and anxiety (32,40,50-54). In fact, anxiety problems are common among healthy individuals and have been associated with many job related factors (7-9,19,23,25). There are numerous data indicating that AT has an impact on stress and anxiety reduction in any kind of participants: male or female, young or old, with or without psychological disorders (36,55-58). Most of the studies are conducted on other health professionals, while testing the effects of relaxation techniques on pharmacists are missing (47). The most common inventory to measure state anxiety is Spielberger's State-Trait Anxiety Inventory (47,59). There is a lack of research to measure the state anxiety using the BAI, which is a self-assessed inventory.

Some healthcare professionals had already advocated that AT should be utilized as a relaxation method to help workers cope with stress. Although knowledge about AT has spread among occupational healthcare staffs, there are only a small number of companies whose employees regularly practice AT. In order to overcome difficulties, workers without any health problems need to be motivated to learn AT, and to be taught effectively (60). The results from some studies show emotional benefits from relaxation training in a variety of clinical and community samples (47,61,62) and with recent small trials on the use of the new technologies for relaxation purposes (63). We argue that relaxation training improve behavioral and psychological resources; relaxation abilities and perceived self-efficacy.

AT could be cost-effective: it can easily and relatively quickly be taught to groups at no great expense. Replications of this study seem necessary by different research groups, both in pharmacists who seek help for anxiety and in other types of participants (hospital pharmacists, clinical pharmacists). The main limitation of the study is that the participants represented a relatively small sample of community pharmacists, the geographical area was limited. Although our results can be extrapolated to Belgrade city, the anxiety situation on the country level cannot be predicted. Another possible limitation is the group homogeneity and a fact that participants were not specifically seeking help with stress, but those who responded to an invitation to learn AT. No other studies on AT for reducing occupational state anxiety among pharmacists have been reported since this study was planned and undertaken and these findings should encourage us to repeat this study in other regions of Serbia in order to put the whole picture more clearly. An additional qualitative research might have helped us to understand the underlying factors of the state of anxiety among pharmacists. Replication of this study would be justified with follow up. Further research into the effects of AT improving pharmacists' quality of work life could offer some insight of the cost effectiveness point of view because AT can be taught and practice with no great expense. Relationship between pharmacists' personality characteristics and state anxiety can be analyzed in future research as well.

Conclusions

Pharmacists working in community pharmacies are in constant interaction with patients and they are often exposed to numerous stress factors that can lead to state anxiety. In order to provide adequate health care and ultimately enhance patient care and safety, it is important that pharmacists reduce the degree of state anxiety to a minimum. AT as relaxation technique has an impact on state anxiety reduction and at least a short-term effect in alleviating occupational stress in community pharmacists. AT is a simple, short term technique that can be easily adopted, and applied daily. It is therefore desirable for pharmacists working in community pharmacies to have organized training courses for the application of relaxation techniques. Further research priorities should enhance the understanding of the variability and clinical significance of state anxiety reduction outcomes after different relaxation trainings, but AT in particular. It is also of interest to consider the impact of AT in relation to other psychological work-related outcomes in community pharmacy practice.

Acknowledgments

We would like to thank all study participants for their contribution to this study. We especially thank an anonymous reviewer for his careful reading, valuable comments and constructive criticism. The author DK gratefully acknowledges funding support from the Ministry of Science and Environmental Protection of the Republic of Serbia (project No. 41004). The funding agreement ensured the authors' independence in designing the study, interpreting the data, writing, and publishing the report.

References

1. *Bell HM, McElnay JC, Hughes CM. A self reported work sampling study in community pharmacy practice. Pharm World Sci 1999; 21(5):210-216. doi: 10.1023/A:1008760306052.*
2. *Roberts AS, Hopp T, Sorensen EW, Benrimoj SI, et al. Understanding practice change in community pharmacy: a qualitative research instrument based on organisational theory. Pharm World Sci 2003; 25(5): 227-234.*
3. *Taris WT , Ybema FJ, Beckers GJD, Verheijden WM, et al. Investigating the Associations among Overtime Work, Health Behaviors, and Health: A Longitudinal Study among Full-time Employees. Int J Behav Med 2011;18(4):352-360.*
4. *Ortmeier BG, Wolfgang AP. Career commitment, career plans, and job-related stress: a follow-up study of pharmacy students as pharmacists. Am J Pharm Educ 1993;57:25–28.*
5. *McNeely E. The consequences of job stress for nurses' health: time for a check-up. NursOutlook 2005;53:291–299.doi:10.1016/j.outlook.2005. 10.001.*
6. *Lapane KL, Hughes CM. Baseline job satisfaction and stress among pharmacists and pharmacy technicians participating in the Fleetwood Phase III study. Consult Pharm 2004;19:1029–1037.*
7. *Wolfgang AP, Perri M, Wolfgang CF. Job-related stress experienced by hospital pharmacists and nurses. Am J Hosp Pharm 1988;45:1342–1345.*
8. *McCann L, Adair CG, Hughes CM. An exploration of work-related stress in Northern Ireland community pharmacy: a qualitative study. Int J Pharm Pract 2009; 17:261–267.*
9. *Dowell AC, Westcott T, McLeod DK, Hamilton S. A survey of job satisfaction, sources of stress and psychological symptoms among New Zealand health professionals. N Z Med J 2001;114:540–543.*
10. *Newbury-Birch D, Kamali F. Psychological stress, anxiety, depression, job satisfaction, and personality characteristics in preregistration house officers. Postgrad Med J 2001;77(904): 109–111.*
11. *Mott DA, Doucette WR, Gaither CA, Pedersen CA, et al. Pharmacists' attitudes toward worklife: results from a national survey of pharmacists. J Am Pharm Assoc 2004;44: 326–336. doi:10.1331/154434504323063968.*
12. *Rothman S, Malan M. Occupational stress of hospital pharmacists in South Africa. Int J Pharm Pract 2007;15:235–242. doi: 10.1211/ijpp.15.3.0011.*

13. *Willett VJ, Cooper CL. Stress and job satisfaction in community pharmacy: a pilot study. Pharm J 1996; 256:94–98.*

14. *Harpham T. Urbanization and mental health in developing countries: a research role for social scientists, public health professionals and social psychiatrists. Soc Sci Med 1994; 39(2):233-245.*

15. *Phipps DL, Ashcroft DM. Psychosocial influences on safety climate: evidence from community pharmacies. BMJ Qual Saf. 2011;20:1062-1068. doi:10.1136/bmjqs.2011.051912.*

16. *Gupchup GV, Wolfgang AP. The health professions stress inventory: factor structures for pharmacists. Percept Mot Skills 1994;79:515–519.*

17. *Schell KL, Grasha AF. State anxiety, performance accuracy, and work pace in a simulated pharmacy dispensing task. Percept Mot Skills 2000; 90:547-561.*

18. *Marine A, Ruotsalainen J, Serra C, et al. Preventing occupational stress in healthcare workers. Cochrane Database Syst Rev 2006; (4): CD002892.*

19. *Ruotsalainen J, Serra C, Marine A, et al. Systematic review of interventions for reducing occupational stress in health care workers. Scand J Work Environ Health 2008;34(3): 169-178.*

20. *Royal Pharmaceutical Society of Great Britain. Stress: It's not just patients who get stressed…Leaflet produced by the Benevolent Fund (2006).*

21. *Gaither CA, Kahaleh AA, Doucette WR, Mott DA, et al. A modified model of pharmacists' job stress: The role of organizational, extra-role, and individual factors on work-related outcomes. Res Soc Admin Pharm 2008; 4: 231–243.*

22. *Hassell K, Seston E, Shann P. Measuring job satisfaction of UK pharmacists: a pilot study. Int J Pharm Pract 2007:259-264.*

23. *Jocić D, Krajnović D, Kostadinović Milošević K. Correlation of pharmacists' anxiety and their perception of patients' in relation to residence place. World Congress of Pharmacy and Pharmaceutical Sciences 2010, 70th International Congress of FIP, Lisboa 2010, abstract.*

24. *Schell KL, Grasha AF. State anxiety, performance accuracy, and work place in a simulated pharmacy dispensing task. Percept Mot Skills 2000; 90:547-561.*

25. *Jocić D, Krajnović D, Milošević Kostadinović K et al. The influence of pharmacists' anxiety on the perception to patients in a community pharmacy: a pilot project. 16th International Social Pharmacy Workshop. Pharmacy Practice 2010;8:112-113, abstract.*

26. *Spielberger CD. Trait-state anxiety and motor behavior. J Mot Behav 1971;3: 265-279.*

27. *Tovilović S, Novović Z. Anxiety as a trait. In: Buro M, Smederevac S, Novović Z (eds.) Assessment of psychological and psychopathological phenomena, Belgrade 2009: CPP. [in Serbian]*

28. *Cox RH. Psychology of Sport. Circulation Slap, Zagreb, Croatia, 2005. ISBN: 953-191-156-8. [in Croatian]*

29. *Miu AC, Heilman RM, Miclea M. Reduced heart rate variability and vagal tone in anxiety: trait versus state, and the effects of autogenic training. Auton Neurosci 2010;157(1-2):91-95.*

30. *Kröner B, Frieg H, Niewendiek U. Use of various programs of autogenic training in test anxiety. Z Klin Psychol Psychother 1982;30(3):254-266.*

31. *Yurdakul L, Holttum S, Bowden A. Perceived changes associated with autogenic training for anxiety: A grounded theory study. Psychology and Psychotherapy: Theory, Research and Practice 2009; 82: 403–419.*

32. *Kanji N, White A, Ernst E. Autogenic training to reduce anxiety in nursing students: randomized controlled trial. J Adv Nurs 2006;53(6):729-735.*

33. *Pagnini F, Manzoni GM, Castelnuovo G, Molinari E. The efficacy of relaxation training in treating anxiety. International Journal of Behavioral Consultation and Therapy 2009;5(3,4):264-269.*

34. *Vlajkov M. On the trail of their own. Relaxation and meditation. Novi Sad, 1990. ISBN: 86-81617-01-X. [in Serbian]*

35. *Stetter F, Kupper S. Autogenic Training: A Meta-Analysis of Clinical Outcome Studies. Appl Psychophysiol Biofeedback 2002;27(1):45-98.*

36. *Sutherland G, Andersen MB, Morris T. Relaxation and Health-Related Quality of Life in Multiple Sclerosis: The Example of Autogenic Training. J Behav Med 2005;28(3):249–256. doi: 10.1007/s10865-005-4661-2.*

37. *Ernst E, Kanji N. Autogenic training for stress and anxiety: a systematic review. Complement Ther Med 2000; 8(2):106-110.*

38. *Approval of the Ethics Committee of the Pharmaceutical Chamber of Serbia, No 687/2-2, 18/10/2011. [in Serbian]*

39. *Approval of Faculty of Pharmacy, University of Belgrade, No 1850/2, 31/10/2011. [in Serbian]*

40. *Burns DD. (1989). The Feeling Good Handbook. New York: William Morrow and Co., Plume, 1990, Revised and updated, 1999. ISBN 0-452-28132-6.*

41. *Maric Z. Manual for the advanced course Rational - emotional and cognitive - behavioral therapy. REBT Centar, Belgrade, 2009. [in Serbian]*

42. *Tomioka M, Kubo C: Group autogenic training in psychosomatic medicine: A pretreatment interview reduces the dropout rate. Int Congr Series 2006;1287:235-239.*

43. *Dongre AR, Deshmukh PR, Kalaiselvan G, Upadhyaya S. Application of Qualitative Methods in Health Research: An Overview. Online J Health Allied Scs 2009;8(4):3.*

44. *Berne E. Principles of group treatment. Grove press, INC., New York, 1966. ISBN: 0-394-17603-0.*

45. *Lindemann H. Autogenic training. Prosvjeta, Zagreb, 1988. ISBN: 86-353-0012-2. [in Croatian]*

46. *Morse JM. Designing qualitative research. In: Denzin NK, Lincoln YS, editors. Handbook of qualitative inquiry. Thousand Oaks, CA: Sage, 1994:220-235.*

47. *Kanji N., White AR., Ernst E. Autogenic training for tension type headaches: A systematic review of controlled trials. Compl Ther Med 2006;14 (2):144-150.*

48. *Manzoni GM, Pagnini F, Castelnuovo G, Molinari E. Relaxation training for anxiety: a ten-year systematic review with meta-analysis. BMC Psychiatry 2008;8:41. doi:10.1186/1471-244X-8-41.*

49. *Puryear HB, Cayce CT, Thurston MA. Anxiety reduction associated with meditation: home study. Percept Mot Skills 1976;42(43):527-531.*

50. *Bonadonna R. Meditation's impact on chronic illness. Holist Nurs Pract 2003;17(6):309-319.*

51. *Herrmann JM. Essential hypertension and stress. When do yoga, psychotherapy and autogenic training help? MMW Fortschr Med 2002;144(19):38-41.*

52. *Perlitz V, Cotuk B, Schiepek G, et al. Synergetics of hypnoid relaxation. Psychother Psychosom Med Psychol 2004;54(6):250-258.*

53. *Gonzalez-Jaimes EI, Turnbull-Plaza B. Selection of psychotherapeutic treatment for adjustment disorder with depressive mood due to acute myocardial infarction. Arch Med Res 2003;34(4):298-304.*

54. *Ritz T. Relaxation therapy in adult asthma. Is there new evidence for its effectiveness? Behav Modif 2001;25(4):640-666.*

55. *Zsombok T, Juhasz G, Budavari A, Vitrai J, et al. Effect of autogenic training on drug consumption in patients with primary headache: an 8-month follow-up study. Headache 2003;43(3):251-257.*

56. *Spinhoven P, Kuile MM. Treatment outcome expectancies and hypnotic susceptibility as moderators of pain reduction in patients with chronic tension-type headache. Int J Clin Exp Hypn 2000; 48(3):290-305.*

57. *Wright S, Courtney U, Crowther D. A quantitative and qualitative pilot study of the perceived benefits of autogenic training for a group of people with cancer. Eur J Cancer Care 2002;11(2):122-130.*

58. *Goldbeck L, Schmid K. Effectiveness of autogenic relaxation training on children and adolescents with behavioral and emotional problems. J Am Acad Child Adolesc Psychiatry 2003;42(9):1046-1054.*

59. *Sakai M. Application of autogenic training for anxiety disorders: a clinical study in a psychiatric setting. Fukuoka Igaku Zasshi 1997; 88(3):56-64.*

60. *Mishima N., Goto T., Kubota S., Nagata S. Present conditions and problems of applying autogenic training to promote mental health in the workplace. International Congress Series. April, 2006 (1287): 230-234. ISSN: 0531-513.doi:10.1016/j.ics.2005.11.069 Elsevier Science*

61. *Bagheri-Nesami M, Mohseni-Bandpei MA, Shayesteh-Azar M. The effect of Benson Relaxation Technique on rheumatoid arthritis patients: Extended report. Int J Nurs Pract 2006;12:214-219.*

62. *Parle M, Maguire P, Heaven C. The development of a training model to improve health professionals' skills, self-efficacy and outcome expectancies when communicating with cancer patients. Soc Sci Med 1997;44(2):231-240.*

63. *Freeman J, Lessiter J, Keogh E, Bond FW, et al. Relaxation island: Virtual and really relaxing. Paper presented at: 7th International Workshop on Presence, 2004. Universitat Politecnica de Valencia, Spain.*

Corresponding Author
Dragana Jocic,
Department of Social Pharmacy and
Pharmaceutical Legislation,
University of Belgrade,
Faculty of Pharmacy,
Belgrade,
Serbia,
E-mail: draganajocic@beotel.net

Appendix

Appendix 1 The Burns Anxiety Inventory (40)For each of the interference circle the number that most closely indicates the extent to which it was expressed during the past week.

Category I: Anxious Feelings		not at all	somewhat	moderately	a lot
1	Anxiety, nervousness, worry, or fear	0	1	2	3
2	Feelings that things around you are strange, unreal or foggy	0	1	2	3
3	Feeling detached from all or part of your body	0	1	2	3
4	Sudden unexpected panic spells	0	1	2	3
5	Apprehension or a sense of impending doom	0	1	2	3
6	Feeling tense, stressed, "uptight", or on edge	0	1	2	3
Category II: Anxious Thoughts					
7	Difficulty concentrating	0	1	2	3
8	Racing thoughts or having your mind jump from one thing to the next	0	1	2	3
9	Frightening fantasies or daydreams	0	1	2	3
10	Feeling that you're on the verge of losing control	0	1	2	3
11	Fears of cracking up or going crazy	0	1	2	3
12	Fears of fainting or passing out	0	1	2	3
13	Fears of physical illnesses, heart attacks or dying	0	1	2	3
14	Concerns about looking foolish or inadequate in front of others	0	1	2	3
15	Fears of being alone, isolated or abandoned	0	1	2	3
16	Fears of criticism or disapproval	0	1	2	3
17	Fears that something terrible is about to happen	0	1	2	3
Category III: Physical Symptoms					
18	Skipping, racing or pounding of the heart (sometimes called "palpitations")	0	1	2	3
19	Pain, pressure or tightness in the chest	0	1	2	3
20	Tingling or numbness in the toes or fingers	0	1	2	3
21	Butterflies or discomfort in the stomach	0	1	2	3
22	Constipation or diarrhea	0	1	2	3
23	Restlessness or jumpiness	0	1	2	3
24	Tight, tense muscles	0	1	2	3
25	Sweating, not brought on by heat	0	1	2	3
26	A lump in the throat	0	1	2	3
27	Trembling or shaking	0	1	2	3
28	Rubbery or "jelly" legs	0	1	2	3
29	Feeling dizzy, lightheaded or off balance	0	1	2	3
30	Choking, or a smothering sensations or difficulty breathing	0	1	2	3
31	Headaches or pains in the neck or back	0	1	2	3
32	Hot flashes or cold chills	0	1	2	3
33	Feeling tired, weak, or easily exhausted	0	1	2	3

Add up your total score for the 33 symptoms and record it

here _____

Date: _____

Total Score	Degree of Anxiety
0 - 4	Minimal or No Anxiety
5 - 10	Borderline Anxiety
11 - 20	Mild Anxiety
21 - 30	Moderate Anxiety
31 - 50	Severe Anxiety
51 - 99	Extreme Anxiety or Panic

Gallbladder carcinoma-case series analysis

Mirjana Zivojinov[1,2], Jelena Ilic[3] , Tamara Boskovic[1,3], Srdan Zivojinov[4]

[1] Center for Pathology and Histology, Clinical Center of Vojvodina, Novi Sad, Serbia,
[2] Department of Pathology, Medical Faculty, Novi Sad, Serbia,
[3] Department of Histology and Embryology, Medical Faculty, Novi Sad, Serbia,
[4] Institute of Surgery, Clinical Center of Vojvodina, Novi Sad, Serbia.

Abstract

Gallbladder carcinoma is among the five most common malignancies of the digestive tract. It is more common in female elderly patients over 60 years of age. A common associated finding is the presence of gallstones and chronic cholecystitis. Aim was to examine clinic and pathologic features of gallbladder carcinoma, distribution by gender and by age of patients. The method used for obtaining representative histological specimens for microscopic examination was to select tissue samples from fundus, corpus and neck in order to cover the whole mucosal surface. The patients were 46 women and 18 men between the ages 41 to 81 years (mean ages of diagnosis, 69 years). Grossly 86,2% the cases of malignancy were characterized by infiltrative growth. Adenocarcinoma was the most frequent histological type (79,3%). Perineural invasion was observed in 63,8% and perivascular in 41,4% of cases. The most frequent pathologic stage for this tumor was pT2 (infiltration of the gallbladder wall, with compromise of serosa) and pT3 (extension to hepatic parenchyma). Associated chronic cholecystitis was found in 55 patients (85,9%).

Key words: gallbladder, adenocarcinoma, chronic gallstones cholecystitis, pTNM stage.

Introduction

Gallbladder carcinoma is among the five most common malignancies of the digestive tract. It is more common in women over 60 years of age. Its incidence varies in different parts of the world, and depends on the lifestyle and diet (1). It is considered for genetic factors to have a major impact on the development of the gallbladder carcinoma, as well as environmental factors. The major risk factors for developing gallbladder carcinoma are: gallstones, diet and obesity, pollutants and environmental factors, sex, bile infections, porcelain gallbladder and anomalous pancreatobiliary ductal junction. A common associated finding is the presence of gallstones, which can occur in approximately 90% of cases (2). Often a clinical diagnosis of malignancy is not apparent and the diagnosis becomes an incidental finding after evaluating a specimen removed under the clinical diagnosis of cholecystitis. In about 90% of cases the major risk factor is duration of chronic cholecystitis associated with gallstones. It leads into epithelial dysplasia and carcinoma through the time (3,4). The most frequent histological type is adenocarcinoma, accounting for more than 95% of gallbladder carcinoma, among which almost two-thirds are moderately or poorly differentiated. Other less frequent histological types are described such as squamous, adenosquamous, mucinous, signet ring cell, clear cell carcinoma and small cell carcinoma. Two types of gross morphology may be present: infiltrative and vegetative form. The most common localization of vegetative form is fundus and neck of gallbladder and it could be necrotic, hemorrhagic or ulcerative. Tumor dissemination is mainly via the lymphatic pathway, but also by direct invasion into the liver. Prognostic factors in gallbladder carcinoma are: perineural and perivascular invasion, vein and lymphatic invasion (5).

Aim

Aim of our study was to analyze the distribution of gallbladder carcinoma at the period of five years. To examine:

- Gender
- Age of patients
- Presence of chronic gallstones cholecystitis.
- To analyze presence of tumor tissue in fundus, body and neck of gallbladder.
- To determine number of certain histological types of tumor, stage of differentiation and depth of invasion.

- To determine presence of perineural, perivascular, vein and lymphatic invasions by tumor tissue.

Material and Methods

Sixty four cases of primary gallbladder carcinoma were identified in the files of the department of Pathology at the Clinical center of Vojvodina. The cases were identified after a review of all cholecystectomies performed from 2006 to 2010 (a period of 5 years). All the macroscopic descriptions of the specimens were reviewed as well as all clinical information available. Histological evaluation of all the cases was performed. All gallbladder samples were fixated in 70% formalin and hematoxylin-eosin section were studied in all cases. The method used for obtaining representative histological specimens for microscopic examination was to select tissue samples from fundus, corpus and neck in order to cover the whole mucosal surface. Some of gallbladders were processed by spiral histological method, by wrapping whole gallbladder in the form of the spiral from fundus to neck. The middle part was tied by thread, and peripheral parts were reduced enough for paraffin mold. In that way all the length of gallbladder was continually examined, and diagnosis was performed. The histological classification was based on the World Health Organization system and the stage was determined using the TNM system (UICC International Union Against Cancer, 1997) (2).

Histological parameters were rated semi quantitative, histological type according to standard classification of gallbladder carcinomas, and other parameters had numerical character.

Macroscopy growth

1 Vegetative
2 Ulcerative
3 Infiltrative

Depth of invasion

1 Tumor confined to the mucosa
2 Tumor confined to the mucosa and muscle layer
3 Tumor infiltrates all layers of the serosa, not breaking through it
4 Tumor infiltrates through the serosa into hepatic parenchyma

Perineural invasion

0-No 1-Yes

Perivascular invasion

0-No 1-Yes

Invasion blood vessels

0-No 1-Yes

Invasion lymph vessels

0-No 1-Yes

Gender

1-Female 2-Male

* - Suspicion at carcinoma

Differentiation

1-Well 2-Moderate 3-Poor

All the results were examined and presented by graphics and tables.

Results

The most important clinical features of the 64 cases with gallbladder carcinoma are presented in Table 1 and Table 2. There were 46 females and 18 males, with median age of 69 years (range 41-81 years) (Table 1). The major number of patients were over 60 years of age. The associated gallstones chronic cholecystitis was present in 85,9% (55/64) of cases of gallbladder carcinoma. There was the suspicion at carcinoma in 54,7% (35/64) surgically removed gallbladders.

Grossly, tumor in the majority of cases showed infiltrative growth (Table 2). Pathohistological analysis showed that the most common histological type is nonspecific gallbladder adenocarcinoma (Table 2). Sporadically are registrated partially mucinous adenocarcinoma (Figure 1), squamous (Figure 2), adenosquamous (Figure 3 i 4), colloidal (Figure 5) and anaplastic gallbladder carcinoma (Figure 6). Depth of invasion of gallbladder wall compromises serosa in 57% of cases. The majority of cases are moderately differentiated in 65,5% (Table 2). Perineural (Figure 7) and perivascular invasion, as well as lymphatic invasion are present in the large percentage, while it is not the case with vein (Table 2). The number

of direct invasion into the liver is presented in Table 1. According to pTNM classification, the most common stage is pT2N0Mx (Table 1).

Discussion

The gallbladder adenocarcinoma is the most common gallbladder neoplasm. The mesenchimal and vascular gallbladder tumors were described in the literature, but their appearance is not so often.

Table 1. Clinic and Pathologic Features of Gallbladder Carcinoma

Characteristics	%	
Number of patients	64	
The average age of patients	69	
Number of patients by age		
41-50	1/64	1,6%
51-60	16/64	25%
61-70	19/64	29,7%
71-80	19/64	29,7%
81-90	9/64	14%
Gender		
female	46/64	71,9%
male	18/64	28,1%
Calculosis		
present	55/64	85,9%
Suspicion at carcinoma	35/64	54,7%
Hepatic metastasis		
present	5/64	7,8%
Nodal involvement		
present	9/64	14,1%
Pathology		
T stage		
T1a	2/62	3,2%
T1b	1/62	1,6%
T2	31/62	50%
T3	25/62	40,4%
T4	3/62	4,8%
N stage		
N0	55/62	88,7%
N1	7/62	11,3%
M stage		
Mx	57/62	91,9%
M0	1/62	1,6%
M1	4/62	6,5%

In reviewing the literature on different documented series of gallbladder carcinoma, one can estimate that its incidence is no more than 3%. The gallbladder adenocarcinoma is not so common pathology of gallbladder. There is a result of Uruguay study which shows that there were just 5 cases of gallbladder carcinoma of 802 performed cholecystectomia (2). In our study we found 64 cases in which histological documented carcinoma was present. It is still low incidence compared with other diseases of gallbladder. However, compared with incidence in the other parts of world, in Vojvodina the incidence is higher, which can be explained by specific habits about diet (a lot of fats), which could be one of the major factors of risk for developing gallbladder carcinoma.

It is not rare to mix suspicion to gallbladder carcinoma and chronic gallstones cholecystitis. Previously mentioned study in Uruguay shows that in diagnosed gallbladder carcinoma was a suspicion to carcinoma in more than 50% of cases (2), which is in correlation with results in our study. The mean age found in the present study was 69 years, while results of similar studies show that the mean age ranges from 55,8 years (2) to 74,2 years of age (6,7). The majority of patients are between 60 and 80 years of age (60,4%), which highly correlates with study in Argentina and New York (6,7). According to the literature data women were more frequently affected than men. A study in Japan (2009) shows that this ratio was 1:1 (8), contrary to the result of the study in Argentine (2006), where this ratio was 11:1 in favor of women (7). In most cases gallbladder gallstones were present (85,9%,). It can be concluded that chronic gallstones cholecystitis is common associated with gallbladder adenocarcinoma, or it could be a great risk factor in developing it. An Indian research (2008) lists associated gallstones and gallbladder carcinoma in extremely high percentage (9).

Grossly, the tumor is in 86,2% of cases in infiltrative form, which coincides with results in similar studies (7). Infiltration of the gallbladder wall with compromise of serosa is present in 50 % of cases analyzed by Japanese authors (10), while in our sample it is present in 56,9% and in 39,7 % of cases shows extension to hepatic parenchyma .

From the histopathology point of view, our cases are also similar to those of previous series pre-

Table 2. Macroscopy and Microscopy Characteristics of Gallbladder Carcinoma

Characteristics	Fundus		Body		Neck	
Number of carcinoma	58		63		60	
Macroscopy						
Vegetative	4/58	6,9%	6/63	9,5%	5/60	8,3%
Ulcerative	4/58	6,9%	5/63	7,9%	5/60	8,3%
Infiltrative	50/58	86,2%	52/63	82,6%	50/60	83,4%
Histological type						
Partially mucinous	3/58	5,2%	3/63	4,8%	3/60	5%
Nonspecific	46/58	79,3%	50/63	79,4%	46/60	76,7%
Mucinous	4/58	6,9%	5/63	7,9%	6/60	10%
Squamous	1/58	1,7%	1/63	1,6%	1/60	1,7%
Adenosquamous	2/58	3,4%	2/63	3,2%	2/60	3,3%
Anaplastic	1/58	1,7%	1/63	1,6%	1/60	1,7%
Signet-ring cell	1/58	1,7%	1/63	1,6%	1/60	1,7%
Depth of invasion						
1	0/58	/	1/63	1,6%	0/60	/
2	2/58	3,4%	2/63	3,2%	5/60	8,3%
3	33/58	56,9%	37/63	58,7%	32/60	53,3%
4	23/58	39,7%	23/63	36,5%	23/60	38,4%
Perineural invasion						
present	37/58	63,8%	34/63	54%	14/60	23,3%
Perivascular invasion						
present	24/58	41,4%	20/63	31,7%	9/60	15%
Venous invasion						
present	3/58	5,2%	3/63	4,8%	0/60	/
Lymphatic invasion						
present	20/58	34,5%	19/63	30,1%	5/60	8,3%
Differentiation						
well	5/55	9,1%	6/60	10%	7/57	12,3%
moderate	36/55	65,5%	39/60	65%	36/57	63,1%
poor	14/55	25,4%	15/60	25%	14/57	24,6%

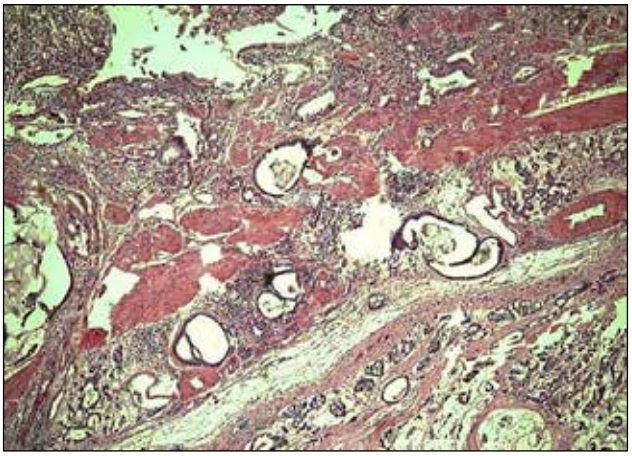


Figure 1. Partially mucinous gallbladder carcinoma (Hematoxylin-eosin stain; magnification x100)

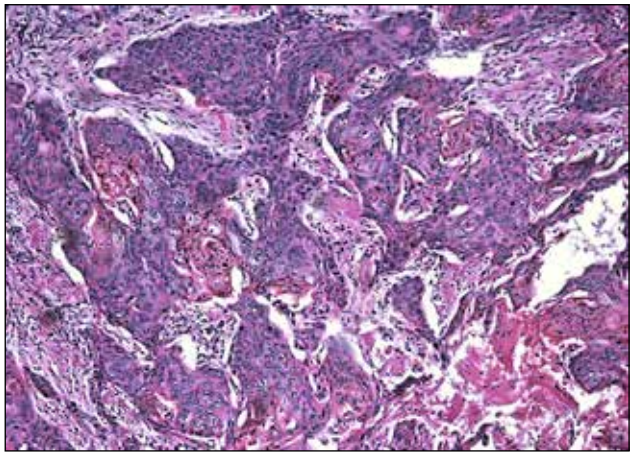


Figure 2. Squamous gallbladder carcinoma (Hematoxylin-eosin stain ; magnification x100)

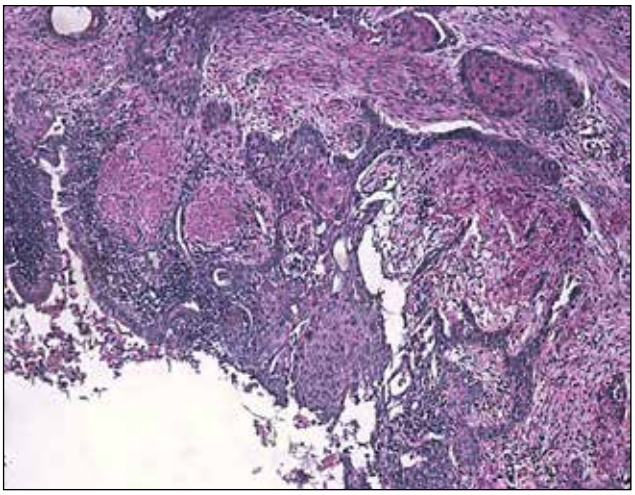


Figure 3. Adenosquamous gallbladder carcinoma (Hematoxylin-eosin stain; magnification x100)

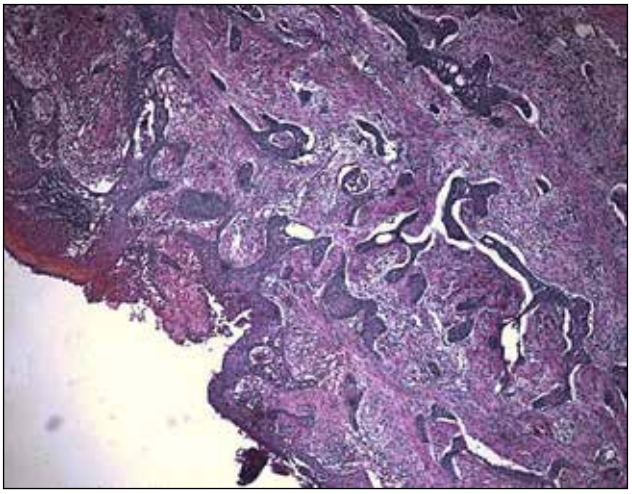


Figure 4. Adenosquamous gallbladder carcinoma (Hematoxylin-eosin stain; magnification x100)

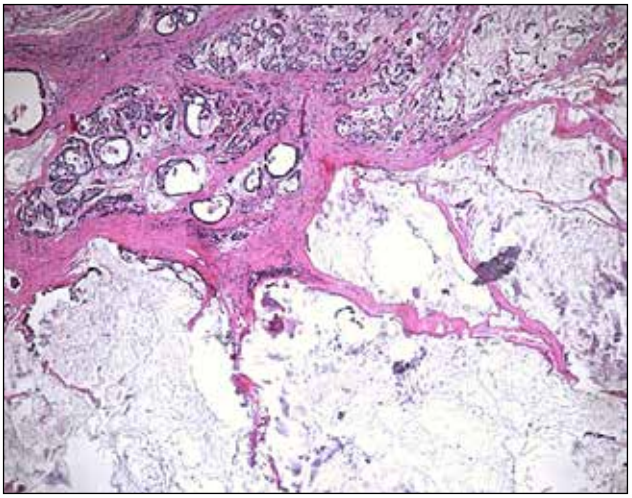


Figure 5. Colloidal gallbladder carcinoma (Hematoxylin-eosin stain; magnification x100)

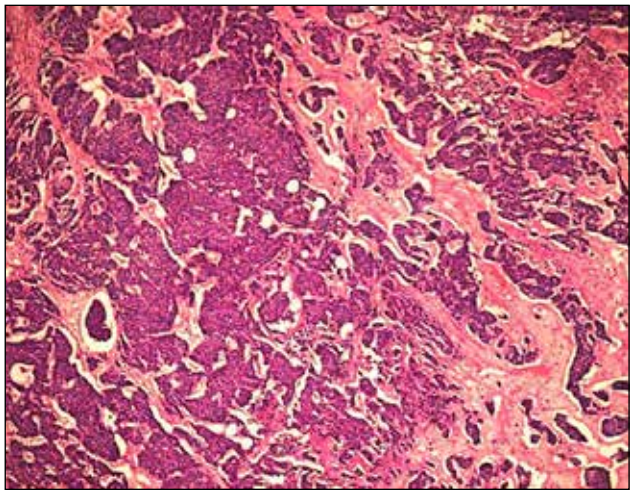


Figure 6. Anaplastic gallbladder carcinoma (Hematoxylin-eosin stain; magnification x100)

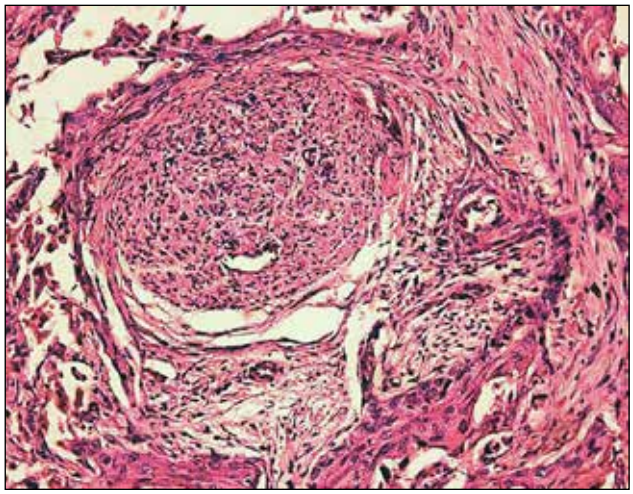


Figure 7. Perineural invasion of tumor tissue (Hematoxylin-eosin stain; magnification x100)

sented in the literature. The most common histological type according to the literature is nonspecific adenocarcinoma with the incidence of 100% (7), while our results show that the incidence of NOS type of gallbladder adenocarcinoma is 79,4%. It is confirmed that there is the presence of sporadic cases of mucinous, partially mucinous, adenosquamous, squamous and anaplastic adenocarcinoma. Those histological types are also described in the literature, like sporadic cases (11,12,13).

Important prognostic factors are perineural and perivascular invasion by tumor tissue. Perineural and perivascular invasion most commonly include fundus, then body and in the end neck of gallbladder. The literature data shows the same results of

study in Japan (2009) (10). Lymphatic invasion is present in more than 30% of cases, while vein invasion is rare (5% of cases). In the current study there is 63,8% of cases with perineural invasion in fundus of gallbladder, and perivascular invasion in 41,4 % of cases. In the body of gallbladder there was 54% of cases with perineural invasion and with perivascular 31,7 % of cases. The lower number of perineural (23,3%) and perivascular (15%) invasion is in the neck of gallbladder. Despite our results, Japanese study shows data that lymphatic and vein invasion were present in 70% of gallbladder carcinoma (10). In the year of 2005 study in Japan showed that liver metastasis were present in 10% analyzed cases (14), which correlates with result in our study (7,8%).

The differentiation stage of tumor is very significant prognostic parameter. In our study the majority of cases were moderately differentiated (65%), while 25% of cases were poorly differentiated. Studies at the territory of New York and Japan show similar results (6,10).

According to the WHO stage classification our sample shows that the most common stage is pT2, which coincides with the study in Tokyo (14), while the study done in New York gives information that the most common is the stage pT3 (6).

Conclusion

Although the gallbladder carcinoma is among the five most common malignancies of the digestive tract, it is very aggressive neoplasm. The majority of cases described were in pT2 and pT3 stage. In conclusion, there was a minimal number of patients detected in early stage, which is very important prognostic parameter. According to our study women were more frequently affected than men. It is important to note that a large number of patients had infiltrative carcinoma in the gallbladder neck, which leads to necessity of additional surgery intervention (liver en block resection). In the population studied, lithiasis is a frequent disease, for this reason patients with chronic cholecystitis should be carefully monitored.

References

1. *Kapoor VK. Gallbladder Cancer: A Global Perspective. J Surg Onc 2006;93:607-9.*
2. *Barcia M, Rodrigez A, Siri L, Masllorens A, Szwebel P,Acosta G. Gallbladder carcinoma in the "Hospital de Clinicas" of Uruguay: 1998-2002. A clinicopathologi study of five cases in 802 cholecystaectomies.Ann Diagn Pathol. 2004;8(1):1-5.*
3. *Anon. Cancer of the Gallbladder and Extrahepatic Bile Ducts. Curr Probl Surg 2007;44:396-482.*
4. *Sikora SS, Singh RK. Surgical Strategies in Patients With Gallblader Cancer:Nihilism to Optimism. J Surg Onc 2006; 93:670-81.*
5. *Goldin RD, Roa JC. Gallbladder cancer: a morphological and molecular update. Histopathology 2009; 55:218-29.*
6. *Ito H, Ito K, D Angelica M, et al. Accurate Staging for Gallbladder Cancer Implications for Surgical Therapy and Pathological Assessment.Ann Surg 2011; 254(2): 320-5.*
7. *Otero JCR, Proske A, Vallilengua C,et al. Gallbladder cancer: surgical results after cholecystectomy in 25 patients with lamina propria invasion and 26 with muscular layer invasion. J Hepatobiliary Pancreat Surg 2006;13:562-6.*
8. *Sakamoto Y, Kosuge T, Shimada K, et al. Clinical Significance of Extrahepatic Bile Duct Resection For Advanced Gallbladder Cancer.J Surg Onc 2006; 94: 298-306.*
9. *Chawla Y, Duseja A. Intrahepatic stones: Is it a lifestyle disease?J Gastroenterol Hepatol 2008; 23: 993-9.*
10. *Nakata T, Kobayashi A, Miwa S, Soeda J, Uehara T, Miyagawa S. Clinical and pathological features of primary carcinoma of the cystic duct. . J Hepatobiliary Pancreat Surg 2009;16:75-82.*
11. *Noske A, Pahl S. Combined adenosquamous and large-cell neuroendocrine carcinoma of the gallbladder. Virchows Arch 2006;449:135-6.*
12. *Krunic AL, Chen HM, Lopatka K. Signet-ring cell carcinoma of the gallbladder with skin metastases. Austral J Derm 2007; 48: 187-9.*
13. *Huang CP, Chiou YY, Chou YH, Chiang JH, Chang CY. Imaging Findings in Mucin-producting Carcinoma of the Gallbladder. J Formos Med Assoc 2006; 105(5): 427-30.*

14. *Yagi H, Shimazu M, Kawachi S, et al. Retrospective analysis of outcome in 63 gallbladder carcinoma patients after radical resection. J Hepatobiliary Pancreat Surg 2006; 13: 530-6.*

Corresponding Author
Jelena Ilic,
Department of Histology and Embryology,
Medical Faculty,
Novi Sad,
Serbia,
E-mail: jelena.ilic1705@gmail.com

Factors influencing the occurrence of denture stomatitis in complete dentures wearers

Tatjana Puskar[1], Michal Potran[1], Dubravka Markovic[1], Slobodan Puskar[2], Danimir Jevremovic[3], Tijana Lainovic[1], Larisa Blazic[1]

[1] University of Novi Sad, Medical faculty, Dentistry department, Republic of Serbia,
[2] Institute for Pulmonary Diseases of Vojvodina, Republic of Serbia,
[3] University Business Academy, School of Dentistry, Pancevo, Republic of Serbia.

Abstract

Introduction: Denture stomatitis is a chronic inflammatory disease of the soft oral tissues that occurs in denture wearing patients. Numerous factors have been proposed to have possible influence on the occurrence of denture stomatitis. Most relevant are: the age of denture, oral and denture hygiene, overnight wear of dentures, smoking habits, presence of Candida and other microorganisms.

Goal: The aim of this study was to investigate factors that influence the occurrence of denture stomatitis in patients with complete dentures.

Material and methods: The research involved 60 patients with complete dentures, residents of a nursing home facility. They were asked to answer a couple of simple questions regarding their age, the age of dentures, cleaning method, smoking habits and overnight wear of dentures. Afterwards a clinical examination of the oral cavity was made, followed by plaque assessment and statistical analysis.

Results: Denture stomatitis was observed in 46,7% of complete denture wearers. The age of dentures, level of denture hygiene and overnight wear of dentures, have proven to be significant factors in the occurrence of denture stomatitis.

Conclusion: Denture stomatitis was more frequently found among patients with old dentures, poor cleaning habits and among those who wore their dentures overnight.

Key words: complete dentures, denture stomatitis, edentulous people

Introduction

Complete dentures are mobile dental restorations used for treatment of edentulous patients. Their purpose is to replace the lost teeth and parts of the alveolar ridge, thus contributing to proper function and aesthetics of chew apparatus [1]. Treatment of edentulous patients is a long term process in which preservation of oral hygiene, as well as the hygiene of dentures, plays a crucial role in maintenance and success of prosthetic therapy.

Denture surface is a susceptible place for plaque accumulation. Due to its intimate contact with oral mucosa, relatively rough surface and prevention of saliva circulation, denture surface presents almost an ideal place for plaque accumulation. Adhered plaque is a good base for bacterial and fungal colonization and contributes to the occurrence of denture stomatitis [2,3,4].

Denture stomatitis is a chronic inflammatory disease of the soft oral tissues that occurs in denture wearing patients (picture 1). Incidence of denture stomatitis is related to many local and systemic factors such as age and misfit of dentures, poor oral hygiene, continuous wear of dentures, smoking, presence of Candida and other microorganism [5,6,7,8]. According to previous studies, denture stomatitis is most often found in the elderly, especially those living in nursing homes. In addition to previously mentioned factors, this can be explained by low immune status, the use of drugs and presence of chronic diseases [9,10,11].

Design of dentures is another factor that can influence the ocurrence of denture stomatitis. It is based on current anatomical condition of the mouth and doesn't follow the continuous dynamics of bone remodelation. Alveolar ridges are prone to resorption and once appropriate dentures may prove to be ill fitting after a period of time. Inadequate dentures distribute uneven load on supporting structures, which can lead to lesions of the mucosa and resorption of the bone [12].

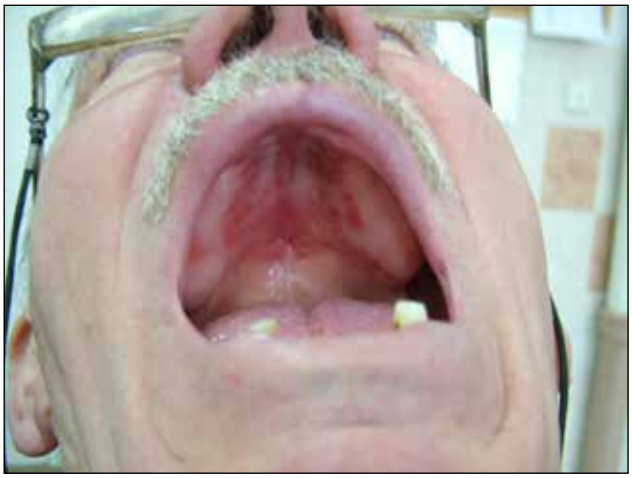
Because of its asymptomatic nature denture stomatitis can last for years, unless diagnosed. Clinical manifestations are usually painless, edematous

and hyperemic areas, which can in more severe cases progress to an inflammatory papillary hyperplasia. It is considered that hyperplastic change of the oral mucosa can go through malignant alteration, which gives diagnostics and therapy of this condition a special meaning [13,14,15].

The aim of this study was to examine the influence of gender, age, cleaning habits and continuous wear of dentures on the occurrence of denture stomatitis.

Material and method

The study included 60 patients that were residents in nursing home in Novi Sad, Serbia. The inclusion criteria were that they had to have both complete dentures and permanent residence in a nursing home. Uncooperative and senile persons were excluded from the study.



Picture 1. Denture stomatitis in the upper jaw

Investigation consisted of a written questionnaire and clinical examination of the oral cavity and corresponding dentures. The questionnaire was composed of simple questions regarding their age, gender, age of their dentures, cleaning and smoking habits and overnight removal of the dentures.The clinical part of the study involved examination of the oral cavity and plaque quantification of corresponding denture, without previous notice. The presence of denture stomatitis was determined by inspection and categorized using a Newton's index [14]. Prior to examination, dentures were rinsed by water and plaque quantification was done with Ambjornsen's index [16]. Statistical analysis was performed by standard statistical methods: mean, standard deviation and chi-square test.

Results

The study involved 60 patients, of which 34 (56,7%) were male and 26 (43,3%) were female. The average age of the examinee was 79,8 years with standard deviation of 5.847 years. Youngest examinee was 69 years old, while the oldest was 92. All patients were divided into two groups. The first one consisted of people bellow the age of 79, while the other included people above the age of 80. According to their cleaning habits, patients were further divided into three groups. The first group consisted of patients that used only toothbrushes, second one additionally used a toothpaste and the third group used chemical products. The results of the questionnaire are presented in table 1.

Table 1. Questionnaire results

		Number of women	%	Number of men	%	Number of whole sample	%
Age of the participants	69-79	12	37,5	20	62,5	32	53,3
	80-92	14	50,0	14	50,0	28	46,7
Do you smoke?	No	20	48,8	21	51,2	41	68,3
	Yes	6	31,6	13	68,4	19	31,7
How old are you dentures?	0-5	8	50,0	8	50,0	16	26,7
	5-10	0	0,0	10	100,0	10	16,7
	10+	18	52,9	16	47,1	34	56,6
How do you clean your dentures?	1	6	33,3	12	66,7	18	30,0
	2	16	47,1	18	52,9	34	56,7
	3	4	50,0	4	50,0	8	13,3
Do you remove you dentures during the night?	No	20	71,4	8	28,6	28	46,7
	Yes	6	18,8	26	81,2	32	53,3

Prevalence of denture stomatitis was 46,7% in the upper jaw and 26,7% in the lower jaw. Denture stomatitis of the lower jaw was always followed by the same condition in the upper jaw, while in 20% of the cases, it appeared solitary in the upper jaw.

Occurrence of denture stomatitis in relation to age of patients, gender, smoking habit, cleaning method, age of dentures and overnight wear of dentures are presented in figures 1-6 (x - occurrence of denture stomatitis in the lower and upper jaw, y - number of patients with denture stomatitis).

Results of plaque index are presented in figure 7 and 8. The mean of plaque was **0.900** for the lower jaw and **0.873** for the upper jaw figure 7,8.

Discussion

Questionnaire used in this study consisted of simple questions that were easy to answer. In the clinical part of the study two indices were used, Ambjornsen's index for quantification of denture plaque [16] and Newton's index for the assessment of oral mucosa condition [14]. Newton's

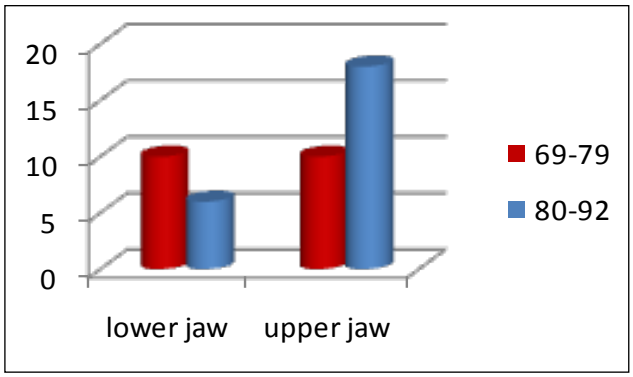


Figure 1. denture stomatitis in relation to age of patients (y-frequency)

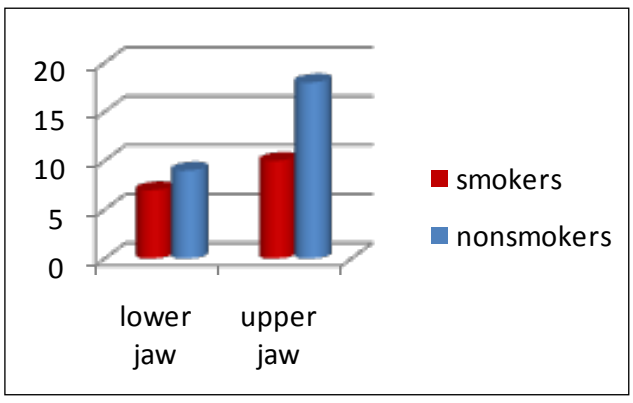


Figure 2. denture stomatitis in relation to smoking habit (y-frequency)

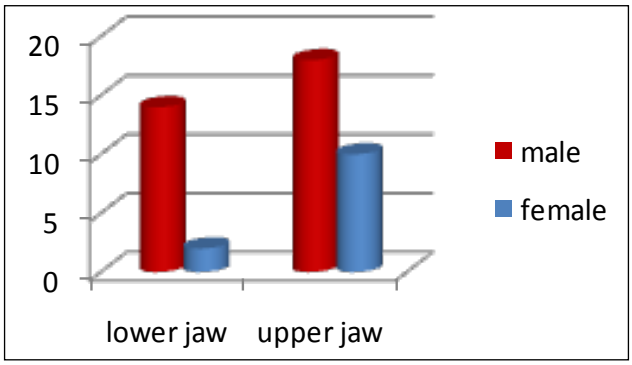


Figure 3. Denture stomatitis in relation to gender (y-frequency)

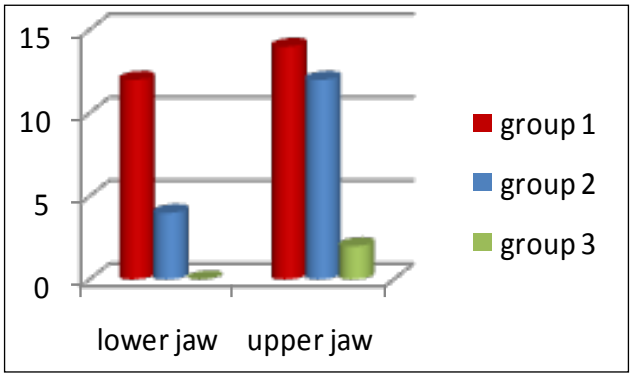


Figure 4. Denture stomatitis in relation to cleaning methods (y-frequency)

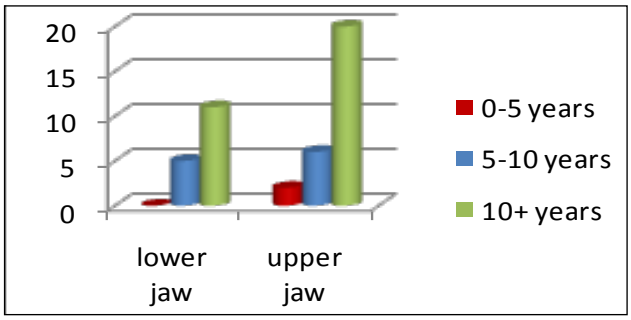


Figure 5. Denture stomatitis in relation to age of dentures (y-frequency)

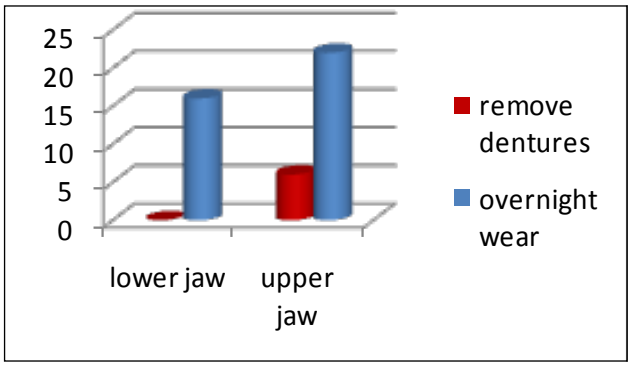


Figure 6. Denture stomatitis in relation to overnight wear of dentures (y-frequency)

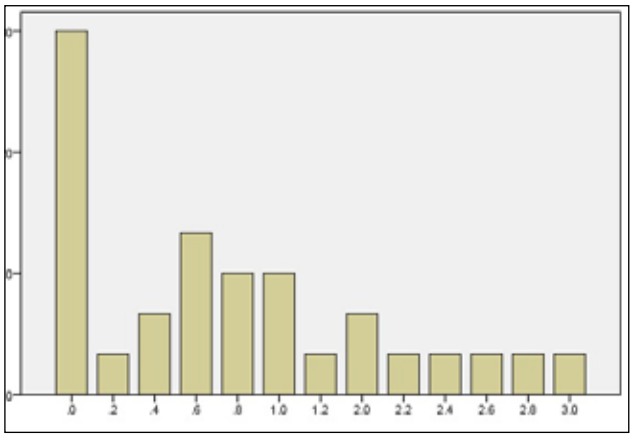


Figure 7. Plaque index of lower complete dentures. x – plaque index y – frequency*

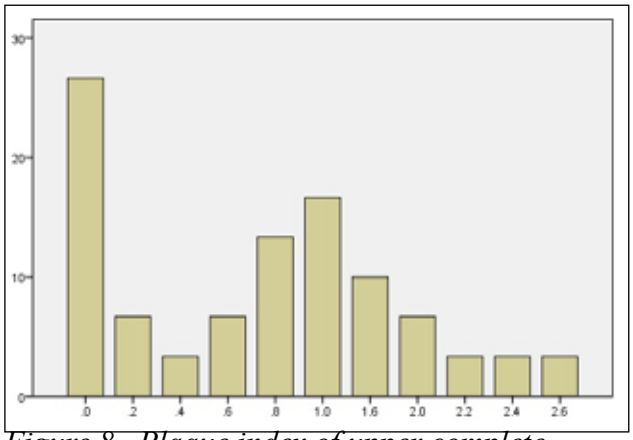


*Figure 8. Plaque index of upper complete dentures. * x – plaque index y – frequency*

index has been used in many previous studies and has shown to be a reliable method for categorization of denture stomatitis [17,18,19].

The latest review article writen by Linda Gendreau, shows that prevalence of denture stomatitis varies among different population samples, but ranges from 15% to 70% [8]. According to research carried out in Scotland, Turkey, England and Canada, among people living in nursing homes, prevalence of denture stomatitis was between 30% and 55% [10, 13, 20, 21]. This concurs with presented study, in which denture stomatitis was registered in 46.7% of the cases.

Some authors suggest that due to a larger contact area between upper denture and underlying tissues, denture stomatitis is more commonly found in the mucosa of the upper jaw [10, 22]. Results of presented study show that 46,7% patients had denture stomatitis in the upper jaw, while 26,7% patients had denture stomatitis in the lower jaw, which supports this claim.

In the presented study the occurance of denture stomatitis is relatively high, as it was found in almost half of the investigated complete denture wearers. Possible cause for such a finding could be inadequate loading of the supporting tissues by old dentures combined with overnight wear of the dentures [20, 23, 24]**.** Supporting tissues of edentulous patients are reduced and thus submitted to higher level of occlusal pressure than that of a healthy parodontium. Additionally, design of dentures doesn't follow the continuous process of bone remodelation [12, 25, 26] and dentures begin to dangle, thus becoming a source of on-going mechanical irritation. Relining of the dentures can temporary resolve this problem, but new dentures should be constructed in every five years. Release of pressure and tissue recuperation can be enhanced by overnight removal of the dentures. This should enhance saliva circulation and provide better nourishment for the underlying tissues [23]. In this study, out of 28 people that had denture stomatitis, 22 of them (78,6%) did not remove their dentures overnight. Overnight removal of dentures should be strongly recommended when giving instructions to patients.

Quantity of denture plaque is another relevant factor that can contribute to the occurence of denture stomatitis [4,6,11,27]. Majority of our examinees had low plaque index, which could explain low incidence of the condition pending on plaque accumulation. More than half of the examined dentures were older than 10 years, but the mean plaque index of the upper and lower denture didn't exceed 0.900. These results indicate high dental awareness, especially if we take into account the age of the examined patients and the fact that examinations were done without previous notice.

Adequate denture hygiene is necessary for prevention of denture stomatitis. Among all of the examinees, the best results were observed in group that cleaned their dentures with tootbrush and toothpaste. The first group that used only a toothbrush had highest prevalence of denture stomatitis with 77,8%, while the second group had 35,3% and the third 25 %. Due to a small number of participants in group three, these results should be considered with caution. The combination of brushing with proper use of chemical products is considered to be most suitable method for plaque

removal, thus contributing to healthy oral mucosa [3, 28]. Some authors suggest that denture stomatitis is more frequently found in women and elderly [29,30], but this statement is not widely accepted [23]. In this study, no significant correlation was found to support this claim. The development of new technologies [31, 32, 33] may lead to improved dental devices and maybe it will also have positive influence on the occurrence of denture stomatitis.

Denture stomatitis is a complex multifactorial disease. Presented study showed that among various factors that contribute to this condition, the age of dentures, cleaning habits and overnight wear of dentures had highest influence on the occurrence of denture stomatitis.

Conclusion

Higher prevalence of denture stomatitis was observed in patients with old dentures, poor cleaning habits and among those who wore their dentures overnight.

Majority of patients had dentures that were older than 5 years.

Prevalence of denture stomatitis was significantly higher in the upper jaw.

Acknowledgement

Results of investigation presented in this paper are part of the research realised in the framework of the project "Research and development of modeling methods and approaches in manufacturing of dental recoveries with the application of modern technologies and computer aided systems"– TR 035020, financed by the Ministry of Science and Technological Development of the Republic of Serbia.

References

1. *Krstić M. Petrović A. Stanišić-Sinobad D. Stošić Z. Stomatološka protetika, Totalna Proteza, treće izdanje, Velarta Beograd 2006, p. 46-46.*

2. *Puri G, Berzins D.W, Dhuru V.B, Raj P.A, Rambhia S.K, Gunjan D.G, Dentino A.R. Effect of phosphate group addition on the properties of denture base resins. Journal of Prosthetic dentistry. 2008; 100: 302-308.*

3. *Iseri U, Uludamar A, Kulak Ozkan Y. Effectiveness of different cleaning agents on the adherence of Candida albicans to acrylic denture base resin. Gerodontology. 2011; 28: 271–276.*

4. *Felton D, Cooper L, Duqum I, Minsley G, Guckes A, Haug S, Meredith P, Solie C, Avery D, Deal Chandler N. Evidence-Based Guidelines for the Care and Maintenance of Complete Dentures: A Publication of the American College of Prosthodontists. Journal of Prosthodontics. 2011; 20: S1–S12.*

5. *Jagger, D.C, Harrison A. Denture cleansing the best approach. Br. Dent. J. 1995; 178: 413–417.*

6. *Shulman JD, Rivera-Hidalgo F, Beach MM. Risk factors associated with denture stomatitis in the United States. J Oral Pathol Med. 2005;34: 340-346.*

7. *Hoshi N, Moi H, Taguchi H, Taniguchi M, Aoki H, Sawada T at al. Management of oral candidiasis in denture wearers. Journal of prosthodontic research. 2011; 55: 48-52.*

8. *Gendreau L, Loewy Z.G. Epidemiology and Etiology of Denture Stomatitis. Journal of Prosthodontics. 2011; 20: 251–260.*

9. *Ramage G, Tomsett K, Wickes BL, Lopez-Ribot JL, Redding SW. Denture stomatitis: a role for Candida biofilms. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2004; 98: 53–9.*

10. *Cumming CG, Wight C, Blackwell CL, Wray D. Denture stomatitis in the elderly. Oral Microbiol Immunol. 1990; 5(2): 82-5.*

11. *Mandali G, Sener I.D, Turker S.B, Ulgen H. Factors affecting the distribution and prevalence of oral mucosal lesions in complete denture wearers. Gerodontology. 2011; 28: 97–103.*

12. *Devlin H, Ferguson MW. Alveolar ridge resorption and mandibular atrophy – a review of the role of local and systemic factors. Br Dent J. 1990; 170: 101–104.*

13. *Frenkel H, Harvey I, Newcombe RG. Oral health care among nursing home residents in Avon. Gerodontology. 2000; 17(1): 33-8.*

14. *Newton AV. Denture sore mouth as possible etiology. Brit Dental J. 1962; 112: 357-60.*

15. *Splieth C.H, Sumnig W, Bessel F, John U, Kocher T. Prevalence of oral mucosal lesions in a representative lesion. Quintessence international 2007; 38: 23-29.*

16. *Ambjornsen E, Valderhaug J, Norheim P, Floystrand F. Assessment of an additive index for plaque accumulation on complete maxillary dentures. Acta Odontol. Scand. 1982; 40: 203-208.*

17. *Aleksov Lj. Stomatitis i totalne zubne proteze. Acta stomatologice Naissi. 1986; 6: 37-38.*

18. *Marković D. Ocena uspeha zdravstveno vaspitnog rada kod nosilaca mobilnih zubnih proteza. Magistarski rad, Novi Sad 1992.*

19. *Morimoto K, Kihara A, Suetsugu T. Clinico-pathological study on denture stomatitis. J Oral Rehabilit. 1987; 14: 513-522.*

20. *Evren B. A, Uludamar A, Iseri U, Kulak Ozkan Y. The association between socioeconomic status, oral hygiene practice, denture stomatitis and oral status in elderly people living different residential homes. Archives of Gerodontology and Geriatrics. 2011; 53: 252-257.*

21. *I.M. Kuc, Samaranayake LP, Van Heyst E.N. Oral health and microflora in an institutionalised elderly population in Canada. International dental journal 1999; 49: 33-40.*

22. *Nikawa H, Jin C, Makihira S, Egusa H, Hamada T, Kumagai H. Biofilm formation of Candida albicans on the surfaces of deteriorated soft denture lining materials caused by denture cleansers in vitro. J Oral Rehabil. 2003; 30(3): 243-50.*

23. *Fenlon M, Sherriff M, Walter JD. Factors associated with the presence of denture related stomatitis in complete denture wearers: a preliminary investigation. Eur J Prosthodont Restor Dent. 1998; 6(4): 145-147.*

24. *Compagnoni MA, Souza RF, Marra J et al. Relationship between Candida and nocturnal denture wear: quantitative study. J Oral Rehabil. 2007; 34: 600–605.*

25. *Tan W.L, Terry L. T. Wong, May C. M. Wong, Niklaus P. Lang. A systematic review of post-extractional alveolar hard and soft tissue dimensional changes in humans. Clinical Oral Implants Research 2012; 23 (s5): 1-21.*

26. *Atwood DA. Reduction of residual ridges: a major oral disease entity. J Prosthet Dent. 1971;26: 266–279.*

27. *Markovic D, Puskar T, Tesic D. Denture cleaning techniques in the elderly affecting the occurrence of denture-induced stomatitis. Medicinski pregled 1999; 1-2: 57-61.*

28. *Lee H.E, LI C.Y, Chang H.W, Yang Y.H, Wu J.H. Effects of different cleaning methods to remove Candida albicans from acrylic resin denture based material. Journal of dental sciences. 2011; 6: 216-220.*

29. *Turker S.B, Sener I.D. Factors triggering the oral mucosal lesions by complete dentures. Arhives of Gerontology and geriatrics. 2010; 51: 100-104.*

30. *Coelho, Sousa, Dare. Denture related oral mucosal lesions in Brazilian school of dentistry. Journal of oral rehabilitation. 2004; 31: 135-139.*

31. *Budak I, Soković M, Kopač J, Hodolič J. Point Data Pre-Processing Based on Fuzzy Logic for Reverse Engineering Modelling. Journal of Mechanical Engineering. 2009; 55: 755-765.*

32. *Muftic O, Kudumovic Dz, Kudumovic L. Biomedical engineering: principles and challenges. Healthmed. 2009; 3(4): 420-427.*

33. *Jevremovic D, Puskar T, Kosec B, Vukelic Dj, Budak I, Aleksandrovic S, Eggbeer D, Williams R. The Analysis of the Mechanical Properties of F75 Co-Cr Alloy for Use in Selective Laser Melting (SLM) Manufacturing of Removable Partial Dentures (RPD). METALURGIJA. 2012; 51(2): 171-174.*

Corresponding Author
Puskar Tatjana,
Klinika za Stomatologiju Vojvodine,
Novi Sad,
Serbia,
E-mail: tatjanapuskar@yahoo.com

Metabolic profile of patients with diabetes in Barbalha, Brazil

Caroline de Almeida Cabral[1], Modesto Leite Rolim Neto[1,2], Juliana Viana Pinheiro[1]

[1] Faculty of Medicine, Universidade Federal do Ceará – Barbalha, Brazil,
[2] Public Health School, Universidade de São Paulo – São Paulo, Brazil.

Abstract

Introduction: Modern life has imposed to people sedentary habits and excessive food consumption, what results into an increase of the incidence of metabolic diseases, which promote the development of atherosclerosis.

Objectives: We aimed to evaluate the metabolic profile of diabetic patients assisted by the endocrinology service from Ceará Federal University, located in Barbalha, Brazil.

Methods: This is a transversal and retrospective study, based on the analysis of patient records. 119 records were reviewed and 35 of them were selected, according to their registers about anthropometric and laboratorial measuring.

Results and discussion: Among the selected records, 65.71% were female patients. It was observed a positive relationship between age and the level of triglycerides, between LDL-cholesterol and the use of tobacco and between blood glucose and glycated hemoglobin.

Conclusion: The superposition of risk factor in this group shows the necessity of an integrated assistance and a follow-up about their metabolic profile, aiming to mitigate or retard serious circulatory pathologies.

Key words: Metabolic profile, diabetes mellitus, cardiovascular risk, endocrinology.

Introduction

Life habits have been transformed heterogeneously, but on a global scale. Modern lifestyle, based mainly on Western culture concepts, has conditioned people to practice sedentary habits and to eat excessive quantities of food. A result of this change is a great increase in the incidence of metabolic diseases worldwide, like obesity, diabetes mellitus and dyslipidemias[1]. Such diseases are interrelated and establish a set of conditions that promote the onset and the progression of atherosclerosis and its complications, important causes of morbidity and mortality.

According to statistics from the Unites States, 58% of deaths in 2002 in that country had cardiovascular disease as the primary cause[2]. In the following years, the improvement in the control and treatment of such diseases led to a slight decrease trend, especially in developed countries. In Brazil, mortality due to this type of pathology is higher than in other countries[3]. They appear more frequently as a cause of death in male individuals, but among women the rates shown in Brazil are above global indices[4]. Due to socioeconomic differences between Brazilian regions, the trend presented by cardiovascular disease incidence rates varies. In São Paulo, since 1980 was seen a decline in cardiovascular mortality numbers. In cities such as Porto Alegre and Curitiba, they are stable. In Rio de Janeiro and in the Northeastern states, there was a slight increase in the participation of circulatory events in the mortality profile[2]. This proportional decrease seen in many centers, however, is not observed among individuals with diabetes mellitus. A North American study that compared data from the 1970 and 1980 revealed that if the death rate from ischemic heart disease was reduced by 44% among non-diabetic men, among those affected by diabetes this fall was only 17%. Among non-diabetic women, the reduction was 20%, compared to an increase of 11% among carriers of such pathology[5].

Dyslipidemias have also emerged as important metabolic diseases. According to several researches conducted in different centers, the reduction in serum levels of total cholesterol and its fraction of low density lipoprotein (LDL) leads to significant reduction in cardiovascular mortality[6,7]. This association was demonstrated for both genders and all ethnic groups and adult ages[2].

The prevalence of dyslipidemia in Brazil has not been studied in order to cover the whole territory of the country. Studies have, however, revealed a prevalence of hypercholesterolemia oscillating about 24% to 30% for men and women[2,5]. Dyslipidemias are classified according to the lipid fraction that is altered. There are isolated hypercholesterolemia (LDL cholesterol> 160mg/dL), isolated hypertriglyceridemia (triglycerides> 150mg/dl), combined dyslipidemia (matching the factors previously exposed) and any of these associated with a reduction in HDL cholesterol (below 40mg/dl for men or of 50mg/dl for women)[6].

Metabolic syndrome is represented by a combination of anthropometric and laboratory findings [7]. It is related to central fat and insulin resistance and its importance, in epidemiological point of view, should be emphasized, because this syndrome is related to an increase in cardiovascular mortality of about 2.5 times[8]. Tracing metabolic profile of the population, especially those presenting a greater cardiovascular risk, such as diabetics, it is important to assess the exposure of patients to harmful and potentially fatal events[9].

Objectives

The main objective of this study is to evaluate the metabolic profile of diabetic patients followed up in the endocrinology clinic of the Ceará Federal University, in Barbalha, Brazil, through anthropometric measurements and laboratory evaluations. Secondary objectives concern to evaluate patent's glycemic and lipidic control, distributing them according to sex and statin use, and to correlate the anthropometric data and metabolic variables.

Methods

This work consists in a cross-sectional and retrospective study[10], based on the analysis of medical records of patients with diagnosed diabetes mellitus, followed up in the service of endocrinology of the Ceará Federal University, in Barbalha, Brazil. A total of 119 patient records were analyzed, out of which only 35 were selected according to the following criteria: all patients should be regularly followed in the ambulatory and have registered the analytical variables (sex, age, weight, height, fasting glucose, glycated hemoglobin, triglycerides, total cholesterol, LDL and HDL. The body mass index (BMI) was calculated as weight divided by square of height, being normal between 18.5 and 25kg/m^2, as defined by the World Health Organization (WHO) for adults[11]. The laboratory variables were considered according to normal standards of the IV Brazilian Guidelines on Dyslipidemia and Atherosclerosis Prevention (2007)[12].

Data were subjected to statistical analysis in the Microsoft Excel 2007 and Prism 2003 Grafpad softwares. Results are expressed as mean and standard deviation and regarded with universal distribution. Gender differences and treatment with statins were evaluated using the T test of Student. Within the groups, we used the method of Pearson and considered statistically significant with a P equal to or less than 0.05%.

Results And Discussion

Among the medical records selected for evaluation, 65.71% were female patients. Diabetes mellitus was the main reason for the clinical follow up for 88.57% of patients. Among all the records, there were 17 active smokers and 23 with hypertension. Table 1 shows the profile of the selected patients, according to studied factors. Patients were divided into two groups according to the lipostatic therapy (statins), users and non-users. Was not considered, however, information about the type of drug they used. There was an association, as expected, between higher levels of total cholesterol and the LDL fraction and the use of such drugs, what can be explained by the fact of the main indication for these drugs is dyslipidemia[11,12].In the analysis of correlations among the studied group, there was positive correlation between age and triglyceride level (r=0.3207, p=0.04) between smoking and LDL-cholesterol (r=0.4506; p=0.02) and between the last result of fasting glucose and glycated hemoglobin (r=0.5104, p=0.02).Among male patients, specifically, was seen a positive statistical correlation between the age factor and the presence of hypertension (r=0.5205, p=0.04). Still regarding the division of genres, among women, the statistical significance was assessed between age and

Table 1. Metabolic profile, according to variables and genders

Variables	All (N=35)	Male (N=12)	Female (N=23)
Age	52.74 (±18.60)	49.91 (±19.74)	54.21 (±18.26)
Blood glucose	137.97 (±87.01)	140.5 (±96.25)	136.52 (±83.73)
Glycated hemoglobin	9.32 (±3.03)	10.45 (±3.29)	8.3 (±2.54)
Total cholesterol	185.3 (±50.56)	169.22 (+/-47.71)	194.15 (+/-51.05)
LDL-cholesterol	110.36 (±44.61)	99.54 (±41.6)	116.44 (±46.38)
HDL-cholesterol	40.6 (±11.68)	37.34 (±6.54)	42.65 (±13.79)
Triglycerides	181 (±89.27)	155.63 (±76.34)	195.7 (±94.76)
BMI	28.53 (±6.33)	26.98 (±6.57)	29.42 (±6.19)

LDL-cholesterol and triglycerides (r=0.4943 and r=5142, respectively, p=0.025).

The greater part of patients was composed by carriers of type 2 diabetes mellitus, female-gendered and presented risk factors such as smoking, hypertension and overweight/obesity, an inappropriate metabolic profile, therefore. According to the Framingham study, are classic risk factors for cardiovascular disease: diabetes mellitus, hypertension, hypercholesterolemia, smoking and some classified as non-modifiable: age, male sex and positive family history of cardiovascular events[13,14]. According to the medical literature, hypertension is detected in 40-60% of patients with type 2 diabetes mellitus between 45 and 75 years[2,15]. This overlap was seen in 65.71% of patients in this study, which presented an average age of 52.74 years (±18.6). There was also a proportion of 48.57% of smokers, adding various risk factors in a population already carrier of an increased cardiovascular risk.

The consensus is that the high plasma concentration of LDL cholesterol - and according to some studies, also low HDL - is one of the most important independent risk factors for atherosclerosis and coronary artery disease[5,16,17]. Therefore, it is noticed that the patients in this study are at high risk for developing heart disease, because the average level of LDL-cholesterol was 110.37mg/dL (±44.61) and HDL-cholesterol, 40.6mg/dL (±11.68).

Conclusion

The patients who formed the group were mostly women, with an age over 50 years, suffering from type 2 diabetes mellitus and presenting overweight. In this description, characteristic of patients with an increased risk for cardiovascular events, many still reported active smoking, for example. The overlap of diseases found in this group draws attention to the need for comprehensive evaluation and monitoring of the metabolic profile of these patients in order to mitigate or delay the onset of disease in catastrophic consequences such as cerebrovascular accidents and ischemic myocardial disease.

Conflicts of interest

All authors declare to have no competing interests.

References

1. *Braga JR, Santos ISO, Flato UP, et al. O impacto do diabetes mellitus na mortalidade em síndromes coronarianas agudas. Arq Bras Endocrinol Metabol. 2007; 51(2): 275-280.*

2. *Pozzan R, Pozzan R, Magalhães MEC, et al. Dislipidemia, síndrome metabólica e risco cardiovascular. Rev Socerj. 2004; 17(2): 97-104.*

3. *Capes ES, Hunt D, Malmberg K, et al. Stress hyperglycemia and increased risk of death after myocardial infarction with and without diabetes: a systematic overview. Lancet. 2000; 355: 773-778.*

4. *Malerbi D, Franco L. Multicenter study of the prevalence of diabetes mellitus and impaired glucose tolerance in the urban Brazilian population aged 30-69 yr. Diabetes Care 1992; 15: 1509-16.*

5. *Moreira RO, Santos RD, Martinez I, et al. Perfil lipídico de pacientes com alto risco para eventos cardiovasculares na prática clínica diária. Arq Bras Endocrinol Metabol. 2006; 50(3): 481-489.*

6. *Horst ICC, Nijsten MWN, Vgetzang M, et al. Persistent hyperglycemia as independent predictor of outcome in acute myocardial infarction. Diabet Med. 2004; 21(4): 305-310.*

7. *Duncan BB, Schimidt MI, Polanczyk CA, et al. Risk Factors for non-communicable diseases in a metropolitan area in south of Brazil: prevalence and simultaneity. Rev Saúde Pública 1993; 27: 43-8.*

8. *Barzilav JI, Spiekerman CF, Wahl P, et al. Cardiovascular disease in older adults with glucose disorders: comparisons of American Diabetes Association of diabetes mellitus with WHO criteria. Lancet 1999; 354: 622-5.*

9. *Gigante DP, Barros FC, Post CLA, Olinto MTA. Prevalência de obesidade em adultos e seus fatores de risco. Rev Saúde Pública 1997; 31: 236-46.*

10. *Coutinho M, Gerstein HC, Wnag Y, et al. The relationship between glucose and incident cardiovascular events. Diabetes Care 1999; 22: 233-40.*

11. *Francisco PMSB, Donalisio MR, Barros MBA, et al. Medidas de associação em estudo transversal com delineamento complexo: razão de chances e razão de prevalência. Rev Bras Epidemiol 2008; 11: 347-55.*

12. *Sposito AC, Caramelli B, Fonseca FAH, et al. IV Diretriz brasileira sobre dislipidemias e prevenção da aterosclerose. Arq Bras Cardiol. 2007; 88(1): 2-19.*

13. *Lee KH, Jeang MR, Kim HM, et al. Benefit or early statin therapy in patients with acute myocardial infarction who have extremely low low-density lipoprotein cholesterol. J Am Col Cardiol. 2011; 58: 1664-1671.*

14. *Siqueira AFA, Almeida-Pititto B, Ferreira SRG. Doença cardiovascular no diabetes mellitus: análise dos fatores de risco clássicos e não-clássicos. Arq Bras Endocrinol Metabol. 2007; 51(2): 257-267.*

15. *Donahoe MS, Stewart GC, Mccabe CH, et al. Diabetes and mortality following acute coronary syndromes. JAMA. 2007; 298: 765-775.*

16. *Hypertension in Diabetes Study Group. HDS 1: Prevalence of hypertension in newly presenting type 2 diabetic patients and the association with risk factors for cardiovascular and diabetic complications. J Hypertens 1993; 11: 309-17.*

17. *Kolankiewcz F, Giovelli FMH, Bellinaso MDL. Estudo do perfil lipídico e da prevalência da dislipidemia em adultos. RBAC. 2008; 40(4): 317-320.*

Corresponding author
Modesto Leite Rolim Neto,
Universidade Federal Do Ceará,
Barbalha Ceará,
Brasil,
E-mail: Modestorolim@Yahoo.Com.Br

Obstructive acute abdomen due to intestinal intussusception in adolescent

Modesto Leite Rolim Neto[1], Edgle Pedro de Sousa Filho[1], Saulo Araujo Teixeira[1], Eduardo Sílvio Gouveia Goncalves[1,2], Joao Antonio de Macedo Junior[1], Alberto Olavo Advincula Reis[3], Luiz Carlos de Abreu[3], Henrique Cesar Nascimento Ramalho Filho[4]

[1] Faculty of Medicine, Ceará Federal University - UFC, Barbalha, CE, Brazil,
[2] Member of Brazilian College of Surgeons (CBC), Brazil
[3] Faculty of Public Health, São Paulo University – USP, São Paulo, SP, Brazil.
[4] Faculty of Medicine – Juazeiro do Norte – FMJ, Brazil

Abstract

Introduction: Intestinal intussusception is a rare disease out of childhood. It is represented by an invagination of a bowel into the lumen of the adjacent segment.

Case Report: This article reports a case of 14 year-old patient presenting intestinal obstruction caused by an intussusception at the level of the terminal ileum. A surgical resection of the invaginated segment was done and the histopathological study disclosed no evidence of malignancy.

Discussion: In children, it is usually idiopathic, but among adolescents and adults it is often related to anatomic lesions, some of them neoplastic with high risk of malignancy. Preoperative diagnosis of intestinal intussusception is difficult due to its nonspecific and subacute symptoms. Computed tomography and ultrassonography can confirm the intussusception through characteristic images.

Conclusion: Intestinal intussusception in adolescents is a rare and often misdiagnosed disease, deserving special attention from surgeons and general doctors.

Key words: acute abdomen, intussusception, small bowel.

Introduction

Intestinal intussusception was first described in XVII century[1]. It is a clinical condition characterized by an invagination of a bowel into the lumen on the adjacent segment, like a telescope. This pathology is more frequent into the pediatric age-group, notably among lactents, and it is rarely observed after the childhood[2]. Between adult patients with intestinal intussusception, 90% present an invagination secondary to any lesion with a high risk of malignancy[3]. Recent researches disclosed that in only 1-5% from all the adults with bowel obstruction it refers to intestinal intussusception.

Among adolescents, intestinal intussusception demonstrates a clinical presentation similar to that seen in children, but, like what occurs in adults, frequently has a causal pathology. Its rarity is a possible reason for the difficult faced by surgeons to manage these patients: pre-operatory diagnosis is correct only in 32% of reported cases[5].

This article aims to report a case of a 14 year-old male patient, previously healthy, who developed an acute abdomen due to intestinal obstruction after an small bowel intussusception. He underwent to segmentar surgical resection.

Case report

N. A. S. T., a fourteen years-old male patient, previously healthy, was admitted complaining of intense abdominal pain, nauseas, vomits and headache for approximately five days. When arrived to the hospital, he showed a bad general status, normal blood pressure (110x60 mmHg), heart frequency (74 per minute) and respiratory rate (16 per minute). He also had no fever (37.4ºC), but presented dehydration (+++/4+) and pallor (+++/4+). At physical examination, the abdomen was distended, diffusely painful at shallow palpation and presented low hydroaerial sounds. In the two subsequent days, he evolved with diarrhea, shivers and unwellness and complained of increasing abdominal pain. Laboratorial evaluation at the admission showed 14.000 leukocytes/μL, with 73% segmented cells. Red series, glucose and the tests for liver and kidney function was compatible with normal levels. Blood amilasis was also evaluated and was normal (116 UI/L).

A videoendoscopic examination showed an important gastric stasis, without other significant signals. Patient underwent to an abdominal computed tomography with contrast, which disclosed an intestinal obstruction characterized by a target image with rounded aspect in small bowel, taking to a severe distention of proximal segments, including stomach.Patient needed a surgical approach for his obstructive acute abdomen. In the laparotomy, were observed distention of small intestine segments, volvulus and ischemic lesions at the level of terminal ileum. Surgical procedure consisted in a segmentary enterectomy of approximately 20 inches of terminal ileum, including volvulus, and further single-plan anastomosis, followed by abdominal wall synthesis and the placement of a Penrose drain. Resected segment of small intestine, product of segmentary enterectomy, was sent to histopathological study. The specimen measured 17 x 1.5 centimeters, presented a lumen with a segment of invaginated bowel and necrotic aspect, and the diagnosis was "ischemic necrosis due to intestinal intussusception, without malignancy, granulomas or parasites".At post-operative period, patient was taken into the Intensive Therapy Unit for four days. He presented hyperglukemia (until 175 mg/dl) and leukocitosis in the first and leucopenia from third to fifth days. He had hospitalar discharge eight days after surgery, asymptomatic. The definitive diagnosis was intestinal intussusception and consequent ischemic necrosis and obstruction, resulting in an obstructive acute abdomen.

Discussion

Intestinal intussusception occurs when a proximal segment of intestine invaginates into the lumen of distal adjacent segment. A vascular oclusion which results from this telescopic invagination (like closing a telescope) is responsible for the further complications. Edema of bowel wall and venous congestion can cause intestinal obstruction, while ischemia, infarction and bowel perforation, if not treated, are potentially lethal[2].

In children, 95% of intestinal intussusception cases are idiopathic events, while in adolescents and adults, are secondary to structural lesions in 80% of cases[3]. Between pediatric population, this clinical condition results from a hyperplasia of lymphatic tissue from Peyer's patch, an aggregation of Mucosa Associated Lymphatic Tissue (MALT). Even in other age-groups, lymphoid hyperplasia can occurs due to Epstein-Barr virus (EBV) infection and non-Hodgkin lymphoma (NHL)[5].Among adolescents and adults, however, an intraluminal tumoration (frequently adenocarcinoma or GIST) often becomes in a traction-point, turning the "head of the intussusception" and, depending on peristaltic movements, results in the invagination[6]. Some non-neoplastic causes involved in small bowel intussusception in adolescents and adults are post-operative adhesions, morphologic abnormalities and Meckel's diverticulum.

Intussusception can develop at several locations, but the most frequent is enteric, at ileocecal topography, responsible for almost 35% of cases[4]. Surgical diagnosis in a study with 745 cases of intestinal intussusception disclosed that 52% of them originated from small intestines, 39% enteroenteric (invagination of two small intestine segments) and 13% ileocolic (invagination of terminal ileum into the colon)[7].Clinical presentation can be different between patients, with unspecific, chronic or subacute symptoms. Abdominal pain is, however, present in 88%, nauseas and vomits in 42% of adolescents with this disease. In adults, often there is partial and intermitent obstruction of bowel lumen. Abdominal palpable mass, constipation, diarrhea, fever and peritonitis can also be found, but with slighter prevalence. Just in 50% of patients there are typical signals of intestinal obstruction, while melena and strawberry-jelly fezes are present in 29% of them[8]. Intussusception can be followed by complications like perforative acute-abdomen and sepsis.Diagnostic investigation is based in imaging: roentgenogram, contrasted exams, computed tomography of the abdomen, ultrassonography and colonoscopy. Definitive diagnosis can be done without invasive methods. Computed tomography is considered the best method for diagnosing an intestinal intussusception[9], although in some countries it is not easily avaliable. Ultrassonography also presents high sensitivity, being near 100% for intussusceptions in pediatric patients[10]. According to the projection of invaginated segment, typical findings on tomography and ultrassonography are the "target sign" (multiple concentric rings) or a cylindric image,

which, although not patognomonical, are very suggestive[11].

Approach to intestinal intussusception in adolescents is similar to adults. Outside pediatric age-group, treatment should consist in a segmentar resection of committed bowel. This resection should be "en bloc", without previous reduction, specially if colon is involved, due to greater risk of malignant neoplasm[12]. The therapeutics should be individualized according to involved segments and their viability. Literature does not recommend more conservative interventions, except in a few selected cases. In some cases, an apendicectomy should be done, aiming to avoid further diagnostic mistakes[13].Anatomopathological and immunohistochemical study of the surgical specimen are fundamental for the definitive diagnosis, specially for discarding the possibility of malignancy. Therefore, these studies have special application for adolescents and adults, for whom malignant neoplastic lesions correspond for an important part of the etiology.

Conclusion

Case reports about intestinal intussusception in adolescents and adults are specially relevant due to the relatively rareness of this disease. Among adults and adolescents, clinical presentation is often subacute and unspecific, what makes difficult a correct pre-operative diagnosis. This misdiagnosing can be decisive, because it is a potentially serious pathology and, in most cases, caused by a malignant neoplasm.In this case, although patient was an adolescent, the surgical resection of a small intestine segment was guided by principles of the approach to intestinal intussusception for adults, due to high risk of malignant neoplasm. This hipothesis was further denied by histopathological analysis.

Acknowledgements

This study was supported by grants the Ceará Federal University – UFC.

References

1 *Lucena MT, Apel A, Silva MJM. Intussuscepção no adulto. Rev Bras Coloproct. 2005; 25(2): 158-161.*

2 *Hanan B, Diniz TR, Luz MMP, Conceição SA, Silva RG, Lacerda-Filho A. Intussuscepção intestinal em adultos. Rev Bras Colo-proctol. 2007; 27(4): 432-438.*

3 *Huppertz HI, Soriano-Gabarro M, Grimprel E, Franco E, Mezner Z, Desselberg U, et al. Intussusception among young children in Europe. Pediatr Inf Dis J. 2006; 25(1 Suppl): 22-29.*

4 *Torricelli FCM, Lopes RI, Dias AR, Marchini GS, Bonafé WW, Lopes JM, et al. Linfoma ileal primário como uma causa de intussuscepção intestinal recorrente. Rev Bras Coloproct. 2008; 28(2): 246-250.*

5 *Brayton D, Norris WJ. Intussusception in adults. Am J Surg. 1954; 88(1): 32-43.*

6 *Batista BN, Maximiano LF. Intussuscepção intestinal em adultos jovens – relato de caso e revisão de literatura. Rev Col Bras Cir. 2009; 36(6): 533-536.*

7 *Alamarthi S, Smith RC. Adult intussusception: case reports and review of literature. Postgrad Med J. 2005; 81(953): 174-177.*

8 *Wang N, Cui XY, Liu Y, Long J, Xu YH, Guo RX, Guo KJ. Adult intussusception: a retrospective review of 41 cases. World J Gastroenterol. 2009; 15(26): 3303-3308.*

9 *Baretta GAP, Matias JEF, Okawa L, Coelho JCU. Intussuscepção, oclusão e perfuração jejunal na síndrome de Peutz-Jeghers: relato de caso. Arq Bras Cir Dig. 2005; 18(4): 145-148.*

10 *Lehnert T, Sorge T, Till H, Rolle U. Intussusception in children-clinical presentation, diagnosis and management. Int J Colorectal Dis. 2009; 24(10): 1187-1192.*

11 *Kim YH, Blake MA, Harinsighani MG, Archer-Arroyo K, Hahn PF, Pitman MB, Mueller PR. Adult intestinal intussusception: CT appearances and identification of a causative lead point. Radiographics. 2006; 26(3): 733-744.*

12 *Zubaidi A, Al-Saif F, Silverman R. Adult intussusception: a retrospective review. Dis Colon Rectum. 2006; 49(10): 1546-1551.*

13 *Araujo PJH, Rangel MF, Batista TP. Intussuscepção íleo-cólica em adulto. Rev Bras Colo-proctol. 2008; 28(4): 470-473.*

Corresponding author
Modesto Leite Rolim Neto,
Universidade Federal Do Ceará,
Barbalha Ceará,
Brasil,
E-mail: Modestorolim@Yahoo.Com.Br

Evaluation of endoscopic findings in patients candidate for renal transplantation

Mohammad Hasan Larizadeh[1], Mohammad Javad Fallah[2], Mohsen Barouni[3]

[1] Research Center for Health Services Management, Kerman University of Medical Sciences, Kerman, Iran,
[2] Isfahan University of Medical sciences, School of medicine, Iran,
[3] Research Center for Health Services Management, Kerman University of Medical Sciences, Kerman, Iran.

Abstract

Patients with end-stage renal disease (ESRD) undergoing hemodialysis demonstrate a number of gastrointestinal lesions and their complications. This was a retrospective study, accomplished during 4 years (from July 2004 to July 2007) on patients with ESRD, awaiting renal transplantation. A total of 300 patients including 174 males (58%) and 126 females (42%) enrolled during the study period. Table 1 shows the demographic characteristics of the patients. Of these, 206 patients (67.8%) had no gastrointestinal complaints.

Key words: Endoscopic, Renal Transplantation, emodialysis

Introduction

Patients with end-stage renal disease (ESRD) undergoing hemodialysis demonstrate a number of gastrointestinal lesions and their complications. In some of these lesions, such as erosions and ulcers, renal transplantation is contraindicated [1-3]. Although some of these may be related to hemodialysis, it seems that most of them are mainly caused by the pathophysiological events related to ESRD [4]. In addition, renal transplantation may also be a contributory factor for many gastrointestinal complications.

Complication of peptic ulcer such as bleeding or perforation, are associated with high mortality rate in renal transplant patients [5, 6]. For this reason, many centers actively screen patients for evidence of peptic ulcer before considering them for renal transplantation [7].

The aim of this study was to determine the prevalence of upper gastrointestinal lesions in patients with ESRD and to evaluate their relationship with some risk factors such as age, sex and gastrointestinal symptoms. Another aim was to evaluate the necessity for all patients to undergo upper gastrointestinal endoscopy (UGIE) before renal transplantation.

Patients and methods

This was a retrospective study, accomplished during 4 years (from July 2004 to July 2007) on patients with ESRD, awaiting renal transplantation. All of these patients referred from nephrologist to consider routine UGIE as a part of their pretransplantation evaluation at the endoscopic clinic in Alzahra and Noor hospitals of Isfahan University of Medical Science. Endoscopic information was collected from endoscopic file-keeping in hospitals.

The minimal standard terminology for digestive endoscopy was used to define the upper gastrointestinal lesions [8]. Upper gastrointestinal tract malignancy and excavated gastric and duodenal lesions, including erosions or ulcers, were considered as potential risk factor for post-transplant complications.

The statistical package for the social science (SPSS) software program version 13 was used for statistical analysis. The chi-squared test was used for evaluation of the relationship between risk factors and endoscopic lesions.

Results

A total of 300 patients including 174 males (58%) and 126 females (42%) enrolled during the study period. Table 1 shows the demographic characteristics of the patients. Of these, 206 patients (67.8%) had no gastrointestinal complaints. The main symptoms of the patients are presented in Table 2.

Upper gastrointestinal endoscopy was normal in 82 patients (27.3%) and abnormal in 218 patients (72.7%). The most common endoscopic lesions are shown in Table 3. Duodenal erosions and antral erosions were the most common positive findings. Chi-square test indicated that the prevalence of hemorrhagic lesions, such as ulcers and erosions in stomach and duodenum were more common in males than females (CI: 95% P value: .019). Age and presence of symptoms were not found to be related to important lesions. It was particulary notable that there was no significant relationship between presence of symptoms and findings of endoscopic lesions. Moreover, of the 35 patients who were found to have duodenal and stomach ulcer, 21 patients did not complain of any gastrointestinal symptoms.

3 patients had hyperplastic polyps in stomach. In one of them, pathologist reported pre-malignant dysplasia changes.

Table 1. Demographic characteristics of patients with end-stage renal disease (ESRD) awaiting renal transplant

Gender, male/female	**174/126**
Mean age ± SD, years	38.83 ± 13.15
Range of age, year	16 - 79

Table 2. Gastrointestinal symptoms of patients with end-stage renal disease awaiting renal transplant

	n	**%**
No symptoms	206	67.8
Symptoms		
Nausea	31	10.3
Heartburn	23	7.7
Abdominal pain	25	8.3
Regurgitation	15	5

Table 3. Endoscopic findings in patients with end-stage renal disease awaiting renal transplant

	n	**%**
Normal	82	27.3
Endoscopic lesions		
Esophagitis	17	5.7
Antral erosions	62	20.7
Duodenal erosions	95	31.7
Gastric ulcer	7	2.3
Duodenal ulcer	28	9.3
Hyper plastic polyp	3	1

Discussion

Previous studies have reported that several gastrointestinal lesions occur in patients with ESRD [3, 9]. Upper gastrointestinal lesions have been found to be present in 25-75% of patients with ESRD [10-13]. The pathogenesis of mucosal lesions in these patients is still unclear. The prevalence of esophagitis in our study was 5.7%. In a similar study it was 8.8% [1]. In two other study investigating asymptomatic ESRD patients undergoing hemodialysis, 17/249 (6.8%) and 8/60 (13%) had endoscopic evidence of esophagitis [14, 15].

In another study similar to our study, Sotoudemanesh R et al. reported esophagitis in 5.9%, antral erosions in 23.2%, duodenal erosion in 32% and duodenal ulcer in 7.7% of patients. No patients had gastric ulcer in their study [16].

In our study, duodenal erosion was present in 31.7%, antral erosion in 20.7%, duodenal ulcer in 9.3% and gastric ulcer in 2.3% of patients.

We could not carry out upper gastrointestinal endoscopy in healthy individuals in order to compare them with patients with ESRD. However, in a prospective study, Akdamar et al. performed UGIE on 355 healthy, asymptomatic male volunteers, aged between 18 and 45 years, and reported abnormal endoscopic findings in 38%. The prevalence in these asyptomatic individuals was 8.5% for erosive esophagitis, 12% for erosive gastritis, 10% for erosive duodenitis, 2% for gastric ulcer and 2% for duodenal ulcer [17]. The population of this study might not be completely comparable to our patients, but the prevalence of the lesions seems to be higher in our patients.

Furthermore, in a study done by Prakash & Agrawal, 182 patients with ESRD were evaluated and it was found that 8.8% had peptic ulcerations [1]. On the other hand, other studies have shown that the prevalence of peptic ulceration in patients with ESRD is nearly similar to that in other population groups [14, 18].

Studies of ESRD patients by Kang et al. and Weet et al reported that peptic ulcer has become more common in uremic patients in recent years [6, 13]. In our study, the prevalence of peptic ulcer was 9.3% which is higher than other studies.

Nowadays, upper gastrointestinal endoscopy is a reliable and suitable method for diagnosing

upper gastrointestinal lesions. Because endoscopy power in diagnosing upper gastrointestinal lesions is more than other methods such as barium meal. In addition, endoscopy is a cost benefit and minimally invasive method for diagnosing lesions that may be missed in barium meal and other methods such as gastritis and erosions [10].

Canadian society of transplantation consensus guidelines on digibility for kidney transplantation advised to use upper gastrointestinal endoscopy before transplant should be considered in selected patients (i.e. those with symptoms or prior peptic ulcer disease) [19]. But in our study 21 from 35 patients who had duodenal and gastric ulcer were asymptomatic. This finding is extremely important because active peptic ulcer disease should be considered a contraindication to renal transplantation [20] and strongly support a recommendation that upper gastrointestinal endoscopy should be performed routinely before transplantation. This finding may be attributed to gastrointestinal symptoms being masked in uremic patients, due to use of antacid medication to control hyperphosphatemia, which is possibly due to uremia-associated neuropathy.

Duodenal erosions (31.7%), antral erosion (20.7%) and duodenal ulcer (9.3%) were common lesions in our patients with ESRD. Male gender was associated with a higher risk of these lesions. A high prevalence of lesions was found at endoscopy in asymptomatic patients. Our study was retrospective, and we were not able to study other risk factors such as H.pylori, serum gastrin level and acid secretion. In addition we did not study other methods for ulcers and erosions detection such as barium meal (radiology) or capsule endoscopy.

Therefore, a study to address these questions is warranted.

References

1. *Prakash J, Agrawal BK. upper gastrointestinal mucosal lesions in chronic renal failure. Indian J Gastroenterol 1991; 10: 131-132*
2. *Gheissari A, Rajyaguru V, Kunashiro R, Matsumoto T. Gastrointestinal hemorrhage in end-stage renal disease patients. Int Surg 1990; 75: 93-95*
3. *Tsai CJ, Hwang JC. Investigation of upper gastrointestinal hemorrhage in chronic renal failure. J Clin Gastroenterol 1996; 22: 2-5*
4. *Miles AM, Friesman EA. Center and home chronic hemodialysis: out-come and complications. In: Schrier RW, Gottschalk CW (eds). Textbook of kidney disease. New York: Little, Brown & Co., 1997; 6th ed: 2807-2839*
5. *Feduska NJ, Amend WJ, Vincenti F et al. Peptic ulcer disease in kidney transplant recipient. Am J Surg 1984; 148: 51-57*
6. *Kang JY, Ho KY, Yeoh KG et al. Peptic ulcer and gastritis in uraemia, with particular reference to the effect of Helicobacter pylori infection. J Gastroenterol Hepatol 1999; 14: 771-778*
7. *Chan L, Kam I. Outcome and complications of renal transplantation. In: Schrier RW, Gottschalk CW (eds). Textbook of kidney disease. New York: Little, Brown & Co., 1997; 6th ed: 2720*
8. *Delvaux M, Korman LY, Armengol-Miro JR et al. The minimal standard terminology for digestive endoscopy: introduction to structured reporting. Int J Med Inf 1998; 48: 217-225*
9. *Benzo J, Matos M, Milanes C et al. Endoscopic findings in the upper digestive tract in patients with terminal chronic kidney failure. G E N 1994; 48: 34-38*
10. *Milito G, Taccone-Gallucci M, Brancaleone C et al. Assessment of the upper gastrointestinal tract in hemodialysis patients awaiting renal transplantation. Am J Gastroenterol 1983; 78: 328-331*
11. *Milito G, Taccone-Gallucci M, Brancaleone C et al. The gastrointestinal tract in uremic patients on long-term hemodialysis. Kidney Int Suppl 1985; 17: S157-S160*
12. *Musoal R, Franzin G, Mora R, Manfrini C. Prevalence of gastrointestinal lesions in uremic patients undergoing dialysis and after renal transplantation. Gastrointest Endoscop 1984; 30: 343-346*
13. *Wee A, Kang JY, Ho MS et al. Gastroduodenal mucosa in uremia: endoscopic and histological correlation and prevalence of helicobacter-like organisms. Gut 1990; 31: 1093-1096*

14. *Andriulli A, Malfi B, Recchia S et al. Patients with chronic renal failure are not at a risk of developing chronic peptic ulcers. Clin Nephrol 1985; 23: 245-248*

15. *Mason EE, Gastrointestinal lesions occurring in uremia. Ann Intern Med 1952; 37:95-105*

16. *Sotoudemanesh R, Endoscopic findings in end-stage renal disease. Endoscopy 2003; 35: 502-505*

17. *Akdamar K, Ertan A, Agrawal NM et al. Upper gastrointestinal endoscopy in normal asymptomatic volunteers. Gastrointest Endosc 1986; 32: 78-80*

18. *Abu Farsakh NA, Roweily E, Rabaa M, Butchoun R. Brief report: evaluation of the upper gastrointestinal tract in uraemic patients undergoing hemodialysis. Nephrol Dial Transplant 1996; 11: 847-850*

19. *Knoll, G, Cockfield, S, Blydt-Hansen, T, et al. Canadian Society of Transplantation: Consensus guidelines on eligibility for kidney transplantation. CMAJ 2005; 173:S1*

20. *Dianne B, McKay EL, Milford NE, Tolkoff R. Management of the patient with renal failure. In: Brenner BM, Rector FC (eds). Brenner & Rector's. The kidney. Philadelphia: Saunders, 2000; 6th ed: 2548*

Corresponding Author
Mohsen Barouni,
Research Center for Health Services Management,
Kerman University of Medical Sciences,
Kerman,
Iran,
E-mail: mohsenbarouni@yahoo.com

Gender differences and trend in in-hospital mortality after acute myocardial infarction: An observational study

Naim Nur

Department of Public Health, Faculty of Medicine, Cumhuriyet University, Sivas, Turkey

Abstract

Background: Acute myocardial infarction (AMI) is a major public health problem. The purpose of this study was to assess the in-hospital mortality rate of acute myocardial infarction (AMI) cases and to assess the impact of age and gender on in-hospital mortality in these subjects.

Methods: In this observational study, all registered data of death cases (3040 males, 2489 females) in the Hospital of Cumhuriyet University during a period from June 1, 2003, to December 31, 2009 were eveluated respectively. A total of 188 death cases after AMI were identified.

Results: The cause- specific proportional mortality ratio depend to AMI for seven years accounted 3.4% of all registration. There were gender differences in age, comorbid conditions and smoking status. Men had a higher in-hospital mortality rate than did women; however, this gender difference disappeared after adjustment for age. Deaths cases from AMI progressively increase in males at 45-54 and in females at 55-64 age groups.

Conclusion: Our study reveals that the AMI in-hospital mortality has constantly decreased over the years and men deaths after AMI have significantly higher in-hospital mortality than women. Public health activities such as community education and prevention programs will lead to substantial reduction in mortality from AMI

Key words: Sex differences, in-hospital mortality, acute myocardial infarction

Introduction

Acute myocardial infarction (AMI) continues to be major cause of death in middle aged and elderly population. The incidence of coronary heart disease, particularly AMI, has increased in most regions of the world over the past decades. According to the World Health Organization it will be the major cause of death in the world as a whole by the year 2020 (1). This trend is associated with a mounting prevalence of conventional cardiovascular risk factors such as obesity, diabetes, hypercholesterolemia, hypertension, and smoking, among others (2-4)

Significant differences in the prevalence of AMI exist with respect to gender, age and ethnicity (5). Despite improved prognosis of patients with AMI in recent years it continues to be the leading cause of mortality in women as well as men (6). Most previous studies that examine mortality rates after AMI by gender and age have reported that women have increased in-hospital mortality risk after AMI even after adjustment for multiple confounders including age (6-8) whereas, in other studies the higher mortality in women was attributed to their older age and higher prevalence of risk factors for coronary heart disease (9-10). Also the risk among women relative to men increases linearly with decreasing age and is not fully explained by differences in AMI severity, comorbidity, or treatment (11).

Since a great deal is known about the personal, genetic, biological, and lifestyle factors, which influence the development of coronary heart diseases, it should be possible to prevent or at least postpone death in the middle ages and elderly populations at increased risk. The main purpose of this study was to assess the in-hospital mortality rate of AMI cases admitted in the Hospital of Cumhuriyet University (the only tertiary health center in Sivas city). The other objective of the study was to assess the impact of age and gender on in-hospital mortality in these subjects.

Materials and methods

In this observational study, all registrated data of death cases (3040 males, 2489 females) in the Hospital of Cumhuriyet University, Sivas-Turkey,

during a period of 7 years (June 1, 2003, through December 31, 2009) were eveluated respectively. A total of 188 death cases after AMI were identified. The inclusion criterion for this study was the diagnosis of AMI established according the definition of the World Health Organization, which requires at least two of the following criteria: 1) typical acute symptoms – chest pain for more than 20 minutes; 2) increased enzyme concentrations – creatine kinase and creatine kinase-MB twice the upper normal value within 72 hours after the onset of acute symptoms, and 3) electrocardiogram changes with or without ST-segment elevation

Trained research medical students studied the information about deaths cases after AMI from the hospital medical records in the hospital archive. Demographic data were extracted from medical records including age, gender, and the prevalence of risk factors such as a positive familial history for coronary heart disease, diabetes, hypertension, alcohol consumption and smoking status. All cases were divided into six categories: < 45, 45-54, 55-64, 65-74, 75-84 and ≥ 85 years

Statistical analysis

All data was analyzed using Statistical Package for Social Sciences version 13.0. Data are presented as mean±standard deviation or proportions (% of in-hospital death). Student t test was applied to analyze continuous variables while Chi-square test for the categorical ones. A p value of <0.05 was considered statistically significant.

Results

The overall *death rate* depend to AMI for seven years accounted 3.4% of all registration. During follow up of seven years, in-hospital mortality was higher in male cases (4 vs 2.6%, p<0.001) (OR 1.57, 95% CI 1.15–2.16), however, this finding disappeared after adjustment for age. The mean age of the study group was 69.1±10.5 years (Table 1). Of 188 in-hospital death from AMI, 97 (51.6%) had hypertension, 66 (35.1%) had diabetes mellitus, 41 (21.8%) had hypercholesterolemia, 85 (45.2%) had smoked (current or extsmokers) prior to admission, 12 (6.4%) had consumed alcohol at least once in their lifetime and 76 (40.4%) had a positive familial history for coronary artery disease. There were 123 (65.4%) males and 65 (34.6%) females. The risk factor profile differed significantly between female and male cases (Table 1). The female subjects were, on average, significantly older than male (73.1 vs 67.0 years, p<0.001), had a higher prevalence of hypertension (63.1 vs 45.5%, p=0.031) and diabetes mellitus (47.7 vs 28.5%, p=0.010), and were less frequently smokers (16.9 vs 60.2%, p<0.001). On the other hand, the proportions of subjects with *family history for coronary* heart *disease*, hypercholesterolemia and subjects who had alcohol consumption did not differ significantly between males and females. During the study period, while there was an *increasing* tendency in death cases (Figure 1), mortality rate related to AMI showed a *decreasing* tendency, this was the case for males and females (Figure 2). The Figure 3 graphically depicts gender and age-related differences in death rates from AMI. Deaths cases from AMI progressively increase in males at 45-54 and in females at 55-64

Table 1. Charecteristic of the subjects by gender (n=188)

	Total	Female	Male	P value
Age (years) (mean±SD)	69.1±10.5	73.1±9.7	67.0±10.2	<0.001
Hypertension	97 (51.6)	41 (63.1)	56 (45.5)	=0.031
Diabetes Mellitus	66 (35.1)	31 (47.7)	35 (28.5)	=0.010
Hypercholesterolemia	41 (21.8)	13 (20.0)	28 (22.8)	NS
Family history for coronary heart disease	76 (40.4)	25 (38.5)	51 (41.5)	NS
Smoking	76 (40.4)	11 (16.9)	74 (60.2)	<0.001
Alcohol consumption	12 (6.4)	1 (1.5)	11 (8.9)	NS
Cumulative number of primary attack of acute myocardial infarction	138 (73.4)	57 (87.7)	81 (65.9)	=0.001
In-hospital mortality	188 (3.4)	65 (2.6)	123 (4.0)	<0.001

age groups. Males showed similar rates at 55-64 and 65-74 age-groups. Also, similar rates were found among females at 65-74 and 75-84 age-groups. Deaths rates from AMI progressively decrease in males at 65-74 and in females at 75-84 age groups. Males and females older than 85 years showed the lowest rates.

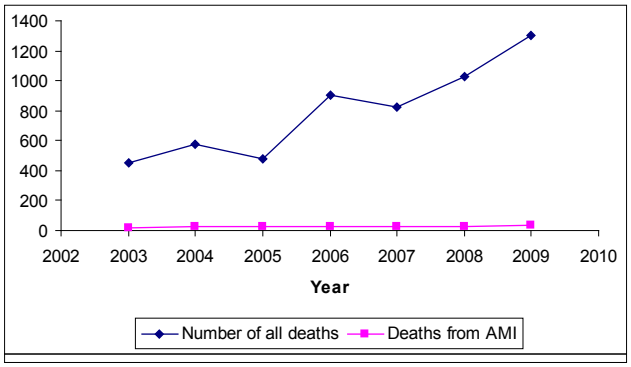


Figure 1. In-hospital mortality rate from acute myocardial infarction in the Sivas city of Turkey, 2003-2009.

Figure 2. Age-adjusted in-hospital mortality rate from acute myocardial infarction in both gender in the Sivas city of Turkey, 2003-2009.

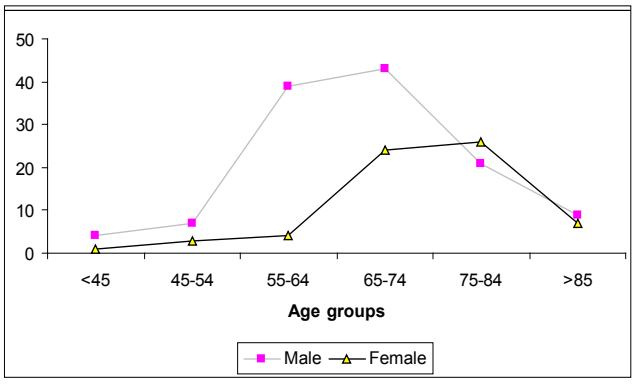


Figure 3. In-hospital mortality rate from acute myocardial infarction in both gender by age groups in the Sivas city of Turkey, 2003-2009.

Discussion

Trends and gender differences in mortality related to AMI have been studied extensively. The obtained results of this retrospective study for the seven-year period, between 2003 and 2009, demonstrates that the average mortality age of cases were consistent with the results of previous studies in suggesting that older age and other baseline variables account for much of the higher in-hospital mortality in women (12-15). Also as expected, similar to a study from Turkey, the prevalent risk factors observed among death cases from AMI in both gender are smoking, diabetes mellitus, hypertension and hypercholesterolemia (Table 1) (16).

This study documents remarkable reductions in hospital mortality after AMI for both men and women during the period of 7 years (Figure 2). This finding is similar to other studies (17-19) have described decreased in-hospital mortality after AMI in recent years, and most attributed such a decrease to improved treatment. This is not surprising because treatment use over time followed similar trends in men and women, both young and old.

Mortality rates of AMI were strongly related to gender and age. In this current study demonstrated that men show higher in-hospital mortality rates than women, particularly at earlier ages (55-64 years old), but these gender differences tend to narrow as they get older (Figure 3). This finding consistent with the some other reports regard to age and sex (2, 8, 14, 20-23), but it contradicts findings of other studies who found a significantly higher mortality rate in female cases (12, 13). Although many studies investigated sex differences in mortality after myocardial infarction (20, 24), the reasons for these differences are still not clear (25). Further research is needed to elucidate these questions.

A number of possible limitations of our study should be mentioned. We only had data on in-hospital mortality; therefore, our results may not be extrapolated to long-term outcomes. In addition, because information on prehospital deaths was not available, we were unable to determine whether sex differences in hospital mortality trends were owing to changing patterns of mortality before hospitalization. Detailed patient-level data, such as socioeconomic factors, functional status, and psychosocial factors, which may have an impact

on sex differences in mortality, were not available for our analysis. A further limitation was that some death cases after AMI may have been missed because they were misdiagnosed. Missed cases would result in underestimation of true AMI deaths. However, these deficits would have little effect on time trends.

Conclusion

This study reveals that the AMI in-hospital mortality has constantly decreased over the years, and men death after AMI have significantly higher in-hospital mortality than women. Men significantly more often die from AMI at the age of 55 to 74, and women at the age of 65 to 84. Public health activities such as community education and prevention programs will lead to substantial reduction in mortality from AMI

References

1. *Lopez AD, Murray CCJL. The global burden of disease, 1990-2020. Nature Med 1998; 4: 1241-3.*

2. *Kirchhoff M, Davidsen M, Brønnum-Hansen H, Hansen B, Schnack H, Eriksen LS, et al. Incidence of myocardial infarction in the Danish MONICA population 1982-1991. Int J Epidemiol 1999; 28: 211-218*

3. *Jones DW, Chambless LE, Folsom AR, Heiss G, Hutchinson RG, Sharrett AR, et al. ARIC. Risk factors for coronary disease in African-Americans. The Atherosclerosis Risk in Communities Study 1987-1997. Arch Intern Med 2002; 162: 2565-2571*

4. *Lee WL, Cheung AM, Cape D, Zinman B. Impact of diabetes on coronary artery disease in women and men: A meta-analysis of prospective studies. Diabetes Care 2000; 23: 962-968*

5. *Tunstall PH, Kuulasmaa K, Amouyel P, Rajakkangas AM, Pajak A. Myocardial infarction and coronary deaths in the World Health Organisation MONICA Project. Registration procedures, event rates and case fatality in 38 populations from 21 countries in 4 continents. Circulation 1994; 90: 583-612.*

6. *Rouleau JL, Talajic M, Sussex B, Potvin L, Warnica W, Davies RF. Myocardial infarction patients in the 1990s—their risk factors, stratification and survival in Canada: The Canadian assessment of myocardial infarction (CAMI) study. J Am Coll Cardiol 1996; 27: 1119-1127.*

7. *Gottlieb S, Harpaz D, Shotan A, Boyko V, Leor J, Cohen M. Sex differences in management and outcome after acute myocardial infarction in the 1990s. Circulation 2000; 102: 2484-2490.*

8. *Vaccarino V, Parsons L, Every NR, Barron HV, Krumholz HM. Sex-based differences in early mortality after acute myocardial infarction. N Engl J Med 1999; 341: 217-225.*

9. *Mahon NG, McKenna CJ, Codd MB, O'Rorke C, McCann HA, Sugure DD. Gender differences in the management and outcome of acute myocardial infarction in unselected patients in the thrombolytic era. Am J Cardiol 2000; 85: 921-926.*

10. *Heer T, Schiele R, Schneider S, Gitt AK, Wienbergen H., Gottwik M. Gender differences in acute myocardial infarction in the era of reperfusion (the MITRA registry). Am J Cardiol 2002; 89: 511-517.*

11. *Vaccarino V, Krumholz HM, Yarzebski J, Gore JM, Goldberg RJ. Sex differences in 2-year mortality after hospital discharge for myocardial infarction. Ann Intern Med. 2001; 134(3): 173-181.*

12. *Trappolini M, Chillotti FM, Rinaldi R, et al. Sex differences in incidence of mortality after acute myocardial infarction. Ital Heart J Suppl 2002; 3(7): 759-66*

13. *Fabijanic D, Culic V, Bozic I, et al. Gender differences in in hospital mortality and mechanisms of death after the first acute myocardial infarction. Ann Saudi Med 2006; 26(6): 455-60.*

14. *Hirakawa Y, Masuda Y, Kuzuya M, Iguchi A, Kimata T, Uemura K. Impact of gender on in-hospital mortality of patients with acute myocardial infarction undergoing percutaneous coronary intervention: an evaluation of the TAMIS-II data. Intern Med 2007; 46(7): 363-366.*

15. *Cheng CI, Yeh KH, Chang HW, et al. Comparison of baseline characteristics, clinical features, angiographic results, and early outcomes in men vs. women with acute myocardial infarction undergoing primary coronary intervention. Chest 2004; 126: 47-53.*

16. *Aksoydan E. Are developıng countrıes ready for ageıng populatıons? An examınatıon on the socıodemographıc, economıc and health status of elderly ın Turkey. Turkish Journal of Geriatrics 2009; 12 (2): 102-109*

17. *Peterson ED, Shah BR, Parsons L; et al. Trends in quality of care for patients with acute myocardial infarction in the National Registry of Myocardial Infarction from 1990 to 2006. Am Heart J 2008; 156(6): 1045-1055.*

18. *Gheorghiade M, Ruzumna P, Borzak S, et al. Decline in the rate of hospital mortality from acute myocardial infarction: impact of changing management strategies. Am Heart J 1996; 131: 250-256.*

19. *Koek HL, de Bruin A, Gast A, et al. Decline in incidence of hospitalisation for acute myocardial infarction in the Netherlands from 1995 to 2000. Heart 2006; 92: 162-165.*

20. *Hammar N, Alfredsson L, Rosen M, Spetz CL, Kahan T, Ysberg AS. A national record linkage to study acute myocardial infarction incidence and case fatality in Sweden. Int J Epidemiol. 2001; 30 Suppl 1: S30-4.*

21. *Heim I, Jembrek-Gostovic M, Kern J, Jonke V, Svetina M. Trends in acute myocardial infarction mortality and morbidity from 1979 to 2001 in the City of Zagreb, Croatia. Croat Med J 2005; 46(6): 970-976.*

22. *Udvarhelyi IS, Gatsonis C, Epstein AM, Pashos CL, Newhouse JP, McNeil BJ. Acute myocardial infarction in the Medicare population: process of care and clinical outcomes. JAMA 1992; 268: 2530-6.*

23. *Vaccarino V, Krumholz HM, Mendes de Leon CF, Holford TE, Horwitz RI, Berkman LF. Sex differences in survival after myocardial infarction in older adults: a community-based approach. J Am Geriatr Soc 1996; 44: 1174-82.*

24. *Demirovic J, Blackburn H, McGovern PG, Luepker R, Sprafka JM, Gilbertson D. Sex differences in early mortality after acute myocardial infarction (the Minnesota Heart Survey). Am J Cardiol. 1995; 75: 1096-101.*

25. *Bell DM, Nappi J. Myocardial infarction in women: a critical appraisal of gender differences in outcomes. Pharmacotherapy. 2000; 20: 1034-44.*

Corresponding Author
Naim Nur,
Department of Public Health,
Faculty of Medicine,
Cumhuriyet University,
Sivas,
Turkey
E-mail: naimnur@yahoo.com

The effect of telephone call reminders on electrodiagnostic laboratory attendance in Korea

Seok-Beom Kwon[1], San Jung[1], Suk Yun Kang[1], Seong-Sook Hong[2], Sung-Hee Hwang[1]

[1] Department of Neurology, Hallym University College of Medicine, South Korea,
[2] Department of Radiology, Soonchunhyang University College of Medicine, South Korea.

Abstract

Background: Non-attendances for outpatient appointments are an important obstacle to providing effective and efficient health care. For the individual, non-attendance results in the delay of effective therapy, increased morbidity, and greater hospitalization. Reminders, such as, telephone calls and letters, have been shown to significantly increase attendance rates.

Objective: This study was undertaken; 1) to measure the effect of telephone reminders on electrodiagnostic (EDX) laboratory attendance, 2) to identify factors associated with poor attendance, and 3) to determine whether reminder strategies can be used universally or whether they are best targeted at particular groups.

Methods: A randomized controlled trial took place during an 8-month period from May 2010 to December 2010. EDX laboratory bookings were randomly assigned to either a reminded groups, members of which were telephoned one day before to appointments, or to a routine booking group (the non-reminded group). Non-attendance was recorded. In addition, demographic and clinical data were evaluated and compared between the reminded and non-reminded groups. **Results:** 404 EDX examination appointments were made during the 8-month study period. Of these, 223 (55.2%) were chosen randomly to receive a telephone reminder and 181 (44.8%) received no reminder. The non-attendance rate in the reminded group was 9.0%, which was not significantly different from the 11.6% rate of the non-reminded group (OR 0.70; 95% CI 0.36, 1.35; P=0.283). However, for needle electromyography (EMG) appointments, the non-attendance rate for those reminded was 2.4%, which was significantly less than the 24.1% of those not reminded (OR 0.068; 95% CI 0.008, 0.605; P=0.016).

Conclusion: Although the effect of telephone reminders was not found to be significant in terms of overall appointment attendances at an EDX laboratory, telephone reminders greatly improved attendance for needle EMG examinations. The effectiveness of telephone reminders for promoting attendance for needle EMG examination raises the question whether reminders are best targeted at specific bookings.

Key Words: Telephone reminder, Electrodiagnostic laboratory attendance, needle EMG

Introduction

Non-attendances at outpatient appointments due to appointment cancellations and broken appointments are an important obstacle to the provision of effective and efficient health care. Clinic non-attendance is an issue that affects most clinical services to some extent. Regarding individuals, non-attendance may result in the delay of effective therapy, increased morbidity, and extended hospitalization. Non-attendance also wastes health care resources, and are largely due to forgetfulness, rescheduling, or an non-communicated cancellation of an appointment.[1-6] Various interventions have been used to promote clinic attendance, such as, postal communication[7], telephone calls[5,6,8-12], and recently using the short message service (SMS)[13-15] for clinical booking systems. Several previous studies on telephone calls (personal and computer-generated) prior to clinic appointments had been shown to effectively reduce non-attendance rates.[5,6,8-12]

Non-attendance at neurological clinics also poses problems concerning the diagnoses and treatments of neurological diseases. However, few studies have addressed the factors that effect attendance for neurologic clinic appointments. Moreover, no study has been conducted on attendance for electrodiagnostic (EDX) examinations in the neurological field. We

considered that non-attendance rates might respond to a telephone reminder a day before a scheduled EDX examination. Therefore, we undertook the present study; 1) to measure the effect of telephone reminders on EDX examination attendance, 2) to identify factors associated with poor attendance, and 3) to determine whether reminder strategies are best used universally or whether they should targeted at particular patient groups.

Material and Methods

This randomized-controlled trial took place during an 8-month period from May 2010 to December 2010. In this study, we tested the effectiveness of a single telephone call reminder on attendance at an EDX laboratory, and compared the attendances of an intervention group with a control group. All patients scheduled to require an EDX examination, such as, a nerve conduction study (NCS), needle electromyography (EMG), or evoked potential (EP) tests, were enrolled in the present study. However, only first ever bookings made were analyzed in order to reduce bias due to possible carry-over effects from previous reminders. Patients requiring an EDX examination were randomly assigned to either a telephone reminder one day prior to appointment (the reminded group), or the routine booking procedure, which involved a written reminder of the appointment time given at first meetings at the neurology outpatient department (OPD) (non-reminded group). Reminded group members were also provided with this paperwork. Randomization was performed by drawing numbered cards. During the study period, a neurology trainee telephoned patients one day before their appointments, asked if they intended to attend, and confirmed the time and date of the EDX examination. The trainee did not have access to patients' medical notes and did not encourage questions related to the reason for the investigation. Telephone numbers were obtained from a computerized hospital information system. Attendances were recorded for reminded and non-reminded groups. Non-attendance was defined as no visit to the EDX laboratory without prior notification by direct visit or telephone communication. When a telephone call was not answered or the number was incorrect or disconnected, no additional attempts were made, and the patients concerned were excluded. Cancellations, defined as non-attendance with notification, were also excluded. The χ^2 test and the student's t test were used to compare categorical and continuous variables of patients randomized to the reminded or non-reminded groups. Non-attendance was the primary outcome measure.

To identify factors that affect non-attendance, we allocated all 404 study subjects to either an attendance or non-attendance group, and then assessed the significances of different study variables (age, sex, telephone reminder, and EDX examination type) on non-attendance rate using multivariate logistic regression analysis. In addition, we also examined patients scheduled for needle EMG, which is performed directly by a neurology specialist, whereas other EDX examinations are usually conducted by an electrophysiology technician. We also assessed attendances rates and attempted to identify predictors of non-attendance for needle EMG.

Results

During the 8-month study period, 411 consecutive EDX examination appointments were included in the study. Among these, seven of the scheduled appointments were excluded due to a failure to answer the telephone, an incorrect telephone number, or cancellation. Thus, 404 appointments were included in the study. Of these 404 examination appointments, 223 appointments (55.2%) were allocated to the reminded group and 181 (44.8%) to the non-reminded group. The characteristics of patients in these groups are shown in Table 1. The overall attendance rate for all 404 appointments was 89.1% (363/404), and rates for the reminded and non-reminded groups were 91.0 % (203/223) and 88.4 % (160/181), respectively. No significant group differences were evident in terms of age, sex, attendance, distance from hospital, or EDX test types. Mean age was 51 years in both groups. EDX examinations were for two types, namely, needle EMG and another such as NCS and EP. Multivariate logistic regression was carried out to assess the effect of a telephone reminder on non-attendance. Non-attendance was adjusted for age, gender, a telephone reminder,

Table 1. Comparison of reminded versus non-reminded groups

		Reminded group (n=223)		Non-reminded group (n=181)		P - value
		n	%	n	%	
Age		51.0±15.3 yrs		50.9±13.9 yrs		0.976
Sex	Female	127	(57.0)	94	(51.9)	
	Male	96	(43.0)	87	(48.1)	0.317
Attendance	No	20	(9.0)	21	(11.6)	
	Yes	203	(91.0)	160	(88.4)	0.411
Distance from hospital	< 5 km	148	(66.4)	126	(69.6)	
	5 - 8 km	54	(24.2)	39	(21.6)	
	> 8 km	21	(9.4)	16	(8.8)	0.779
EDX examination type	Needle EMG	43	(19.3)	29	(16.0)	
	Another tests	180	(80.7)	152	(84.0)	0.434

EDX, electrodiagnostic; needle EMG, needle electromyography; yrs, years old

and EDX examination type (Table 2). Age (OR 0.99; 95% CI 0.97, 1.01; *P*=0.68), gender (OR 1.33; 95% CI 0.68, 2.60; *P*=0.40), a telephone reminder (OR 1.43; 95% CI 0.74, 2.76; *P*=0.28) and EDX examination (OR 1.22; 95% CI 0.53, 2.79; *P* = 0.63) were not found to influence non-attendance. However, unlike other EDX examinations, including NCS and EP, needle EMG is carried out by a neurologist directly. Therefore, we performed subgroup analysis on those scheduled for needle EMG, which accounted for 72 of the 404 appointments. Accordingly, 43 appointments were assigned to the needle EMG reminded group and 29 to the needle EMG non-reminded group. The overall attendance rate for the needle EMG examination was 88.9% (64/72), and all reminded patients attended except one (42/43). Multivariate logistic regression analysis was conducted to assess the association between a telephone reminder and attendance for a needle EMG examination. Attendance for needle EMG was adjusted for age, gender, and a telephone reminder (Table 3). The attendance rate was found to be significantly higher for the needle EMG reminded group (97.6% (42/43) versus 75.9% (22/29)) (OR 0.07; 95% CI 0.01, 0.61; *P* = 0.016).

Discussion

Non-attendances at clinics are troublesome in almost all medical and surgical fields. EDX examinations are ordered by neurology specialists for patients suspected of having a neuromuscular disorder. These tests usually require considerable time and full patient cooperation. Usually, we make appointments at our laboratory several

Table 2. Multivariate analysis of the predictors of non-attendance in EDX examiantions using multiple logistic regression test

		N1/N2	%	*P* - value	Odds ratio	95% CI
Age				0.680	1.01	0.98 - 1.03
Sex	Female	25/196	11.3			
	Male	16/167	8.8	0.404	0.75	0.38 - 1.47
Telephone Reminder	No	21/160	11.6			
	Yes	20/203	9.0	0.283	0.70	0.36 - 1.35
EDX examination type	Needle EMG	8/64	11.1			
	Another tests	33/299	9.7	0.638	0.82	0.35 - 1.88

EDX, electrodiagnostic; needle EMG, needle electromyography; N1, number of non-attendance; N2, number of attendance; %, % of non-attendance

Table 3. Multivariate analysis of the predictors of non-attendance in needle EMG examination using multiple logistic regression test

		N1/N2	%	*P* - value	Odds ratio	95% CI
Age				0.513	1.02	0.96 - 1.09
Sex	Female	4/29	87.9			
	Male	4/35	89.7	0.567	0.63	0.13 - 3.01
Telephone Reminders	No	7/22	75.9			
	Yes	1/42	97.6	0.016	0.07	0.01 - 0.61

Needle EMG, needle electromyography; N1, number of non-attendance; N2, number of attendance; %, % of non-attendance

days or weeks in advance of testing, and because non-attendance rates are high, largely as a result of forgetfulness, more effective booking and reminder systems are required. The majority of studies on this topic subject have concluded that telephone reminders increase attendance rates. For example, in an adolescent clinic setting, O'Brien and Lazebnik[10] reported that a telephone-reminder increased the attendance rate versus non-reminded controls (55.6% vs 44.1%, P=0.002). They also noted that direct communication and automatic messaging were equally effective. Lee and McCormick[5] investigated whether telephone reminders were effective at increasing attendance rates in an outpatient endoscopy clinic. Although they failed to contact 17% of patients, telephone calls were found to increase attendance rates from 76.7% to 94.3% ($P < 0.05$). Telephone-reminders have also been found to be effective when patients are referred from emergency departments to outpatient clinics. According to a report issued by Ritchie et al.[16], patients that received a reminder call showed better attendance rates (70.7% vs 54.4%, $P = 0.002$). Telephone reminders have also been found to be effective in elderly patients with established dementia. A study by Dockery et al.[6] showed a decrease in non-attendance rate by 5% in elderly patients. Although telephone-assisted reminder systems appear to be effective at promoting attendance, other forms of reminding patients, such as, by post[7] and SMS[13,14] may also be effective. However, in contrast to the results of the above studies, overall attendance for all EDX examinations was not found to be increased by a telephone reminder in the present study. This finding is interestingly at odds with previous studies conducted in various clinical settings. The reason why a telephone reminder failed to increase EDX examination attendance is difficult to explain. However, we believe that this might have been due to the fact that EDX examinations are reserved after interviewing patients with neuromuscular problems in a neurology OPD, and patients are apprehensive of tests conducted in an unfamiliar environment. We usually provide patients with a verbal or written description of the EDX examination to explain the technical details of the procedure, and therefore, a telephone reminder probably had little impact on attendance.

In the present study, we also found that patients scheduled for needle EMG responded to the telephone reminder, and were found to be significantly more likely present for appointments than those not telephoned. In the present study, we found that the a telephone reminder led to a 21.7% absolute increase in attendance and about a 10 fold reduction in non-attendance for needle EMG appointments (attendance rates in the reminded and non-reminded groups were 75.9% and 97.6%, respectively). The finding that a telephone call increased attendance to this extent is somewhat surprising, and is higher than results reported by other studies. For example, attendance was increased by 6.9% in a study by Koshy et al.[15], by 11.5% in an attempted intervention analysis study by O'Brien and Lazebnik[10], and by 12% in a study by Sawyer et al.[12] It is difficult to compare our results directly with those of others because of study design, patient, and clinical differences. We propose the following explanations for the increased needle EMG attendance caused by the telephone reminder. First, the present study was conducted in the tertiary care University hospital. EDX examinations are performed using different modalities based on putative clinical diagnoses, NCSs are usually performed in patients suspected to have a peripheral neuropathy, and needle EMG is performed in patients with radiculopathy, plexopathy, or

myopathy. Furthermore, those requiring a needle EMG test, though not always, have a more severe disease condition, and thus, have higher expectations of the neurology clinic. Second, unlike other EDX examinations, such as, EP and NCS, needle EMG is usually performed by a neurologist directly, and patients are made aware this during OPD visits.

The present study has some limitations that deserve consideration. Subgroup analysis of those scheduled for needle EMG involved small patient numbers (all needle EMG tested patients, 72; reminded 43; and non-reminded 29). Accordingly, the design of this study was suboptimal, and a rigorous randomized controlled trial, stratified by socioeconomic characteristics and clinical conditions is required to determine whether the potential benefits identified during this study can be replicated. Knowledge of clinical presentation in the reminded and non-reminded groups is also important as it could affect the 'value' placed on the appointment by patients and potentially affect the likelihood of an appointment being kept. Another limitation is that only one reminder call was made, and in other studies, two or three calls were placed.

In conclusion, to the best of our knowledge, this is the first study to examine the effectiveness of a telephone reminder on attendance rate for EDX examinations. Although a telephone reminder was not found to have a significant effect on overall attendance at the EDX laboratory, a telephone reminder greatly improved needle EMG attendance from 75.9% to 97.6%. The present study suggests that telephone reminders have great potential value in terms of reducing non-attendance rates in EDX laboratories for needle EMG examinations. Nevertheless, the potential benefits of telephone reminders should be confirmed by a larger study with an improved design.

References

1. *Pal B, Taberner DA, Readman LP, Jones P. Why do outpatients fail to keep their clinic appointments? Results from a survey and recommended remedial actions. Int J Clin Pract 1998; 52: 436-437.*
2. *Murdock A, Rodgers C, Lindsay H, Tham TC. Why do patients not keep their appointments? Prospective study in a gastroenterology outpatient clinic. J R Soc Med 2002; 95: 284-286.*
3. *Potamitis T, Chell PB, Jones HS, Murray PI. Non-attendance at ophthalmology outpatient clinics. J R Soc Med 1994; 87: 591-593.*
4. *Herrick J, Gilhooly ML, Geddes DA. Non-attendance at periodontal clinics: forgetting and administrative failure. J Dent 1994; 22: 307-309.*
5. *Lee CS, McCormick PA. Telephone reminders to reduce non-attendance rate for endoscopy. J R Soc Med 2003; 96: 547-548.*
6. *Dockery F, Rajkumar C, Chapman C, Bulpitt C, Nicholl C. The effect of reminder calls in reducing non-attendance rates at care of the elderly clinics. Postgrad Med J 2001; 77: 37-39.*
7. *Can S, Macfarlane T, O'Brien KD. The use of postal reminders to reduce non-attendance at an orthodontic clinic: a randomised controlled trial. Br Dent J 2003; 195: 199-201.*
8. *Burgoyne RW, Acosta FX, Yamamoto J. Telephone prompting to increase attendance at a Psychiatric Outpatient Clinic. Am J Psychiatry 1983; 140: 345-347.*
9. *Tanke ED, Leirer VO. Automated telephone reminders in tuberculosis care. Med Care 1994; 32: 380-389.*
10. *O'Brien G, Lazebnik R. Telephone call reminders and attendance in an adolescent clinic. Pediatrics 1998; 101: E6.*
11. *MacDonald J, Brown N, Ellis P. Using telephone prompts to improve initial attendance at a community mental health center. Psychiatr Serv 2000; 51: 812-814.*
12. *Sawyer SM, Zalan A, Bond LM. Telephone reminders improve adolescent clinic attendance: a randomized controlled trial. J Paediatr Child Health 2002;38:79-83.*
13. *Downer SR, Meara JG, Da Costa AC, Sethuraman K. SMS text messaging improves outpatient attendance. Aust Health Rev 2006;30:389-396.*
14. *Chen ZW, Fang LZ, Chen LY, Dai HL. Comparison of an SMS text messaging and phone reminder to improve attendance at a health promotion center: A randomized controlled trial. J Zhejiang Univ Sci B 2008; 9:34-38.*

15. *Koshy E, Car J, Majeed A. Effectiveness of mobile-phone short message service (SMS) reminders for ophthalmology outpatient appointments: observational study. BMC Ophthalmol 2008; 8: 9 DOI: 10.1186/1471-2415/8/9.*

16. *Ritchie PD, Jenkins M, Cameron PA. A telephone call reminder to improve outpatient attendance in patients referred from the emergency department: a randomised controlled trial. Aust N Z J Med 2000; 30: 585-592.*

Corresponding Author
Sung-Hee Hwang,
Department of Neurology,
Hallym University,
College of Medicine,
Seoul,
South Korea,
Email: hwang@hallym.ac.kr
neukwon@hallym.ac.kr

The Insertion allele of angiotensin converting enzyme increases the risk for coronary artery ectasia

Ibrahim Tekedereli[1], Murat Kara[2], Necati Dagli[3], Mehmet Sait Gurevin[3], Mehmet Ali Kobat[4]

[1] Department of Medical Biology and Genetics, School of Medicine, Inonu University, Malatya, Turkey,
[2] Department of Medical Genetics,Faculty of Medicine, Firat University, Elazig, Turkey,
[3] Department of Cardiology,Faculty of Medicine, Firat University, Elazig, Turkey,
[4] Department of Cardiology,ElazigResearch and Training Hospital, Elazig, Turkey.

Abstract

Coronary artery ectasia(CAE) is characterized by dilation of the coronary arteries, exceeding the 1.5-fold of normal adjacent segment in coronary angiography. A common polymorphism in the angiotensin converting enzyme (ACE) gene is insertion/deletion (I/D) polymorphism. The presence of D allele has been shown to be associated with higher blood ACE concentrations. One hundred CAE patients and the 100 healthy controls were enrolled in the study. The frequencies of DD, ID and II genotypes were 42, 48 and 10% for CAE patients, 65, 33 and 2% for healthy controls, respectively (p=0.0014). The allele frequencies for D and I allele were 0.815 and 0.185 for the control group and 0.660 and 0.340 for the patient group (p=0.0004). In conclusion, our data suggest that the I allele which represents lower ACE levels leads to a decrease in vascular tone and increase in the susceptibility to CAE.

Key Words: Coronary artery ectasia, Angiotensin converting enzyme, Polymorphism

Introduction

Coronary artery ectasia (CAE) is characterized by localized or diffuse, irregular, saccular, or fusiform dilation of the coronary arteries exceeding the 1.5-fold of normal adjacent segment in coronary angiography (1, 2). The incidence has been reported 1.5 - 5 % in different series and men are more prone than women (3). The etiopathogenesis has not been fully understood. While some cases reported to be congenital, some has been found to be related to atherosclerosis, inflammation and connective tissue diseases (3).

The angiotensin-converting enzyme (ACE) is expressed in many tissues such as heart, kidney, lung, vascular endothelium, skin and immune cells (4, 5) and plays a major role on the control of vascular tonus by converting angiotensin I into angiotensin II (6). A common polymorphism in the ACE gene is insertion/deletion (ID) polymorphism which is characterized by the presence or absence of a 287-bp DNA fragment (7). The presence of D allele has been shown to be associated with higher blood ACE concentrations. The role of renin-angiotensin system has been well documented in circulatory system. It has been reported that many organs have their own paracrine renin angiotensin system which is responsible for organ specific effects (8). It has also been reported that ID polymorphism of ACE is related to many disorders including hypertension and type 2 diabetes, panic disorder, systemic lupus erythematosus and lung cancer (9, 10). In this study, we aimed to investigate the role of the ID polymorphism of ACE in etiopathogenesis of CAE in a group of Turkish patients.

Methods

The study was conducted in accordance with the Declaration of Helsinki. The project was approved by the ethical committee at Firat University, Faculty of Medicine and all participants gave their informed consent.One hundred patients with CAE and the 100 controls were enrolled in this study. Patients who had diabetes, cardiac failure, myocardial infarction were excluded.

Genomic DNA was extracted from peripheral blood leukocytes using Promega DNA isolation Kit (Madison, WI, USA) according to

manufacturer's instructions and kept at -20°C until use. The gene region which includes the ID polymorphism has been amplified by PCR using specific primers below.

(forward;5'CTGGAGACACTCCCATCC TTTCT 3' and reverse; 5'ATGTGGCCATCA-CATTCGTCAGAT 3').

The PCR protocol was briefly consisted of an initial step of 94 ºC for 2 min, followed by 35 cycles of 94 ºC for 15 sec for denaturation, 58 ºC for 30 sec for annealing, 72 ºC for 30 sec for extension, and a final extension at 72 ºC for 3 min. The PCR product were run on 2% agarose gel and visualized under UV light.

The expected bands were a 190-bp fragment for the DD genotype or a 490- bp fragment for the II genotype or a combination of 490- and 190-bp fragmentsfor the ID genotype. In order to increase the specificity for the DD genotype, PCR products were subjected to a second PCR amplification with a insertion-specific primer set below.

(forward;5'-TGGGACCACAGCGCCCGC CACTAC-3',

reverse;5'-TCGCCAGCCCTCCCATGCCCA-TAA-3').

PCR amplification was performed for 30 cycles with denaturation at 94 ºC for 30 sec, annealing at 63 ºC for 30 sec and extension at 72 ºC for 30 sec, followed by a final extension at 72 ºC for 10 min. The PCR products were analyzed by agarose gel electrophoresis followed by UV visualization. A 335-bp PCR product was determined in the presence ofan I allele and no bands for the D allele.

Statistical analyses were performed using SPSS for Windows (Release 11.0.1, SPSS Inc., Chicago, IL). Chi-square, fisher's exact test and one-way ANOVA analysis were used to compare the genotypeand allele differences between the patients and control group. The differences were considered statistically significant if the p value was less than 0.05.

Results

A cohort of 100 patients with CAE who were followed up at Firat University Department of Cardiology were evaluated for their ACE genotype. The healthy control group consisted of 60 women, 40 men and the patient group consisted of 36 men, 64 women. The mean age of control and patient group were 53.82±1.24 and 59.13±1.31 years, respectively. There was no statistically difference between the groups regarding body mass index (BMI), blood concentrations of HDL, LDL cholesterol and triglyceride (Table 1).

The frequencies of DD, ID and II genotypes were 42 (42%), 48 (48%) and 10 (10%) for patients with CAE, 65 (65%), 33 (33%) and 2 (2%) for healthy controls, respectively (p=0.0014) (Table 2). The allele frequencies for D and I allele were 0.815 and 0.185 for the control group and 0.660and 0.340 for the patient group, respectively

Table 1. The characteristics of the participants

	Control Group	Patient Group	P value
Sex (M/F)	40/60	64/36	
Age, years	53.82±1.24	59.13±1.31	
BMI	26.63±3.37	27.32±3.97	0.282
LDL cholesterol (mg/dl)	116.98±27.95	124.75±34.04	0.151
HDL cholesterol (mg/dl)	47.04±29.07	45.58±11.52	0.698
Triglycerides (mg/dl)	166.62±113.01	163.90±77.10	0.869

Table 2. The genotype frequencies of ACE

	Angiotensin converting enzyme genotypes*§		
	DD	ID	II
Control Group	65	33	2
Patient Group	42	48	10

** Statistically significant difference between control and patient groups, p=0.0014*

§ Genotypes are in agreement with Hardy-Weinberg equilibrium

Table 3. Allele frequencies of ACE

	Angiotensin converting enzyme Alleles[+]	
	D allele	I allele
Control Group	163 (0.815)	37 (0.185)
Patient Group	132 (0.660)	68 (0.340)

[+] *Statistically significant difference between control and patient groups p=0.0004*

(p=0.0004) (Table 3). The genotype and allele distributions were in agreement with Hardy-Weinberg equilibrium.

Discussion

Although, in many cases, it is related to atherosclerosis, the pathogenesis of CAE has not been fully understood. In this study, we have shown that the functional polymorphism of angiotensin converting enzyme gene could play a role in coronary artery ectasia etiopathogenesis. It has been shown that the D allele of ACE I/D polymorphism is related to higher levels of ACE as compared to I allele (11). It has been reported that this polymorphism is related to various renal pathologies, cancers and cardiovascular diseases (12-14). In addition to increased angiotensin II plasma levels due to the D allele, there have been evidences suggesting increased production of angiotensin II within the atherosclerotic lesions which promotes the lesion (15). Additionally, Prasad et al. have reported that the D allele is associated with increased vascular smooth muscle tone (16). There are studies suggesting the contributory role of ACE I/D polymorphism in cardiac pathologies such as ischemic heart disease, hypertrophic and idiopathic dilated cardiomyopathy (17). In another study by Shim et al. reported that the I allele was more frequent than the D allele in Kawasaki disease, however, there was no statistically significant relationship with coronary dilations (15). It has been shown that the DD genotype is associated with premature coronary artery disease and acute coronary syndrome (18, 19). In a large study, Gulec et al. have shown that the DD genotype could be a potent risk factor for development of CAE (1). Conversely, in our study, we found that patients with CAE have more I allele as compared to control group. In conclusion, we suggest that the I allele leads to a decrease in vascular tone and increase in the susceptibility to CAE, since the I allele represents less amount of ACE therefore less angiotensin II, a potent vasoconstrictor and higher amount of bradykinin, a vasodilator.

References

1. *Gulec S, Aras O, Atmaca Y, Akyurek O, Hanson NQ, Sayin T, et al. Deletion polymorphism of the angiotensin I converting enzyme gene is a potent risk factor for coronary artery ectasia. Heart. 2003; 89(2): 213-4.*

2. *Balin M, Celik A, Kobat MA. The association between soluble lectin-like oxidized low-density lipoprotein receptor-1 levels and patients with isolated coronary artery ectasia. Journal of thrombosis and thrombolysis. 2012.*

3. *Akyel A, Sahinarslan A, Kiziltunc E, Yildiz U, Alsancak Y, Akboga MK, et al. Neutrophil gelatinase-associated lipocalin levels in isolated coronary artery ectasia. The Canadian journal of cardiology. 2011; 27(6): 773-8.*

4. *Kaufman KM, Kelly J, Gray-McGuire C, Asundi N, Yu H, Reid J, et al. Linkage analysis of angiotensin-converting enzyme (ACE) insertion/deletion polymorphism and systemic lupus erythematosus. Mol Cell Endocrinol. 2001; 177(1-2): 81-5.*

5. *Ozkur M, Erbagci Z, Nacak M, Tuncel AA, Alasehirli B, Aynacioglu AS. Association of insertion/deletion polymorphism of the angiotensin-converting enzyme gene with psoriasis. Br J Dermatol. 2004; 151(4): 792-5.*

6. *Kranzhofer R, Schmidt J, Pfeiffer CA, Hagl S, Libby P, Kubler W. Angiotensin induces inflammatory activation of human vascular smooth muscle cells. Arterioscler Thromb Vasc Biol. 1999; 19(7): 1623-9.*

7. *Rigat B, Hubert C, Alhenc-Gelas F, Cambien F, Corvol P, Soubrier F. An insertion/deletion polymorphism in the angiotensin I-converting enzyme gene accounting for half the variance of serum enzyme levels. J Clin Invest. 1990; 86(4): 1343-6.*

8. *Kehoe PG, Miners S, Love S. Angiotensins in Alzheimer's disease - friend or foe? Trends in neurosciences. 2009; 32(12): 619-28.*

9. *Zarouk WA, Hussein IR, Esmaeil NN, Raslan HM, Reheim HA, Moguib O, et al. Association of angiotensin converting enzyme gene (I/D) polymorphism with hypertension and type 2 diabetes. Bratislavske lekarske listy. 2012; 113(1): 14-8.*

10. *Bayoglu B, Cengiz M, Karacetin G, Uysal O, Kocabasoglu N, Bayar R, et al. Genetic polymorphism of angiotensin I-converting enzyme (ACE), but not angiotensin II type I receptor (ATr1), has a gender-specific role in panic disorder. Psychiatry and clinical neurosciences. 2012; 66(2): 130-7.*

11. *Tiret L, Rigat B, Visvikis S, Breda C, Corvol P, Cambien F, et al. Evidence, from combined segregation and linkage analysis, that a variant of the angiotensin I-converting enzyme (ACE) gene controls plasma ACE levels. American journal of human genetics. 1992; 51(1): 197-205.*

12. *Rudnicki M, Mayer G. Significance of genetic polymorphisms of the renin-angiotensin-aldosterone system in cardiovascular and renal disease. Pharmacogenomics. 2009; 10(3): 463-76.*

13. *Liu SY, Sima X, Wang CH, Gao M. The association between ACE polymorphism and risk of colorectal cancer in a Chinese population. Clinical biochemistry. 2011; 44(14-15): 1223-6.*

14. *Lukic S, Nikolic A, Alempijevic T, Popovic D, Sokic Milutinovic A, Ugljesic M, et al. Angiotensin-converting enzyme gene insertion/deletion polymorphism in patients with chronic pancreatitis and pancreatic cancer. Digestive surgery. 2011; 28(4): 258-62.*

15. *Daugherty A, Manning MW, Cassis LA. Angiotensin II promotes atherosclerotic lesions and aneurysms in apolipoprotein E-deficient mice. J Clin Invest. 2000; 105(11): 1605-12.*

16. *Prasad A, Narayanan S, Waclawiw MA, Epstein N, Quyyumi AA. The insertion/deletion polymorphism of the angiotensin-converting enzyme gene determines coronary vascular tone and nitric oxide activity. Journal of the American College of Cardiology. 2000; 36(5): 1579-86.*

17. *Shim YH, Kim HS, Sohn S, Hong YM. Insertion/deletion polymorphism of angiotensin converting enzyme gene in Kawasaki disease. Journal of Korean medical science. 2006; 21(2): 208-11.*

18. *El-Aziz TA, Hussein YM, Mohamed RH, Shalaby SM. Renin-angiotensin system genes polymorphism in Egyptians with premature coronary artery disease. Gene. 2012.*

19. *Chen YH, Liu JM, Hsu RJ, Hu SC, Harn HJ, Chen SP, et al. Angiotensin converting enzyme DD genotype is associated with acute coronary syndrome severity and sudden cardiac death in Taiwan: a case-control emergency room study. BMC cardiovascular disorders. 2012; 12: 6.*

Corresponding Author
Ibrahim Tekedereli,
Inonu Universitesi Merkez Kampusu,
Tip Fakultesi, TibbiBiyoloji AD,
Malatya,
Turkey,
E-mail: itekedereli@yahoo.com

Determining quality of life, depression and anxiety levels of hemodialysis patients

Nezihe Ugurlu[1], Dilara Bastug[2], Ayse Cevirme[3], Derya D.Uysal[1]

[1] Mugla University, Mugla School of Health Sciences, Department of Nursing Mugla,Turkey,
[2] Kosuyolu Higher Education Training and Research Hospital Department of Cardiovascular Surgery, İstanbul, Turkey,
[3] Sakarya University, School of Health Sciences, Sakarya, Turkey.

Abstract

Background/Aims: The aim of this study was to determine quality of life, depression and anxiety levels of the patients receiving hemodialysis treatment at Muğla (Turkey) State Hospital Hemodialysis Unit and to determine the relationships of SF-36 Quality of Life Inventory, Beck Depression Inventory and Beck Anxiety Inventory with various variables such as age, gender, employment, family type and marital status. This is a descriptive study.

Methods: Data was collected using individual information form developed by the researcher containing socio-demographic characteristics to determine the demographic data of the patients, SF-36 Quality of Life Inventory, Beck Depression Inventory and Beck Anxiety Inventory developed by Beck. In data analysis, SPSS 15.00 package program was used. For statistical analyses, correlation analysis, frequency distribution, Independent-Samples t test, one-way variance analysis-ANOVA and LSD analysis which is a Post Hoc Test were performed.

Participants/Setting: The study was carried out on a total of 43 patients receiving hemodialysis treatment at Muğla State Hospital Hemodialysis Unit in January 2009.

Results: It was found that among general quality of life sub-scales, physical functioning average score was 59.65±22.10, role limits due to health problems average score was 71,5 1±43.50, body pain average score was 65.93±26.47, general health average score was 46.86±20.44, vitality average score was 36.74±14.59, social functioning average score was 85.80±20.28, role limits due to emotional problems average score was 81.39±37.30, mental health average score was £-l=16.37.

Conclusion: It was found that there was a statistically significant relationship between the ages, quality of life scores, depression and anxiety scores of the patients. Anxiety scores increased in parallel to age. As for the quality of life scores, it was observed that the males had higher scores than females.

Clinical Relevance: This study can help healthcare providers to understand factors affecting of levels quality of life, depression and anxiety of hemodialysis patients.

Keywords: Patient; hemodialysis; quality of life, depression; anxiety

Introduction

Physical illnesses in people can sometimes bring about many psychological reactions. When these physical illnesses become chronic, the patient and his/her relatives might encounter many difficulties and reactions. Chronic renal failure (CRF) and a regular dialysis program have a special importance among chronic diseases[1-3]. Three basic treatments applicable for patients with renal failure include hemodialysis (HD), peritoneal dialysis (PD) and renal transplant. These three treatments are called renal replacement therapy (RRT) in combination[4]. Since the patient is connected to a hemodialysis center for a life time, hemodialysis (HD) is important in terms of the adaptation of the patient and the changes it creates in the life of the patient[5]. Hemodialysis causes role limits and deterioration of the general health perception depending on physical problems in the short term; however it causes role limits depending on physical and emotional problems due to the deterioration in physical functioning and general health perception[6,7]. Hemodialysis changes the life it saves; it significantly deteriorates normal life order and quality of life of the patients[8]. Among chronic renal failure patients, approximately 10%

of the end stage renal failure patients who were hospitalized due to medical reasons have a psychiatric disorder. The most serious psychological problems in dialysis patients include depression, dementia, drug and alcohol-related disorders, anxiety and personality problems. Depression, which is a reaction to some real, potential or imagined losses, is the most common psychological complication among dialysis patients[9]. The incidence of depression varies between 5-60%. The symptoms of depression include the feelings of hopelessness or pessimism, sleeping disorder or excessive sleeping, fatigue, lack of interest, lack of appetite or excessive eating, body pain and colic, difficulty in concentration, thinking of death or committing suicide, the feeling of guiltiness and useless, psychomotor agitation or retardation[10]. The terms "sıkıntı", "bunaltı", "kaygı" are Turkish equivalents of the term anxiety The individual is anxious and is anxious that something bad will happen, however can not indicate a objective source of danger or threat to explain this situation[11]. These psychiatric disorders deteriorate the adaptation and quality of life of the patient and also affect the progress of the disease, response to treatment, complications, the course and quality of life of the patient. It was reported that when compared to PD and renal transplant patients, HD patient had a lower quality of life [12].In a polycentric study carried out on a total of 5256 patients receiving dialysis in 253 centers due to ESRD in the US and European countries, according to the medical records of the last one year, 20% of the patients had depression. The percentage of depression increased in females, young people and white people, however it decreased in married, working people and students. It was also found that the ratio of duration of dialysis and accompanying physical disease increased in patients with depression[13]. In a 4-year follow-up study carried out on HD patients, psychological disorders had an annual incidence of approximately 11%[14]. In another study, it was found that according to DSM-III-R, diagnosis of psychological disorder significantly increased in HD group (55%); the most common diagnosis were major depressive seizure (35%) and common anxiety disorder (20%)[15]. The aim of this study was to determine the effects of various variables on quality of life, depression and anxiety levels of CRF patients receiving HD treatment.

Methods

Selection and Description of Participants

Study Population and Selection of the Sampling: The population of the study consisted of 48 patients receiving treatment in Muğla State University hemodialysis unit in center of Muğla province. As 5 patients did not give consent to participate in the study, the sampling consisted of 43 patients. The questionnaire was administered to the patients between the dates of 14.01.2008-17.01.2008. The questionnaire was administered through face-to-face interview with a total of 43 patients, 15 of whom were female and 28 of whom were male. The duration of the questionnaire was 15 minutes on average.

Technical Information

Data collection tools

In the study a questionnaire form consisting of four sections was used. In the first section personal information form was used; in the second section SF-36 Quality of Life Inventory was used; in the third section Beck Depression Inventory was used and in the fourth section, Beck Anxiety Inventory was used.SF-36 Quality of Life Inventory; SF-36 Quality of Life Inventory was used to evaluate quality of life of the patients. SF-36 Quality of Life Inventory is an individual evaluation inventory developed by Ware in 1987 to evaluate health policies and general population surveys in clinical applications and researches. SF-36 was translated into various languages. In Turkish version, its validity and reliability in patients with physical illnesses were performed by Koçyiğit [16].SF-36 is a short questionnaire which can be used on both patients and healthy population. As its name denotes, the questionnaire contains 36 items which measure 8 scales. These scales include physical functioning (10 items), social functioning (2 items), role limits due to health problems (4 items), role limits due to emotional problems (3 items), mental health (5 items), energy/vitality (4 items), body pain (2 items) and general health perception (5 items). Furthermore, it contains an item on the perception of changes in health in the last 12 months, which is not currently used in the measurement. Apart from the mentioned item, the inventory is evaluated

considering the last 4 weeks. In SF-36, as the score of each health domain increases, health-related quality of life increase as well. For example, high scores in pain scale indicate reduced pain. All scales of quality of life and global quality of life can be evaluated with this inventory. The score of each scale varies between 0-100; total score is between 0-100. While 0 indicates the worst health condition, 100 indicates the best health condition. *The higher the score*, the *better is the quality of life*.

Beck Depression Inventory; This is a self-evaluation inventory which determines depression risk and measures the level of depressive symptoms and severity changes. The inventory was developed by Beck and was adapted into Turkish by Hisli[17].

Beck Anxiety Inventory

This is a self-evaluation inventory determining the frequency of anxiety symptoms experienced by the individuals. It was developed by Beck and was adapted in Turkish by Ulusoy [18].

Ethical Considerations

Since the ethics committee was not available on the date when the study was carried out, after taking necessary permits from authorized bodies in writing, verbal consents were taken from the patients who agreed to participate in the study.

Data Analysis

Statistical Package for Social Sciences (SPSS) version 15.00 was used in data analysis. For statistical analyses, correlation analysis, frequency distribution, Independent-Samples t test, one-way variance analysis-ANOVA were used (in groups with number of n below 30, LSD analysis which is a Post Hoc Test was performed). $p<0.05$ was considered as statistically significant.

Results

Of the 43 patients who participated in the study, 34.9% were female, 65.1% were male. Average age of the participants was 56.00±11.90. It was found that 88.4% were married, 51.2% were primary school gradate, 62.8% were not working, 53.5% had a monthly income of 500-999 TL. It was found that only 1 of the participants had no health insurance while 46.5% were registered to social security organization.As for the personal characteristics of the patients with CRF, it was found that they were CRF patients for minimum 5, maximum 180 months; they received HD treatment for minimum 4, maximum 180 months. Statistical average of both parameters was found to be 42 months and the table was arranged according to average 42-month criteria.It was found that 30 (69.8%) of the participants had no depression; 12 (27.9%) had a mild level of depression and 1 (2.3%) had a severe level of depression. None of the participants had a moderate level of depression. A total of 42 (97.7%) of the patients had a low level of anxiety, 1 (2.3%) had moderate level of anxiety. None of the patients had a high level of anxiety (Table 1).

An analysis of the quality of life scores of the patients revealed that average physical functioning score was 59.65±22.10 between 10 and 90. Average role limits due to health problems score was 71.51±43.50 between 0 and 100. Average body pain score was 65.93±26.4 between 31 and 100. Average general health score was 46.86±20.44 between 10 and 100. Average vitality score was 36.74±14.59 between 5 and 65. Average social functioning score was 85.80±20.28 between 25 and 100. Average role limits due to emotional problems scores was 81.39±37.30 between 0 and 100. Average mental health score was 63.84±16.37 between 20 and 90.An analysis of the depression severity scores of the patients indicated that average depression severity score was 8.60±4.43 between 0 and 24. An analysis of the anxiety level scores indicated that average anxiety level score was 5.30±4.63 between 0 and 21

Table 1. Depression and Anxiety Levels of the Patients

The severity of depression according to BDI score	**n**	**%**
No Depression	30	69.8
Mild Depression	12	27.9
Moderate Depression	-	-
Severe Depression	1	2.3
Total	43	100
BAI scores according to level of anxiety	**n**	**%**
Mild Anxiety	42	97.7
Moderate Anxiety	1	
Severe Anxiety	-	-
Total	43	100

Table 2. Quality of Life of the Patients, Distribution of Depression and Anxiety Scores

Scales	n	Minimum	Maximum	X ±SD
SF-36				
Physical Functioning	43	10	90	59.65±22.10
Role Limits due to Health Problems	43	0	100	71,51±43.50
Body Pain	43	31	100	65.93±26.47
General Health	43	10	100	46.86±20.44
Vitality (Energy)	43	5	65	36.74±14.59
Social Functioning	43	25	100	85.80±20.28
Role Limits due to Emotional Problems	43	0	100	81.39±37.30
Mental Health	43	20	96	63.84±16.37
Beck Depression Scale	43	0	24	8.60±4.73
Beck Anxiety Inventory	43	0	21	5.30±4.63

(Table 2).There was a statistically significant relationship (F=7.081 and p<0.05) between age and physical functionality scores among demographic characteristics. It was found that this relationship resulted from the differences between 30-39 age group and 60-69 and 70-79 age groups; 40-49 age group and 60-69 and 70-79 age groups; and 50-59 age group, 60-69 and 70-79 age groups. Physical functioning scores according to gender was found to be X=48.00 in females and X=65.89 in males. There was a negative statistically significant relationship between gender and physical functionality (t=-2.571 and p<0.05).

There was a statistically significant relationship between occupation and quality of life (F=2.598 and p<0.05). It was found that this significant relationship resulted from the differences between pensioner group and worker group, pensioner group and farmer group, pensioner group and self-employed group. There was a statistically significant relationship between age and role limits due to health problems (F=1.214 and p<0.05). It was found that this significant relationship resulted from the difference between 40-49 age group and 70-79 age groups. Physical role functioning scores according to gender was found to be X=53.33 in females and X=81.25 in males. There was a negative statistically significant relationship between gender and role limits due to health problems (t=-1.924 and p<0.05). There was a statistically significant relationship between age and body pain (F=2.834 and p<0.05). It was found that this significant relationship resulted form the differences between 40-49 age group and 50-59, 60-69 and 70-79 age groups. Body pain scores according to gender were X=47.40 in females, X=75.86 in males. There was a statistically negative relationship between gender and body pain (t=-4.275 and p<0.05). There was a statistically significant relationship between age and general health perception (F=1.638 and p<0.05). It was found that this significant relationship resulted from the difference between 40-49 age group and 60-69 age groups. There was a significant relationship between age and vitality (F=2.860 and p<0.05). It was found that this significant relationship resulted from the differences between 40-49 age group and 50-59, 60-69 and70-79 age groups.

There was a statistically significant relationship between age and social functioning (F=1.810 and p<0.05). It was found that this significant relationship resulted from the differences between 40-49 age groups and 70-79 age group. Role limits due to emotional problems scores according to gender were found to be X=80.13 in females, X=90.47 in males. There was a negative statistically significant relationship between gender and role limits due to emotional problems (t=-1.945 and p<0.05). There was a statistically significant relationship between monthly net income and role limits due to emotional problems (F=2.848 and p<0.05). It was found that there was a statistically significant relationship between age and mental health (F=2.190 and p<0,05). It was found that this significant re-

Table 3. Comparison of SF-36 Quality of Life Inventory Scores and Demographic Characteristics of the Patients in the Study

Physical Functioning	n	X	SD	Significance Level
Age Groups				
30-39	3	75.00	8.66	
40-49	13	73.85	13.25	F=7.081
50-59	12	63.75	20.24	p<0.05
60-69	8	40.00	8.86	
70-79	7	42.14	27.12	
Gender				
Female	15	48.00	22.97	t=-2.571
Male	28	65.89	19.24	p<0.05
Profession				
Unemployed	27	54.44	23.01	
Retire	5	47.00	14.40	
Government employee	1	80.00	-	F=2.598
Farmer	3	80.00	13.22	p<0.05
Self employed	4	77.50	8.66	
Role Limits due to Health Problems				
Age Groups				
30-39	3	66.67	57.73	
40-49	13	88.46	29.95	F=1.214
50-59	12	75.00	45.22	p<0.05
60-69	8	62.50	46.29	
Gender				
Famale	15	53.33	48.97	t=-1.924
Male	28	81.25	37.65	p<0.05
Body Pain				
Age Groups				
30-39	3	75.00	30.51	
50-59	12	62.67	26.70	p<0.05
60-69	8	50.13	17.42	
70-79	7	55.00	31.59	
Gender				
Famale	15	47.40	18.13	t=-4.275
Male	28	75.86	25.02	p<0.05
General Health				
Age Groups				
30-39	3	43.33	20.20	
40-49	13	56.15	20.93	F=1.638
50-59	12	45.42	21.36	p<0.05
60-69	8	33.75	14.57	
Vitality (Energy)				
Age Groups				
30-39	3	35.00	22.91	
40-49	13	46.54	9.87	F=2.860
50-59	12	35.42	12.14	p<0.05
60-69	8	28.13	8.42	

Social Functioning	7	31.43	20.55	
Age Groups				
30-39	3	95.83	7.21	
40-49	13	92.31	15.76	F=1.810
50-59	12	89.58	16.71	p<0.05
60-69	8	76.56	22.59	
70-79	7	73.50	28.23	
Role Limits due to Emotional Problems				
Gender				
Female	15	64.44	47.91	t=-1.945
Male	28	90.47	27.00	p<0.05
Monthly income				
0-499 TL*	15	64.44	47.91	F=2.848
500-999 TL	23	92.75	22.38	p<0.05
1000-1499 TL	5	80.00	44.72	
Mental Health				
Age Groups				
30-39	3	49.67	16.50	
40-49	13	70.46	12.17	F=2.190
50-59	12	68.00	15.90	p<0.05
60-69	8	60.50	11.98	
70-79	7	54.29	22.49	

** Turkish currency*

lationship resulted from the difference between 30-39 age group and 40-49 age group; 40-49 age group and 70-79 age group (Table 3).

There was a statistically significant relationship between age and depression (F=3.341 and p<0.05). It was found that this significant relationship resulted from the differences between 40-49 age group and 60-69 age group; 40-49 age group and 70-79 age group; and 50-59 age group and 60-69 age group. Depression scores according to gender was found to be X=10.47 in females, X=7.61 in males. There was a statistically significant relationship between gender and depression (t=2.141 and p<0.05).

Depression scores according to family type were found to be X=7.83 in members of nuclear family and X=12.57 in members of large family. There was a statistically negative relationship between family type and depression resulting from the difference between nuclear family and large family (t=-2.662 and p<0.05). There was a statistically significant relationship between occupation and depression (F=2.180 and p<0.05). It was found that this significant relationship resulted from the differences between unemployed group and the worker group; the unemployed group and the farmer group; the pensioner group and the worker group; the pensioner group and the farmer group (Table 4). There was a statistically significant relationship between age and anxiety (F=4.733 and p<0.05). It was found that this significant relationship resulted from the differences between the 30-39 age group and 60-69 age group; 40-49 age group and 60-69 age group; 40-49 age group and 70-79 age group. Anxiety scores according to gender were found to be X=7.73 in females, X=4.00 in males. There was a statistically significant relationship between gender and anxiety (t=2.524 and p<0.05). Anxiety scores according to marital status were found to be X=5.26 in married patients, X=0.50 in single patients, and X=9.00 in widowed patients. There was a statistically significant relationship between marital status and anxiety (F=2.138 and p<0.05). It was found that this significant relationship resulted from the difference between the married group and the single group (Table 5).

Discussion

Psychological diseases like depression and anxiety are among the quite common problems in dialysis patients. When compared to the normal population, depression and anxiety are more common in dialysis patients. Levenson and Glocheski [19] reported that depression was a very common physiologic symptom in chronic diseases and that it varied significantly in dialysis patients (between 30% and 100%). The researchers also stated that this difference might have resulted from the definitions and measurements used in identification of depression. For example, Smith et al., indicated that in their studies which used Beck Depression Inventory, 47% of the dialysis patients were found to have depression; when they used Multiple Affect Adjective Checklist, 10% of the patients were found to have depression and according to DSM-III criteria, 5% of the patients were found to

Table 4. Comparison of Depression Scores and Demographic Characteristics of the Patients in the Study

Age Groups	n	X	SD	Significance Level
30-39	3	8.67	7.37	
40-49	13	6.15	2.64	F=3.341
50-59	12	7.33	3.96	p<0.05
60-69	8	11.88	2.99	
70-79	7	11.57	6.68	
Gender				
Female	15	10.47	3.66	t=2.141
Male	28	7.61	4.99	p<0.05
Family type				
Nuclear family	36	7.83	4.46	t=-2.662
Large family	7	12.57	4.27	p<0.05
Profession				
Unemployed	27	9.85	4.86	
Retire	5	10.20	3.83	
Government employee	1	5.00	-	F=2.180
Workers	3	4.33	1.52	p<0.05
Farmer	3	4.67	1.15	
Self employed	4	5.25	3.86	

Table 5. Comparison of Anxiety Scores and Demographic Characteristics of the Patents in the Study

	n	X	SD	Significance Level
Age Groups				
30-39	3	1.67	2.08	
40-49	13	2.85	2.26	F=4.733
50-59	12	4.83	3.48	p<0.05
60-69	8	7.38	2.97	
70-79	7	9.86	7.49	
Gender				
Female	15	7.73	4.93	t=2.524
Male	28	4.00	3.97	p<0.05
Marital status				
Married	38	5.26	4.58	F=2.138
Single	2	0.50	0.70	p<0.05
Widowed	3	9.00	4.35	

have depression. In the present study which used BDI and BAI, it was found that 27.9% (N=12) of dialysis patients had a mild level of depression; 2.3% (n=1) had a severe level of depression. In our study it was found that 97.7% (n=42) of the patients had a low level of anxiety and 2.3% (n=1) had a moderate level of anxiety. In a study carried out in Turkey, it was found that 45.8% of the patients had a low level of anxiety, 25.4% had a moderate level of anxiety and 28.8% had a high level of anxiety [9,11]. Averages of quality of life sub-dimensions were found to be higher than the averages of the hemodialysis patients in the study of Sağduyu [12]. It is known that old age is a risk factor for HD patients. In the present study, the comparison of the ages of the patients and quality of life scores indicated that there was a statistically significant difference (Table 3). Previous studies carried out particularly on hemodialysis indicated that quality of life was affected by age [20]. Other studies reported that there was no relationship between age and quality of life [21-23]. In the present study, when the quality of life scores were analyzed, it was found that excluding mental health score, the males had higher scores than females (Table 3).

The reason for this can be that since the females have more responsibility at home in Turkish community and that no matter what, they have to pursue this responsibility, they might be experiencing a weakness about this. While our findings show parallelism with the results of some previous studies[21-26], they are inconsistent with the results of some other studies[27-32]. The studies indicating that quality of life varied according to gender reported that physical quality of life dimension was higher in males[29,30,32]. Whether there is a significant difference between the genders or not, it is an interesting findings that the majority of the abovementioned studies report a higher quality of life dimension in males.It was found that there was a significant difference between age and depression and anxiety. However, it was found that depression scores did not increased in parallel to age. While the lowest depression score was expected to be observed in 30-39 age group, it was observed in 40-49 age group; while the highest score was expected to be observed in 70-79 age group, it was observed in 60-69 age group (Table 4). It was found that anxiety scores increased in parallel to age. The lowest anxiety score was observed in 30-39 age group; while the highest anxiety score was observed in 70-79 age group (Table 5).There was a statistically significant difference between gender factor and depression and anxiety. It was found that depression and anxiety score was higher in females (Tables 4-5). This difference between BDI according to gender is consistent with other studies in the literature. In a previous study carried out by Çelik & Acar[11] it was reported that depression was more common in females than males. The results of the study of Diaz-Buxo,[32] on the quality of life and its psychosocial effects in females with ESRD support the findings of our study. The fact that the females undertake the roles of mother, spouse and businesswomen simultaneously and they are exposed to more stress can be considered as a more important factor in this issue.

It was found that there was a statistically significant difference between marital status and anxiety. Single patients had the lowest anxiety scores. In a previous study it was reported that the single people had a higher tendency of anxiety than the married ones[20]. This result is not consistent with our study.

Conclusion

This study indicated that hemodialysis patients did not have a high tendency towards physiological problems like depression and anxiety and that their quality of life was not very low. Although the obtained percentages are based on the statements of the patients, considering that missing or erroneous statements can be made, a close follow-up of the patients not only in internal, but also in psychiatric terms will reduce morbidity and increase their life qualities. Analyzing the physiological and cognitive functions of the patients within a holistic approach will contribute to the solving of psychosocial problems of the patients and will help them increase their quality of life.

References

1. *Sertbaş, G., & Çuhadar, D. (2004). Diyalize giren kronik böbrek yetmezliği hastalarında görülen psikiyatrik sorunlar. Hemşirelik Forumu Dergisi, 7(3), 27-31.*

2. *Mok E., Lai, C., & Zhang, Z.X. (2004). Coping with chronic renal failure in HonKong.*

3. *International Journal of Nursing Studies, 41(2), 205-213.*

4. *Ünal, G., & Bilge, A. (2005). Hemodiyaliz tedavisindeki son dönem böbrek yetmezlikli hastaların ruhsal durumlarının ve yaşam kalitelerinin değerlendirilmesi. Ege Tıp Dergisi, 44 (1), 35 – 38.*

5. *Arık, N., Ateş, K., Süleymanlar, G., Tonbul, H.Z., Türk, S., et al. (2009).Hekimler İçin Hemodiyaliz Kaynak Kitabı. TND ile Sağlık Bakanlığı ortak yayını Ankara.*

6. *Özgür, B., Kürşat, S., & Aydemir, Ö. (2003). Hemodiyaliz hastalarında yaşam kalitesi ile anksiyete ve depresyon düzeyleri yönünden değerlendirilmesi. Türk Nefroloji Diyaliz Ve Transplantasyon Dergisi,12 (2), 113-116.*

7. *Markus, M.P., Jager, K.J., Dekker, F.W., Haan, R.J., Boeschoten, E.W., et al. (1997). Quality*

8. *of life in patients on chronic dialysis: self-assessment 3months after the start of the treatment. The Necosad Study Group. Am J Kidney Dis, 29, 584-592.*

9. *Meyer, K.B., Espindle, D.M., DeGiacomo, J.M., Jenuleson, C.S., Kurtin PS., et al. (1994). Monitoring dialysis patients' health status. Am J Kidney Dis, 24, 267-279.*

10. *Okanlı, A., Erdem, N., & Yılmaz, E.K. (2008). Hemodiyaliz Hastalarında Duygu Kontrolü ve Etkileyen Faktörler. Anatolian Journal of Psychiatry, 9, 156-161.*

11. *Daugirdas, J.T., Blake, P.G., & Ing, T.S. (2003). Diyaliz El Kitabı. Bozfakıoğlu S (Çeviren) 3. Baskı. Ankara, Güneş Kitapevi.*

12. *Levy, J., Morgan, J., & Brown, E.(2002). Oxford Diyaliz El Kitabı. Uslan İ (Çeviren). İstanbul: Nobel Tıp Kitapevleri.*

13. *Çelik, CH., & Acar, T. (2007). Kronik hemodiyaliz hastalarında depresyon ve anksiyete düzeylerinin çeşitli değişkenlere göre incelenmesi. Fırat Tıp Dergisi,12(1): 23-27.*

14. *Sağduyu, A., Şentürk, V., Sezer, S., Emiroğlu, R., & Özel,S. (2006). Hemodiyalize giren ve böbrek nakli yapılan hastalarda ruhsal sorunlar, yaşam kalitesi ve tedaviye uyum. Türk Psikiyatri Dergisi,(1), 22-31.*

15. *Lopes, A.A., Bragg, J., Young, E., Goodkin, D.A., Mapes, D., et al. (2002). Dialysis outcomes and practice patterns study (DOPPS). Depression as a predictor of mortality and hospitalization among hemodialysis patients in the United States and Europe. Kidney Int, 62, 199-207.*

16. *Fukunishi, I., Kitaoka, T., Shiari, T., Kino, K., Kanematsu, E., et al. (2002). Psychiatric disorders among patients undergoing hemodialysis therapy. Nephron, 91, 344-347.*

17. *Aghanwa, H.S., & Morakinyo, O. (1997). Psychiatric complications of hemodialysis at a kidney center in Nigeria. J Psychosom Res, 42 (5), 445-451.*

18. *Koçyiğit, H., Aydemir, Ö., Fişek, G., Ölmez, N., & Memiş, A. (1999). Kısa Form-36 (KF 36)'nın Türkçe versiyonunun güvenilirliği ve geçerliliği. İlaç ve Tedavi Dergisi, 12, 102-106.*

19. *Hisli, N. Beck (1989). Depresyon Envanterinin üniversite öğrencileri için geçerliliği, güvenilirliği. Psikoloji Dergisi, 7, 3-13.*

20. *Ulusoy, M., Şahin, N., & Erkman, H. (1998) Turkish version of the Beck Anxiety Inventory: psychometric properties. J Cognitive Psychotherapy, Int Quaterly, 12: 28- 35.*

21. *Levenson, J.L., & Glocheski S. (1991)Psychological factors affecting end-stage renal disease. A review. Psychosomatics, 32, 382-389.*

22. *Şentürk, A., Levent,B.A., & Lut, T. (2000). Hemodiyalize giren kronik böbrek yetmezliği olan hastalarda psikopatoloji. Ondokuz Mayıs Üniversitesi Tıp Dergisi, 17, 163-17.*

23. *Akyol, A. (1993).Yaşam kalitesi ve yaklaşımları. Ege Üniversitesi Hemşirelik Yüksekokulu Dergisi, 9, 75-79.*

24. *Chubon, R.A. (1986). Quality of life and persons with end-stage renal disease. Dial Transplant, 15(8), 450-452.*

25. *Kalantar-Zadeh, K., Kopple, J.D., Block,G., & Humphreys, M. H. (2001). Association among SF-36 quality of life measures and nutrition, hospitalization and mortality in hemodialysis. J Am Soc Nephrol, 12(12), 2797-2806.*

26. *Durna, Z., Özcan, Ş., Erdoğan, N., &Yeşiltepe, G. (2000). Düzenli hemodiyaliz tedavisi gören hastaların yaşam kalitesi ve sosyal destek düzeyleri. Hemşirelik Forumu, 3(2), 6-14.*

27. *Altıntepe, L., Güney, İ., Türk, S., Tonbul, Z., &Yeksan, M. (2005). Hemodiyaliz ve sürekli ayaktan periton diyalizi hastalarında yaşam kalitesi ve etkileyen faktörler. Türk Nefroloji Diyaliz ve Transplantasyon Dergisi, 14(2), 85-89.*

28. *Mozes, B., Shabtai, E., & Zucker, D. (1997). Differences in quality of life among patients receiving dialysis replacement therapy at seven medical centers. J Clin Epidemiol, 50(9), 1035-1043.*

29. *Harris, L.E., Luft, F.C., Rudy, D.W., & Tierney, W.M.(1993). ;Clinical correlation of functional status in patients with chronic renal insufficiency. Am J Kidney Dis, 21(2), 161-166.*

30. *Mingardi, G., Cornalba, L., Cortinovis, E., Ruggiata, R., Mosconi, P., et al. (1999). Health-related quality of life in dialysis patiens. A report from an Italian study using the SF-36 health survey. Nephrol DialTransplant, 14(6), 1503-1510.*

31. *Mittal, S.K., Ahern, L., Flaster, E., Maesaka, J.K., & Fishbane, S. (2001). Self-assessed physical and mental function of haemodialysis patients. Nephrol Dial Transplant, 16(7), 1387-1394.*

32. *Moreno, F., Lopez ,G.J.M., Sanz, G.D., Jofre, R., & Valderrabano, F. (1996). Quality of life in dialysis patients: a Spanish multicentre study. Nephrol Dial Transplant, 11(Suppl.2), 125-129.*

33. *Suet-Ching, W.L. (2001). The quality of life Hong Kong dialysis patients. J Adv Nurs, 35(2), 218-227.*

34. *Walters, B.A.J., Hays, R.D., Spitzer, K.L., Fridman, M., & Carte, W.B. (2002). Healthrelated quality of life, depressive symptoms, anemia and malnutrition at hemodialysis initiation. Am J Kidney Dis, 40(6), 1185-1194.*

35. *Diaz-Buxo, J. A., Lowrie, E. G., Lew, L. N., Zhang, H. Y., & Lazarus, J.M. (2000). Quality of life evaluation using short form 36: comparison in hemodialysis and peritoneal dialysis patients. Am J Kidney Dis, 35, 293-300.*

Corresponding Author
Nezihe Ugurlu,
Muğla University,
Muğla School of Health Sciences,
Department of Nursing Muğla,
Turkey,
E-mail: nugurlu@mu.edu.tr

The effect of low-dose ketamine on ephedrine requirement following spinal anesthesia in cesarean sections: a randomised controlled trial

Nurcin Gulhas[1], Ulku Ozgul[1],Feray Erdil[1], Mukadder Sanli[1], Hamza Nakir[1], Saim Yologlu[2], Mahmut Durmus[1], Mehmet Ozcan Ersoy[1]

[1] Inonu University, School of Medicine, Department of Anesthesiology and Reanimation, Malatya, Turkey,
[2] Inonu University, School of Medicine, Department of Biostatistics, Malatya, Turkey.

Abstract

Background: We aimed to assess the effectiveness of subanesthetic doses of ketamine on ephedrine requirement in patients scheduled for Cesarean section under spinal anesthesia.

Methods: ASA I-II, 105, patients were enrolled in the study. Spinal anesthesia was achieved with 12.5 mg hyperbaric bupivacaine and 15 μg fentanyl. Following spinal anesthesia, patients were randomly allocated to three groups. Group Placebo: 2 mL of intravenous physiological saline, Group Ketamine 0.25: 0.25 $mg.kg^{-1}$ of intravenous ketamine, and Group Ketamine 0.5: 0.5 $mg.kg^{-1}$ of intravenous ketamine was received.

Results: The systolic and mean blood pressures were similar in the groups. There were no significant differences between the groups, number of hypotensive attacks, as well as the amount of ephedrine used. The sedation scores in Group Ketamine 0.25 and Group Ketamine 0.5 were significantly higher than Group Placebo (p=0.001)

Conclusions: Subanesthetic dose of ketamine is not effective on decreasing ephedrine requirement in Cesarean section under spinal anesthesia.

Key words: ketamine, maternal hypotension, spinal anesthesia, Cesarean section

Introduction

The incidence of hypotension following spinal anesthesia in Cesarean sections is 80%, and despite intravenous fluid loading and use of vasopressor drugs, the incidence remains as high as 35%.[1,2] Due to the fact that long-lasting infusion of ephedrine may result in metabolic acidosis in the fetus, ephedrine is not recommended in the prophylaxis of hypotension, and phenylephrine use is emphasized in general.[2-6] However, phenylephrine is unavailable in many countries. It is important to find any technique that decrease the ephedrine requirement and studies regarding to this area are maintaining.

The techniques regarding decrease the ephedrine requirement in Cesarean section anesthesia are decreasing local anesthetic dose,[7] sitting position after spinal anesthesia administration,[8] hydration with colloid versus kristalloid.[9] All these techniques are some disadvantages that decrease the effectiveness of spinal anesthesia.

Ketamine hydrochloride is a well-known anesthetic agent, that has been in clinical use for more than 3 decades.[10] Ketamine is an antagonist at N-methyl-D aspartate receptors, which are considered important in the mechanism of blood pressure. It has good hemodynamic properties results from its indirect sympathomimetic activity. It is an excellent choice in patients with modest hypovolemia.[11,12] In addition, it has been demonstrated that subanesthetic doses (10-20 mg) of ketamine can be used safely for labor analgesia and following a failed block during Cesarean section, without any negative effect on the fetus. Ketamine does not cause uterine contractions unless given at doses > 1.5-2 $mg.kg^{-1}$. It does not affect Apgar scores or blood gas values of the fetus, either.[13-14] Ketamine does not induce hallucinations unless the dose exceeds 0.5 $mg.kg^{-1}$.[15]

Therefore, we aimed to assess the effectiveness of subanesthetic doses of ketamine on ephedrine requirement in patients scheduled for Cesarean section under spinal anesthesia.

Methods

Trial design and patients

The present study was a single-centre, balanced randomized [1:1:1], double-blinded, parallel group, phase IV study conducted at Inonu University Hospital (Malatya, Turkey) between November 2010 and July 2011. Following guidelines of the ethics committee of Turkish Republic of Ministry of Health, approval (24.09.2010 / N°71; chairperson Professor F. Avsar, MD) and written consent 105 American Society of Anesthesiologists (ASA) physical status I or II, aged between 18 and 45 years, pregnant women presenting for scheduled Cesarean delivery under spinal anesthesia were enrolled in this study. Patients were excluded from the study for the following reasons: contraindication to regional anesthesia; an ASA score > I-II; being < 18 years of age; multiple gestation; being < 150 cm or > 170 cm in height; preeclampsia; eclampsia; diabetes mellitus; intrauterine anomalies; using medications containing ephedrine or phenylephrine. The patients spinal anesthesia was failed excluded from the study and general anesthesia was administered. None of the methods changed after commencement of the study.

Randomisation and allocation of the participants into intervention groups was performed using computerised numbers (Excel; Microsoft, Remond, Washington, USA) by an anesthesiologist not participating in the trial. Both care providers on the ward and the anesthesiologists assessing outcomes were blinded to the study groups.

None of the patients received premedication. Non-invasive blood pressure, pulse oximetry and ECG monitoring were performed in the operating room. Following routine monitoring, all parameters were measured 3 times and the mean values were calculated. These were recorded as the baseline values. During the operation, the same parameters were continued to be monitored at 2-minute intervals.

Patients were prehydrated with 10 mL.kg^{-1} of lactated Ringer's solution and solution was continued at 4 ml/kg/h. For spinal anesthesia 12.5 mg hyperbaric bupivacaine and 15 μg fentanyl administered through the L4-L5 or the L3-L4 intervertebral space using a 25-gauge Whitacre spinal needle while the patient was in the lateral position. The patients were immediately returned into the supine position with left lateral tilt. Following spinal anesthesia, the patients were randomly allocated to three groups. Group Placebo (n=35): 2 mL of intravenous physiological saline, Group Ketamine 0.25 (n=35): 0.25 mg.kg^{-1} of intravenous ketamine, and Group Ketamine 0.5 (n=35): 0.5 mg.kg^{-1} of intravenous ketamine, a total of 2 mL study drug, was administered to each group. The sensory block was evaluated by pinprick method using a 22-G hypodermic needle. Modified Bromage scale was used to evaluate motor block (Bromage scale: 0= no paralysis, able to flex hips, knees /ankles, 1= able to move knees, unable to raise extended legs, 2= able to flex ankles unable to flex knees, 3= unable to flex ankles, knees, hips). Sensory and motor block were assessed at 2 min intervals until the block level of T4, then they were repeated every 5 min until the level had stabilized for four consecutive tests. This level was recorded as the peak sensory block level.

A ± 20% change in systolic blood pressure from baseline was allowed. Bolus of ephedrine 10 mg was given when there was a decrease greater than this value. This dose was repeated in patients who did not respond. Atropine 0.5 mg was administered to patients with a heart rate of < 45 beats. min-1, regardless of their systolic arterial pressure, as well as to patients with ephedrine-resistant hypotension and a heart rate of < 50 beats.min^{-1}.

Maternal data and observations, including, sedation, shivering, pruritus, pain, nausea and vomiting, hallucination were recorded at 3 minutes intervals. Sedation was assessed using Ramsey sedation score (1=awake; 2= drowsy, arouses easily with verbal stimuli; 3= arouses to tactile stimuli; 4= unconscious, unresponsive to verbal or tactile stimuli).

Hallucination as a side-effect was defined as a false sensory experience where the patients reported they saw, heard, smelled, tasted and felt something that was non-existent.

Apgar scores at 1 and 5 minutes were assessed and recorded. Blood samples were obtained from the umbilical vein and artery, and blood gas values were recorded. After completion of the operation, the patient stayed at the postoperative care unit for at least 30 minutes, and following stabilization of the vital signs, the patient was transferred to the ward.

Statistical analysis

The SPSS 13.0 program was used to analyze the statistical data (SPSS Inc., Chicago, IL). According to α=0.05, β=0.05, and power=0.95, it was found that for each group at least 32 patients were required to assume a 50% decrease in ephedrine requirement. Parametric data are expressed as mean ± SD and categorical data are expressed as number or rate. Shapiro Wilk test was used to determine normal distribution of parametric data. Parametric data were analyzed with unpaired t test or paired t test. Categorical data were compared with Pearson Chi-square or Fisher's exact tests. A *P* value of < 0.05 was considered as significant.

Results

During the study, 108 patients were eligible for the study. Three of the patients were excluded from the study due to a spinal block failure. A total 105 patients participated in and completed this study. The number of patients lost to follow-up is shown in Figure 1.

The demographic findings of the three groups were similar (Table 1).

The systolic and the mean blood pressures were decreased from baseline in all three groups. However, no significant differences among the groups (Figure 2). The heart rate and oxygen saturation were similar in three groups.

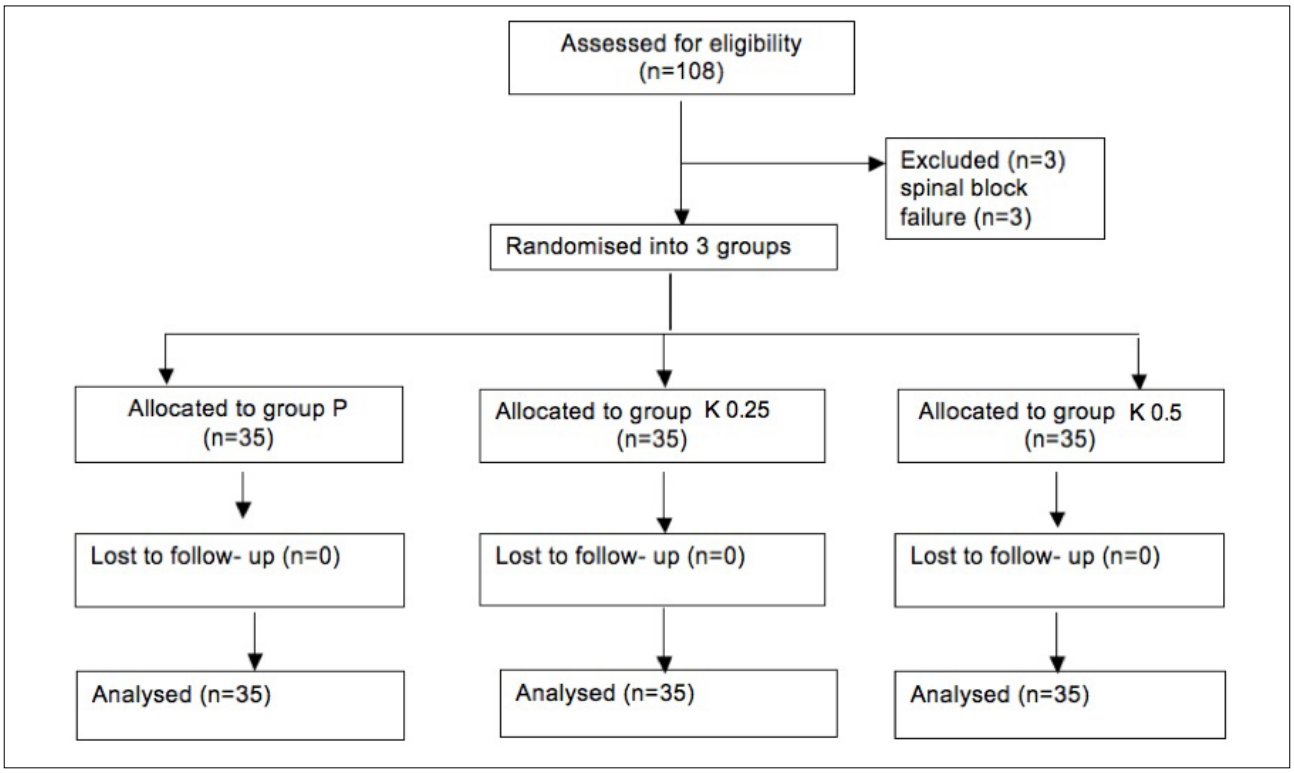


Figure 1. Flow chart of the study. P, placebo; K, katemine

Table I. Maternal characteristics, anesthetic and surgical times

	Placebo (n=35)	Ketamine 0.25 (n=35)	Ketamine 0.5 (n=35)	P Value
Age (years)	30.5 (4.1)	31.3 (5.0)	30.8 (4.9)	0.051
Weight (kg)	75.3 (17.3)	75.1 (10.3)	72.8 (11.2)	0.069
Height (cm)	159.2 (15.9)	161.6 (4.3)	161.6 (5.2)	0.070
Gestation (weeks)	38.6 (1.3)	38.5 (1.1)	38.4 (1.4)	0.060
Spinal-supine time (s)	58.1 (10.5)	59.6 (9.1)	58.6 (9.4)	0.063
Spinal-start surgery (min)	4.8 (1.1)	4.5 (1.0)	4.4 (1.2)	0.056
Spinal-end surgery (min)	38 (1.5)	40.2 (1.6)	40.0 (1.3)	0.059

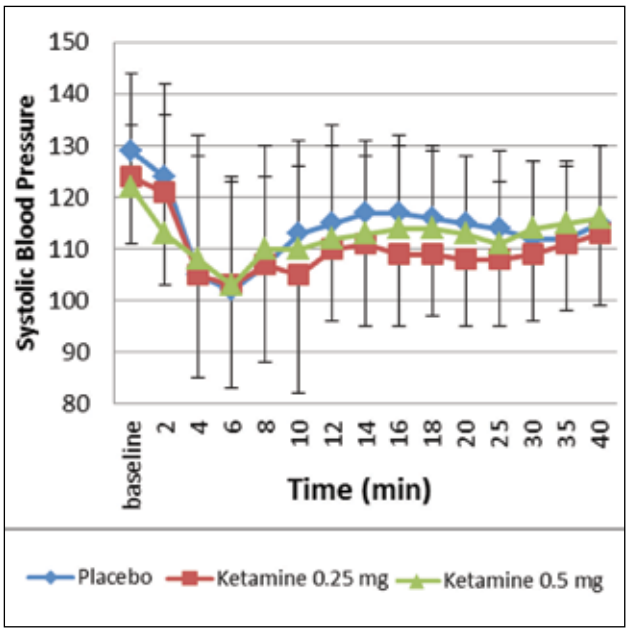


Figure 2. Mean systolic blood pressure at different time intervals in patients given placebo, ketamine 0.25 mg/kg or ketamine 0.5 mg/kg; error bars are SD. No significant difference between groups

The incidence of hypotension in Group Placebo was 80%; in Group Ketamine 0.25, the incidence was 69 %, and in Group Ketamine 0.5, the incidence was 58 %. There were no differences between the three groups with respect to the time of first hypotensive episode, number of hypotensive episode, as well as the amount of ephedrine used (Table II). The incidence of hypotension before delivery were similar.(Table 2).

The Apgar scores at 1 and 5 minutes and the umbilical vein and artery pH values were similar in all three groups (Table 2). The sedation scores in Group Ketamine 0.25 and Group Ketamine 0.5 were significantly higher than that in Group Placebo (p=0.01). (Table 3). While no hallucination was noted in any of the patients in Group Placebo, it was noted in three patients in Group Ketamine 0.5 (9.4%), and in one patient in Group Ketamine 0.25 (2.9%); there was no significant difference between the groups.

The groups were similar with respect to pruritus, shivering, and nausea-vomiting rates (Table III). None of our patients required supplemental analgesia.

Discussion

In the current study, we found that administration of 0.25 mg.kg^{-1} and 0.5 mg.kg^{-1} intravenous ketamine following spinal anesthesia increased the sedation scores; however, the use of ketamine did not affect the incidence of hypotension and ephedrine requirement.

Ketamine has unique cardiovascular effects. Ketamine increases the blood pressure, heart rate and the cardiac output by stimulating the cardiovascular system.[16] The hemodynamic changes are not related to the dose of ketamine. There is no hemodynamic difference between ketamine iv administration of 0.5 mg.kg^{-1} and 1.5 mg. kg^{-1}.

Table 2. Sensory block height, ephedrine requirement, characteristics of hypotension, fetal parametres

	Placebo (n=35)	Ketamine 0.25 (n=35)	Ketamine 0.5 (n=35)	P value
Peak sensory block height; dermatome	T5(T7-T4)	T5(T7-T4)	T5(T7-T4)	0.60
Ephedrine given (mg)	16.4 (9.8)	15.9 (10.0)	12.1 (9.9)	0.80
Time to first hypotension (min)	4.9 (1.5)	4.9 (1.3)	6.6 (1.2)	0.43
Episodes of hypotension (n)	2 (1.8-3.5)	2 (1.6-2.8)	2 (1.3-2.5)	0.08
Number of hypotensive patients (n,%)	28 (80%)	24 (69%)	20 (58%)	0.34
Hypotension before the delivery (n)	23/28	21/24	16/20	0.53
Apgar 1 min	8 (7-9)	8 (7-9)	8 (7-9)	0.32
Apgar 5 min	9 (8-10)	9 (8-10)	9 (8-10)	0.07
Umbilical arterial (pH)	7.31 (0.2)	7.30 (0.4)	7.32 (0.3)	0.12
Umbilical venous (pH)	7.38 (0.3)	7.36 (0.5)	7.37 (0.4)	0.25

Values are mean (SD) or median [range], percentage.

Table 3. Side effects. Values are (n)

	Placebo (n=35)	Ketamine 0.25(n=35)	Ketamine 0.5 (n=35)	P value
Sedation	1(1-1)	2(1-2)*	3(2-3)*	0.01
Hallucination	0	2	1	0.15
Nausea-vomiting	17	15	12	0.57
Pruritus	3	3	1	0.91
Schivering	1	1	1	0.60

**=p<0.05, Group placebo versus Group Ketamine 0.25 and Group Ketamine 0.5*

Ketamine can also be used as a supplement to regional anesthesia. It can be used when spinal anesthesia is not sufficient, and it can be used safely to provide analgesia at doses of 10-15 mg.[17] In this study, we chose the lowest dose of ketamine since we used it for prophylactic purposes.

In order to avoid stimulation of the cardiovascular system by ketamine, ketamine can be administered in combination with adrenergic antagonists (α and β), vasodilators and clonidine. Benzodiazepines may be administered in advance of ketamine. General anesthetics, particularly inhalation anesthetics and propofol, may suppress the hemodynamic effects of ketamine.[17] In the current study, arteriolar and venous vasodilation due to sympathetic blockade created by administration of spinal anesthesia, might have suppressed the hemodynamic effects of low-dose ketamine.

With the aim of decreasing the incidence of hypotension and ephedrine consumption, Gregory et al.[18] decreased the dose of local anesthetic used for spinal anesthesia. The authors reported that there was no decrease in the incidence of hypotension following spinal anesthesia using isobaric bupivacaine 4.5 mg, fentanyl 50 μg and morphine 200 μg; however, they reported a faster motor recovery. Although reported incidences of hypotension 74% in that particular study were comparable with those in this study. Quantities of ephedrine administered were similar in the 4.5 and 12 mg dose groups, respectively. Supplemental analgesia was required in five patients (4.5 mg group) in Gregory et al 18 study.

Yet in another study, performed by Turhanoglu et al.19 in which the authors investigated whether or not there was an advantage in using low-dose intrathecal bupivacaine for Cesarean section, it was found that the use of bupivacaine 4 mg and fentanyl 25 μg was not effective in preventing hypotension, but it decreased the severity of hypotension, the number of ephedrine treatments and the total dose of ephedrine. In that particular study, the incidence of hypotension in the control group (100%) was higher than that in our study. In patients receiving low-dose anesthetics, the incidence decreased to 75%, similar to our study. However, three of their patients required supplemental analgesia in low-dose bupivacaine group, whereas none of our patients required supplemental analgesia. Mebazaa et al 7 reported that a low dose of 7.5 mg of isobaric bupivacaine reduced incidence hypotension and 60% decreasing of ephedrine requirement. Using Ketamine 0.5 $mg.kg^{-1}$ 25% decreasing of ephedrine requirement while using 12.5 mg hyperbaric bupivacaine for spinal anesthesia in our study. El-Hakeem et al 8 sitting the patient up for five minutes rather than laying the patient down immediately after spinal anesthesia for Caeserean delivery decreased ephedrine requirement 40%.

In a study of Sen et al.20 in which the authors evaluated the effect of low-dose ketamine on postoperative pain control following spinal anesthesia in Cesarean sections, ketamine 0.15 mg/kg, a dose lower than to that used in this study, was administered following spinal anaesthesia, and it was found that ketamine had no effect on ephedrine consumption and blood pressure. This finding is consistent with the findings of our study. Similar to our study, they also used hyperbaric bupivacaine; however, unlike them we did not record postoperative analgesic consumption in our study.

According to the Ramsay Sedation Scale, conscious sedation developed in cases receiving 0.25 $mg.kg^{-1}$ and 0.5 $mg.kg^{-1}$ doses of ketamine.

Deep sedation was not observed in any of our patients. Similar to our study, Sen et al.20 and Bauchat et al.21 administered low-dose ketamine following spinal anesthesia in their reports, and

observed a moderate level sedation in patients receiving ketamine. This study has some limitations. The primary purpose of this study was to investigate the effect of ketamine on ephedrine requirement, the postoperative analgesic requirements of patients did not include in that study as an additional parameter.

It was concluded that subanesthetic dose of 0,25 and 0,5 mg.kg^{-1} ketamine is not effective in decreasing ephedrine requirement in patients scheduled for Cesarean section under spinal anesthesia.

References

1. *Allen TK, Muir HA, George RB, Habib AS. A survey of the management of spinal-induced hypotension for scheduled caesarean delivery. Int J Obstet Anesth 2009; 18: 356-61.*

2. *Mohta M, Janani SS, Sethi AK, Agarwal D, Tyagi A. Comparison of phenylephrine hydrochloride and mephentermine sulphate for prevention of post spinal hypotension. Anaesthesia 2010; 65: 1200-5.*

3. *Ngan Kee WD, Khaw KS, Tan PE, Ng FF, Karmakar MK. Placental transfer and metabolic effects of phenylephrine and ephedrine during spinal anesthesia for caesarean delivery. Anesthesiology 2009; 111: 506-12.*

4. *Ngan Kee WD, Lee A, Khaw KS, Ng FF, Karmakar MK, Gin T. A randomized double-blinded comparison of phenylephrine and ephedrine infusion combinations to maintain blood pressure during spinal anesthesia for caesarean delivery: the effects on fetal acid-base status and hemodynamic control. Anesth Analg 2008; 107: 1295-302.*

5. *Ngan Kee WD. Prevention of maternal hypotension after regional anaesthesia for caesarean section. Curr Opin Anaesthesiol 2010; 23: 304-9.*

6. *Ngan Kee WD, Khaw KS, Lau TK, Ng FF, Chui K, Ng KL. Randomized double-blinded comparison of phenylephrine vs ephedrine for maintaining blood pressure during spinal anaesthesia for non-elective caesarean section. Anaesthesia 2008; 63: 1319-26.*

7. *Mebazaa MS, Ouerghi S, Ben Meftah R, Ben Cheikh M, Mestri T, Ben Ammar MS. Reduction of bupivacaine dose in spinal anaesthesia for caesarean section may improve maternal satisfaction by reducing incidence of low blood pressure episodes. Middle East J Anesthesiol 2010; 20: 673-8.*

8. *El Hakeem EE, Kaki AM, Almazrooa AA, Al-Mansouri NM, Alhashemi JA. Effects of sitting up for five minutes versus immediately lying down after spinal anesthesia for Cesarean delivery on fluid and ephedrine requirement; a randomized trial. Can J Anaesth 2011; 58: 1083-9.*

9. *Madi- Jebara S, Ghosn A, Sleilaty G, Richa F, Cherfane A, Haddad F, Yazigi A, Antakly MC. Prevention of hypotension after spinal anesthesia for caesarean section: 6% hydroxyethyl starch 130/0.4 (Voluven) versus lactated Ringer's solution. J Med Liban 2008; 56: 203-7.*

10. *Reza FM, Zahra F, Esmaeel F, Hossein A. Preemtive analgesic effect of ketamine in patients undergoing elective caesarean section. Clin J Pain 2010; 26: 223-26.*

11. *Baraka A, Louis F, Dalleh R. Maternal awareness and neonatal outcome after ketamine induction of anaesthesia for Caesarean section. Can J Anaesth 1990; 37: 641-4.*

12. *Ngan Kee WD, Khaw KS, Ma ML, Mainland PA, Gin T. Postoperative analgesic requirement after caesarean section: a comparison of anesthetic ınduction with ketamine or thiopental. Anesth Analg 1997; 85: 1294-8.*

13. *Wakefield ML. Systemic analgesia: parenteral and inhalational agents. In: Editor Chesnut DH. Obstetric anesthesia principles and practice. St. Louis: Mosby,1999: 355.*

14. *Joselyn AS, Cherian VT, Joel S. Ketamine for labour analgesia. Int J Obstet Anesth 2010; 19: 122-3.*

15. *Schmid RL, Sander AN, Katz J. Use and efficacy of low-dose ketamine in the management of acute postoperative pain. A review of current techniques and outcomes. Pain 1999; 82: 111-125.*

16. *Katzung BG. Basic & Clinical Pharmacology.11 th ed. McGraw-Hill Medical 2009.*

17. *Reves JG, Glass PSA, Lubarsky DA, McEvoy MD, Martinez Ruiz R. Intravenous anesthetics. In: Editor Miller RD. Miller's Anesthesia.USA: Churchill Livingstone, 2010:745.*

18. *Bryson GL, MacNeil R, Jeyaraj LM. Small dose spinal bupivacaine for caesarean delivery does not reduce hypotension but accelerates motor recovery. Can J Anesth 2007; 54: 531-7.*

19. *Turhanoglu S, Kaya S, Erdogan H. Is there an advantage in using low-dose intrathecal bupivacaine for caesarean section? J Anesth 2009; 23: 353-7.*

20. *Sen S, Ozmert G, Aydin ON, Baran N, Calışkan E. The persisting analgesic effect of low-dose intravenous ketamine after spinal anaesthesia for caesarean section. Eur J Anaesthesiol 2005; 22: 518-23.*

21. *Bauchat JR, Higgins N, Wojciechowski KG, McCarthy RJ, Toledo P, Wong CA. Low-dose ketamine with multimodal postcesarean delivery analgesia: a randomized controlled trial. Int J Obstet Anesth 2011; 20: 3-9.*

Corresponding author
Nurcin Gulhas,
T. Ozal Tıp Merkezi Anesteziyoloji,
ve Reanimasyon AD,
Malatya,
Turkey,
E-mail: nurcin.gulhas@inonu.edu.tr

Numerically coded learning objectives: a simple solution to follow-up problem of outcomes-based curriculain medical education

H. Omer Tontus, M. Yasin Selcuk, A.Haydar Sahinoglu,

Ondokuz Mayis University, Medical Faculty, Medical Education Department, Tip Fakultesi Dekanlik, Samsun, Turkey

Abstract

Demonstrating specific competencies in order to graduate from medical schools is essential for students and identifying ways to demonstrate students have had these competencies for medical schools. Medical education is making a fundamental transition from a focus on teaching to a focus on learning. Therefore, students and schools can be held increasing accountable for their learning outcomes and objectives. Establishing learning objectives to guide the design and content of an educational program is a very important principle which supported by educational theory and practice. The degree of applicability of numerical coding system needs to be described on block/system based integrated entire curriculum of faculty. Learning Objectives play roles as a guide and framework for medical students in their efforts on graduation from medical schools. These will assist students with understanding the scope of knowledge, skills, values and attitudes expected of them by the end of undergraduate medical education. Well-defined learning objectives will lead the faculty to development of appropriate systems of student evaluation.

Key words: Learning objectives, curriculum, medical education, numeric code

Introduction

The most important responsibility of the Medical Faculties is to provide students with a valid, reliable, manageable, comprehensive, assessable and individually satisfying medical education at the highest quality. This education optimally prepares medical students as future's good professionals and doctors; who equipped with caring, motivated, competent, productive and humanitarian attitudes in their chosen career. Medical Faculties are committed to educate students in the full range of medical disciplines, with emphasis on practice in the primary care specialties. Curriculum mapping has been instigated as a move towards curriculum management and improved quality assurance processes for future's medical practitioners (1). Some recent publications have outlined approaches taken by specific medical schools or associations, whether they have created custom built systems or made use of existing solutions such as CurrMIT (curriculum management information tool) (1). A curriculum map can guide its users (students, faculty members, teachers, and curriculum planners, evaluators and coordinators) through the various elements of the curriculum and their interconnections as navigation devices (2).Learning objectives are fundamental to education at any level and simply define what is to be learned (3).When needed, to engage and lead teachers in a curriculum change or designing process is not done easily and the road is mostly chaotic. Acceptance of the basis and the need for change is the second most essential condition (4). Educators across the world are charged with the responsibility of producing core learning outcomes for their medical curricula (5). But core outcomes are too wide to assess students' knowledge in any exams. Deeper level of learning objectives is more feasible when evaluating a school's program.This paper is focused on analysing the issue of control within the curriculum from an ideological education perspective with detailed learning objectives model. According to Rees, medical schools in the UK aredeveloping outcomes-based or product-orientatedcurricula (5). Same things happen in Turkey like many other countries and we tried move forward from core outcome to smaller learning objectives. Researcher accepts, outcomesbased education as a very effective way of designing

courses/programs, delivering teaching and documenting the results of students' learning (5, 6).

In recent years, many researchers on medical education have expressed concerns that new graduates are not as well equipped as they should be to encounter people expectations of them. To address these concerns, medical teachers must understand how changes in people's views of on changes in the healthcare organization, financing, and delivery of health care (7). Medical schools have to get information from community in a routine basis and then use these to update the design, content, and conduct of medical curriculums. Medical education is making a fundamental transition from a focus on teaching to a focus on learning (8). Therefore, students and schools can be held increasing accountable for their learning outcomes and objectives (8). This means demonstrating specific competencies in order to graduate from medical schools is essential for students and identifying ways to demonstrate students have these competencies for medical schools.Although studies have shown variant results concerning the effectiveness of learning objectives (LOs) in increasing learning success and extended memory, all agree that the defining of learning objectives is important for effective teaching and learning (9). Establishing LOs to guide the design and content of an educational program is a very important principle which supported by educational theory and practice (7). In the early post war period, the Association of American Medical College (AAMC) itself developed a set of objectives to assist medical faculties in changing their curricula in response to the changes in medical practice. Addressing the goal of medical education is to produce physicians who are prepared to serve the fundamental purposes of medicine.Coding has been seen as an unimportant number applied to a curriculum file where the written explanation supersedes any numerical coding representation of the curriculum. But depending Fulks, this belief is entirely wrong (10). In practical educational life, reporting quality or accuracy does not necessary to show that faculty is doing the job of managing curriculum accurately. The conclusions of this study strongly invite medical teachers to reflect on their current practices. This information is widely available and discussed by the program committee to ensure and agree some changes are needed.

Aim

The main reason for producing curriculum with numerically coded LOs is to track of what is being taught, where, when, by whom, and how. A curriculum map can help to identify gaps and redundancies in a curriculum by providing answers to the question: What, When, Where, How do we teach? (11). Help students, teachers, curriculum planners and examiners.

Methods

In 2001, a group of Medical Faculties announced the definition of goals of undergraduate training "The National Core Curriculum (NCC)" for medical schools in Turkey. NCC consists of three main sections. The first section is "Diseases, Symptom and Condition List (DSCL)" (409 items) (Table 1). This list gave clue to medical faculties that students need to gain knowledge and they supposed to teach students in medical school before graduation. DSCL is put too much weight on knowledge and too little on social competence, attitudes, and ethical aspects. Other main sections of NCC are focused on two domains which are "skills" and "attitudes and behaviour". The crucial intention of the NCC project was to reach agreement on the main learning outcomes (here is DSCL) that clearly outline the expected abilities of the Turkish medical graduate. PBL based undergraduate medical curriculum composed in 2003 in Ondokuz Mayıs University Medical Faculty (OMU/MF) with announced LOs. These objectives scheduled in blocks and fellowship period to prepare students as future's good doctors. Course content has been restructured and the combination of new teaching methods, such as problem -based learning, has been increased. However, despite these efforts, LOs for the complete curriculum have not been definite consistently. Medical Education Department founded in July 2009 and first of all we tried to revise curriculum with Curriculum Designing Committee. After one year we redesigned curriculum for undergraduate medical education. Detailed learning outcomes were set for educational and training programmes by curriculum committee which the committee is responsible designing and revising curriculum. Now, it is clear what knowledge, skills, attitudes and behaviours students must have before graduating from our me-

dical faculty.Undergraduate medical education in Turkey takes six years. In OMU/MF, educational program divided in 24 modules which called as block in first 3 years. Following two years called as fellowship period and constructed with TASK groups in total 11 groups. The sixth year is called as internship period and students studies in clinics and outpatients department under observation of clinical educators.In OMU, LOs customized like a journey itinerary from nature of life to pathophysiology of diseases than through management of diseases. Allocated LOs passed to block committee to manage content of educational program and order lectures or scenario based education from department. In OMU/MF educational concept, block committee was assigning lectures to lecturers and then same lecturers prepare questions of their lecture contents for "end block exam" and send questions to block committee. In first look everything was working smoothly until first progress test done in December 2009. Progress test prepared by "progress test committee" which independent from block committee. Progress test questions targeted to LOs and did not ask block committee to whether the objectives assigned to any lecture or scenario based small group educational activities or not. Progress test results when presented to dean's office for evaluation,the results were found disappointing and medical education department ordered to evaluate why "end of block exam results" and "progress test results" are located far away from each other. But after 2 months of discussion with educational board and committees, medical education department offered numeric coding of each LOs in order to follow up and comparison of exam results depending on targets. Which educational activities will include which number of LOs and which DSCL targeted at the end of 5th year of undergraduate medical education? First step is taking on account of DSCL to match with our LOs. All 2500 highly detailed LOs grouped under DSCL in order to organize curriculum & evaluate outcomes. In 2009-2010 educational years we conducted 3 progress tests and first two test result evaluated depending on coded LOs.

What was done?

Although not formalized, national expectations for undergraduate medical education have already been set,we used 409 items DSCL as starting marker points (Table 1). This is the list which medical schools obliged to teach different level of knowledge to students before graduation. We have another list having nearly 2500 items to match or connect to DSCL which are LOs of undergraduate medical education (Table.2). After finishing NCC matched curriculum by medical education department, new coded curriculum represented to Curriculum Committee. The coding processes at OMU/MF havebegun two years ago when coding had only minimal importance/acceptance; they were only a way to describe the curriculum to a database in medical education department.Objectives are written in detail but measurable terms.After coming up with a list of objectives, each individual objective re-evaluatedtogether with curriculum committeeto make themmore specific. When first study results revealed, we found that some of the LOs are not mentioned as expected as in block schedules, all the block committee accepted importance of evaluating easy to use coded curriculum. We tried to find answer to following questions:

- Are all important LOs enclosed in curriculum or some of them are missing?
- How is a LOs integrated into the PBL based curriculum?
- Are there any planning errors which LOs embedded in unrelated block programs?
- What are the priorities of the curriculum (numbers of repeated LOs)?

National Core Curriculum Main Objectives as Diseases-Condition-Symptom based list (Sample list). Original list prepared in alphabetical order in Turkish.Some researchers also asked same or similar questions in theirs publications (9). In order to find answer to these questions, a curriculum map based on specific LOs and standard catalogues (depending on NCC list) was established. Block programs and lecture orders constructed by block committee by guidance of given numeric codes. In same manner, the entire exam questions which tagged by LOs number collected from testing committee members for future exams. Beside of these, medical education department started to tag previous years' exam questions with LOs number. Examinations which designed with coded questions give chance to curriculum committee to

Table 1. National Core Curriculum Main Objectives as Diseases-Condition-Symptom based list (Sample list). Original list prepared in alphabetical order in Turkish

National core curriculum objectives (selected sample list)			
NCC No	**Diseases, Symptom and Condition List (DSCL)**	**NCC No**	**Diseases, Symptom and Condition List (DSCL)**
1	Addison Disease	**101**	Congenital respiratory tract and lung malformations
2	Inappropriate ADH Secretion Syndrome	**102**	Congenital anomalies, structural
3	Approach to Forensic Medicine Cases	**139**	Glomerulonephritis, acute
4	Adrenal hyperplasia, congenital	**140**	Glomerulonephritis, chronic
5	Acute Adrenal Insufficiency Crisis	**141**	Chest wall anomalies
6	Aphasia; motor and sensory	**142**	Refractive disorders
7	Affective disorder, bipolar	**165**	Hypercalcemia
8	AIDS and HIV	**166**	Hyperlipidemia
9	FMF	**167**	Hyperparathyroidism
28	Angina pectoris	**168**	Hypertension
29	Anxiety	**198**	Hearing impairment
30	Anuria	**199**	Constipation
31	Aortic aneurysm	**200**	Increased ICP Sydrome (acute serebrovascular accidents)
32	Arithmia, supraventricular	**238**	Febril convulsion
48	Head & Neck Malignancies	**239**	Corpulmonale
49	Behchet' Disease	**240**	Caustic substance ingestion
50	Back Pain	**283**	Osteoporosis
51	CerabralEdema	**284**	Otitis
67	Sexually trasnmitted diseases	**298**	Peptic ulcer
68	Crush injury	**299**	Perianal abcess, fissur, fistula in ano
69	Cushing disease &sydrome	**300**	Peripheral vascular diseases
70	Enviromental& Health	**315**	Premenstrual syndrome
71	Luxation, extremity	**316**	Prenatal diagnosis
79	Atopic dermatitis	**317**	Benign prostatic hypertrophy/hyperplasia
82	Attention deficit, hyperactivity disorder and unconsciousness	**353**	Upper respiratory tract infections, chronic
99	Perinatal asphixia / Birth asphixia	**408**	Food intoxication
100	Perinatal fetal distress	**409**	Intoxications (non-food)

evaluate on-going educational activities by block, departments, individual lecture or lecturers.

Numeric coded LOs provide the following functions:

- Teachers can make their course program and examination questions with given LOs codes;
- The LOs codes have to be connected to blocks, departments/divisions and DSCL;
- Using coded LOs enable a minimum standardisation in order to follow up continuing curriculum;
- Learners can access the coded LOs and obtain information about their curriculum,
- Curriculum planners can analyse the codded curriculum and can manage revise if needed.Identified major deficiencies in curricula while coding or after coding:
- Some LOs are not covered in blocks curricula which cause lack of expected knowledge in certain domain;
- Some LOs are covered in blocks curricula but they are irrelevantly placed to schedule;
- Although some LOs are unnecessarily covered multiple times, some of them scheduled inadequate repeating
- Not organized in the correct time period in on-going curricula

Some exam questions were irrelevant with LOs.Questions referring same LOs were repeatedly used by different departments (ie: origin of

	NCC No 232	Learning objectives (los)	Block name	Department	Year	Lecture Code	System
Diseases, Symptoms or Conditions:Cholecystitis	**232.01**	Liver anatomy and functions	Energy	Anatomy	Y1	E1A	GIS
	232.02	Histology of liver: embryology, structure, specifications of hepatocyte, Kupffer and Ito cells	Energy	Histology	Y1	E1H	GIS
	232.03	Gall bladder anatomy	Nutrition	Anatomy	Y1	B2A	GIS
	232.04	Enterohepatic circulation	Nutrition	Anatomy	Y1	B2A	GIS
	232.05	Intra andextrahepatic biliary tract anatomy	Nutrition	Anatomy	Y1	B2A	GIS
	232.06	Bile; synthesis, composition and function	Nutrition	Biochemistry	Y1	B1B	GIS
	232.07	Functions of gallbladder and regulation of bile secretion to intestine	Nutrition	Biochemistry	Y1	B1B	GIS
	232.08	Bilirubin metabolism	Nutrition	Biochemistry	Y1	B1B	GIS
	232.09	Sympathetic and parasympathetic effects on biliary tract	Movement	Anatomy	Y1	M3A	GIS
	232.10	Sympathetic and parasympathetic effects on biliary tract	Upper Level Control	Anatomy	Y2	M4A	GIS
	232.11	Gallbladder stones: epidemiology, composition, risk factors, pathogenesis	Digestive	Gastroenterology	Y3	D1IG	GIS
	232.12	Acute cholecystitis , chronic cholecystitis, cholangitis, cholelithiasis, choledocolithiasis diagnosis and differential diagnosis	Digestive	Gastroenterology	Y3	D1IG	GIS
	232.13	Biliary atresia: ethiopathogenesis, congenital and perinatal forms of biliary atresia	Digestive	Paediatric Surgery	Y3	D1PS	GIS
	232.14	Biliary atresia: diagnosis, differential diagnosis, laboratory tests and other diagnostic procedures	Digestive	Paediatric Surgery	Y3	D1PS	GIS
	232.15	Congenital anomalies of intra and extrahepatic biliary tracts: (choledochal cysts, Caroli syndrome, Cong. hepatic fibrosis etc.)	Digestive	Paediatric Surgery	Y3	D1PS	GIS
	232.16	Chronic abdominal pain: causes, history, physical examination and diagnostic tests	GIS	Gastroenterology	Y4	G2IG	GIS
	232.17	Chronic abdominal pain: ethiology and treatment modalities	GIS	Gastroenterology	Y4	G2IG	GIS
	232.18	Malignancy and chronic abdominal pain	GIS	Gastroenterology	Y4	G2IG	GIS
	232.19	Bilirubin metabolism and liver cells	GIS	General Surgery	Y4	G1GS	GIS
	232.20	Jaundice: definition and types of jaundice	GIS	General Surgery	Y4	G1GS	GIS
	232.21	Obstructive jaundice: causes, clinical features, diagnostic tests and diagnosis	GIS	General Surgery	Y4	G1GS	GIS
	232.22	Biliary tract clinical anatomy and clinical importance of anomalies	GIS	General Surgery	Y4	G1GS	GIS
	232.23	Clinical features and diagnosis of gallbladder and bile duct diseases	GIS	General Surgery	Y4	G2GS	GIS
	232.24	Acute cholecystitis: diagnosis, differential diagnosis, treatment	GIS	General Surgery	Y4	G2GS	GIS
	232.25	Biliary colic and chronic cholecystitis: risk factors, pathogenesis, clinical signs	GIS	Gastroenterology	Y4	G3IG	GIS
	232.26	Biliary colic, acute and chronic cholecystitis: diagnostic tests, abdominal ultrasonography, ERCP	GIS	Gastroenterology	Y4	G3IG	GIS
	232.27	Biliary colic, acute and chronic cholecystitis: complications, medical and surgical treatment	GIS	Gastroenterology	Y4	G3IG	GIS
	232.28	Chronic abdominal pain in childhood: causes, history, physical examination and diagnostic tests	Paediatrics	Paediatric Gast.	Y4	P1PG	GIS

III. Cranial nerve was asked by Anatomy, then Ophthalmology and they Neurology departments in same year exams)The item analysis is an important phase in the development of an exam program. In this phase statistical methods are used to identify any test items that are not working well. The most common statistics in an item analysis like the item difficulty, the item discrimination and distractor analysis are studied for each individual item of exams. Evaluating curriculum, depending on coded LOs one by one takes many years but early results indicated that ordering targeted lectures from lecturer does not meaning ordered lecture presented to students. As an example of question showing in Figure.1 resulted with disappointing correct answer rate by students. There are many examples with similar results by this question. These are guiding us through establish a curriculum evaluation model like students assessment.

Discussion

Each medical school should develop mechanisms for monitoring and evaluating its curriculum. Although test results have some limitations, the information gained from them is valuable in recognizing problematic areas. To be beneficial, there has to be a comparatively high answer rate, and the tests must be carefully designed and evaluated. Feeding the information back to responsi-

Figure 1. Sample question with low correct answer rate

SampleItem 1: Which of thefollowingeventswould be mostlikelytopredisposetoectopicpregnancy?

a. Induction of ovulation
b. Pelvicinflammatorydisease (PID)
c. Use of a contraceptiveuterinedevice (IUD)
d. Exposure in uterotodiethylstilbestrol (DES)
e. Previoustubalsurgery

Block Name	Pregnancy
Department	Gynaecology&Obstetrics
Year	Y4
System	Reproduction
LOscode	130.02
CorrectAnswer Rate%	12.2%

SampleItem 2: Whichlaboratory test is lowestdiagnosticvaluecomparingwiththeother in a childhoodlymphomatypewhichlocates in mediastineumandcausescaugh, dypnea, pleuraleffusionand SVCS?

a.Plasma LDH level
b. Ascitesfluidlaboratoryexamination
c.Pleuralandpericardialfluidlaboratoryexaminations
d. CSF laboratory
e.Lymphnodebyopsy

Block Name	Tumors
Department	Pathology
Year	Y3
System	Hematopoetic-Lenfoid
Los code	**247.11**
CorrectAnswer Rate%	5.6%

ble persons for designing and teaching individual block or block components is one of the most important post-test activities. Medical education provides students with an understanding of health issues and the skills needed for confident participation as professionals. This enables students to make responsible decisions about health and to promote their own and others' well-being. DSCL is a framework for outcome-based education. Outcome-based education focuses on the end-product and defines what the learner is accountable for (6). Using DSCL like, learning outcomes leads to community based curriculum design that states what students are to learn, and provides a clear and undisputable statement of what the graduates will be like.None of the medical faculties was free of errors in one area or another (10). Learning objectives are widely considered to be a valuable tool for both instructor and student. Many researchers stated in their publication that learning objectives are statements of preferred, observable, teachable, and learnable behaviours that are evidence of learning. One step beyond of these main domains is LOs must be assessable to promote students learning behaviours and evaluate curriculum. Joint Commission of the Swiss Medical Schools defined discipline related objectives based on discipline and clinical pictures (12). This concept found to be problematic for our educational program due to similar clinical pictures in different departments or disciplines. Integrated curriculum guided us toward the DSCL basedcoding.A national set of learning objectives provides guidelines for the breadth and depth of knowledge in the medical education principles that are essential for further progress. Regardless of the specific didactic or educational approach used by any given institution, that institution must develop mechanisms to assure that the students are being coached with these objectives at an appropriate depth of understanding (13).Our conclusion is that the coding process at OMU/MF have begun two years ago when coding had only minimal importance/ acceptance; they were only a way to describe the curriculum to a database in medical education department. But nowadays, the job of assigning the lectures to lecturers and designing PBL scenarios even choosing questions for exams with numerically coded learning outcomes is essential. In fact, as Fulks, we discovered that coding is so important and specific that in many cases even a well-informed curriculum committee member may not be qualified to correctly code a course (10).The person who must do this is the department expert for TASK period and block chair for the first three years, not the dean, not the curriculum chair, but the person creating the curriculum in department/ block (10). If that creator does not understand the numeric coding structure, then responsible department of coding (such as medical education department) must do some professional development meeting in the purpose of the explanation of the coding and must do professional assistance to departmental/block based creators. There may be good explanations for a test question about a LO of the block being answered incorrectly with a large proportion of students, but at least such LO should be identified and the reasons for the students' views should be scrutinized. Student tests such as progress tests should be obtained regularly for each evaluation of LOs of the block/curriculum and evaluated by the appropriate committee. Medical schools can also evaluate their curriculum by "pass rates" in individual block. If student selection is appropriate, a high failure rate in a block suggests that the block content is inappropriate, or that there are problems with the teaching or that the examination is set at inappropriate standards. The responsible committee or department should oversee the correct answer rates in individual LOs of the block, and investigate circumstances where these are inappropriately low. Theoretically, the best method of evaluating the relevance and effectiveness of the medical course is to examine the quality of the graduates (14). Medical schools should have follow-up mechanisms for obtaining feedback from the exams bodies where their students sit as medical doctor to be a resident or researcher in any university after graduation. In Turkey, there is a national exam called as TUS (Exam for Specialising in Medicine) for getting a position in postgraduate education which provides important data for medical schools to check their comparative position. The LOs also are meant to reveal the "Mission Statement" for undergraduate medical education (15). The roles of LOs are important for the education of physicians (15). Depending on Christadoulou, learning objectives

will assist students with understanding the scope of knowledge, skills, behaviours, values and attitudes expected of them by the end of medical school. Also LOs will lead the faculty to development of appropriate systems of student evaluation (15). Matejic at al noted that even if medicine (including medical education) does not respond to the ideas of postmodernism, it may become increasingly irrelevant to the needs of a changing society (16). Development in any area of education corresponds to the postmodern trends in developed societies and it should be supported (16) The degree of applicability of numericalcodingsystemneedsto be described on block/system based integrated entire curriculum of faculty. Learning Objectives play roles as a guide and framework for medical students in their efforts on graduation from medical schools.Medical schools will assess and evaluate their curricula, in order to confirm that the LOs are being met by students at all levels of education. Conjoining by National Core Curriculum goals, coded curriculum will cover the expectations are in keeping with accepted national and "latterly" international standards in the field of medical education.At the completion of the undergraduate medical education, a student will be expected to demonstrate an understanding of the ways health condition changes from beginning to end and how these changes are reflected in physiology, pathology and wellbeing (physical, psychosocial and behavioural). The overall objective will be met through participation in any kind of educational activities and with a program of self-directed learning which will result in the ability to perform required competencies.Numerically collected data from learning objectives systems based assessment can be integrated easily with data from other administrative tools to create a more rapid, open and truthful overview of the curriculum to faculties and students. Stages of the curriculum lifecycle can then be guided by evaluated information because of its easy to use numeric pattern. Further studies will determine how useful the using coded LOs are for comparing curricula, developing examination and evaluation of educational outcomes.

Acknowledgment

Thanks to all members of Curriculum Committee and Progress Testing Committee

References

1. *Willett T.G. ; Current status of curriculum mapping in Canada and the UK; Medical Education 2008: 42: 786–793*
2. *Harden RM. AMEE Guide No. 21. Curriculum mapping: a tool for transparent and authentic teaching and learning. Med Teach 2001;21:123–37.*
3. *M. J. Burke, A.C. Brodkey, Trends in Undergraduate Medical Education: Clinical Clerkship Learning Objectives; Academic Psychiatry 2006; 30:158–165.*
4. *Fullan, M., G., "The New Meaning of Educational Change", New York: Teachers College Press, 1991*
5. *Charlotte E Rees, The problem with outcomes-based curricula in medical education: insights from educational; Theory; Medical Education 2004; 38: 593–598*
6. *The Scottish Deans' Medical Curriculum Group; Learning Outcomes for the Medical Undergraduate in Scotland: A foundation for competent and reflective practitioners, 2010; 1-20*
7. *Association of American Medical Colleges, Medical School Objectives Project ; January 1998; Report I; Learning objectives for Medical Student Education Guidelines for Medical Schools*
8. *David T. Stern, AndrzejWojtczak, M. Roy Schwarz; Accreditation of Medical Education: A Global Outcomes-Based Approach ; www.healthprofessionals21.org/docs/AccredMedEd.pdf*
9. *Inga Hege, Matthias Siebeck& Martin R Fischer; An online learning objectives database to map a curriculum; Medıcal Educatıon 2007; 41: 1083–1111*
10. *Fulks J., Curriculum, Coding and our Professional Responsibility: Revise Your Process, 2009, http://asccc.org/content/curriculum-coding-and-our-professional-responsibility-revise-your-process*
11. *Denny JC, Smithers JD, Armstrong B, Spickard A.; 'Where do we teach what?' Finding broad concepts in the medical school curriculum. JGIM 2005;20 (10):943–6.*
12. *Working Group under a Mandate of the Joint Commission of the Swiss Medical Schools, Swiss Catalogue of Learning Objectives for Undergraduate Medical Training, 2nd Edition (2008) http://sclo.smifk.ch/downloads/sclo_2008.pdf*

13. *R. G. Carroll, design and evaluation of a national set of learning objectives: the medical physiology learning objectives project; Advan in PhysiolEdu2001; 25:2-7.*

14. *WHO Guidelines for Quality Assurance of Basic Medical Education in the Western Pacific Region; 2001, Manila, Philippines, pp 11-12*

15. *C. Christadoulou, UndergraduateMedicalEducation Learning Objectives, Uni. Of Manitoba; 2010: UGME, Faculty of Medicine, University of Manitoba, Version7.0; FINALhttp://umanitoba.ca/faculties/medicine/education/opas/media/UGME_Learning_Objectives__Final.pdf*

16. *B. Matejic, D. Vukovic, M. S. Milicevic, Z. T. Supic, A. J.Vranes,B. Djikanovic, J. Jankovic, V. Stambolovi; Student-centred medical education for the future physicians in the community: An experience from Serbia; HealthMED - Volume 6 / Number 2 / 2012; 517-524*

Corresponding Author
H. Omer Tontus,
Ondokuz Mayis University,
Medical Faculty,
Medical Education Department,
Tip Fakultesi Dekanlik,
Samsun,
Turkey,
E-mail: healthmedjournal@gmail.com

Sources of stress among future helper professionals in human services

Sladjana J.Jovic[1],Slavica S. Ristic[2], Dragan C. Bogdanovic[3], Olivera Radulovic[1], Aleksandar M. Visnjic[1], Cedomir R.Sagric[1]

[1] Department of Social medicine and hygiene with medical ecology, Medical Faculty, University of Nis, Serbia,
[2] Department of biochemistry, Medical Faculty Foca, University of East Sarajevo, Serbian Republic, Bosnia and Hercegovina,
[3] The State University of Novi Pazar, Serbia.

Abstract

Studies confirm the high stress exposure in students who are studying for ''helper'' professions (medicine, nursing, social work, dentistry, law, psychology). Studies have been conducted mainly in Western societies, while in the Republic of Serbia and neighboring countries this type of research is rare.The aim of study was to determine the most common sources of stress (academic and non-academic) in university students and to compare results with similar studies.

Design and Settings: Cross-sectional questionnaire survey was performed to collect data of most frequent sources of stress among university students.

Methods: The study included 194 students of the third and fourth year of the Faculty of Security Studies, University of Belgrade, 98 males (50.5%) and 96 females (49.5%). Authorized questionnaire was used where students rated the intensity of certain stressful situations on a scale of 1 to 10 and ranked them on an individual stress scale.

Results: Ten most frequently cited sources of stress were: 1. Death of a family member, 2. Serious illness of a family member, 3. Misfortune of my loved one, 4. Lies and deception by people who are close to me, 5. Unwanted pregnancy, 6. Disagreement with parents, 7. Partner's infidelity, 8. Permanent loss of a friend, 9. Separation from a loved one, 10. Financial problems, economic crisis.. The higest ranked situations derived from non-academic sources of stress. They mainly derived from the family or close persons and social-economic problems. The highest ranked academic sources of stress were Exams, at the 12th place. Statistically significant gender differences were found.

Conclusions: The results represent a starting point for designing of health promotion and stress management programs for university students.

Key words: university students, helper professions, sources of stress

Introduction

Studies confirm the high stress exposure in students who are studying for ''helper'' professions, future members of human service professions (medicine, nursing, social work, dentistry, law, psychology, law enforcement, educational institutions), which are expected to care for health, safety, and lives of the clients.[1, 2, 3, 4, 5, 6] Studies have been conducted mainly in Western societies, while in the Republic of Serbia and neighboring countries this type of research is rare. Stress can initiate the development of depression, depressive disorders, anxiety, professional burn-out, depersonalization, distress, emotional exhaustion and related mental health problems, as well as other indicators of psychological distress in students. [7] Increased student exposure to stress can impair their mental and physical health, quality of life and life satisfaction, and affect their capacity to adequately meet client's needs in their future ''helper'' professional practice.[8,9,10,11,12,13] Helper professionals should be able to assist themselves first, and then their clients, to avoid harmful effects of stress on health. [14, 15, 16]

Academic sources of stress are related to conditions at a faculty that provides education and training of students, including the examination, meeting the next year of study entry requirements, teachers' and staff behavior toward students and the relationship with staff and clients in different institutions during professional practice. [17] Students are also exposed to non-academic stressors, related to the social environment, family members, relationship with persons who are important to them, and environmental problems. [2] It is recognized that the influence on environmental factors

is possible in the terms of their modifications, but individual factors related to the student's gender are not satisfactorily clarified yet. [18,19,20] The aim of study was to determine the most common sources of stress in university students, future helper professionals in human services, as well as rankings of stressful situations on the stress scale, depending on the intensity of their estimated impact. A special aim of this study was to determine whether there are gender differences in the estimated intensity impact, and ranking of certain stressful situations by female and male students.

Methods

The study included 194 students of the third and fourth year of the Faculty of Security Studies, University of Belgrade, whose future title is "Manager of human and social resources in the civilian sector". In the sample there were 98 males (50.5%) and 96 females (49.5%). Authorized questionnaire YSS -30 (Youth Stress Scale – 30) was used where students rated the intensity of certain stressful situations on a scale of 1 to 10 and ranked them on an individual stress scale. The study was conducted during March and April 2010. There is no ethical research committee at the Faculty of Security at the moment, but the study was approved by the Faculty committee and the Dean. Students filled in the stress events questionnaire at the end of their lectures, and a researcher had previously explained to the students the purpose and importance of the research, that their participation is voluntary and that they were guaranteed anonymity and confidentiality of data. The students' interest to participate in the study was high, so the response of students was 100%. Completing the questionnaire required about 20 minutes. The questionnaire was filled in by 201 students, but 6 questionnaires (2.98%) were not completely filled and therefore had not been taken for analysis. The authorized questionnaire was a combination of standard Holmes Rashe Life Events Scale, also known as Social readjustment Rating Scale – PRS. [21] and life events that are cited by students as stressful and specific to their population, and do not adhere to a standard stress scale. The questionnaire included demographic characteristics of the sample - gender and year of study. This questionnaire was previously tested on a sample of 1273 medical students of the Medical Faculty in Nis (Serbia) in the period 1996 to 2006 and 269 medical students of Medicine, University of East Sarajevo (Foca, Republic of Srpska, Bosnia and Herzegovina) in the period 2007 to 2010. The questionnaire contained 30 stress events, the most common cited in the previous studies, with the possibility for students to add three events which represented a significant source of stress for them, but were not mentioned in questionnaire. Students were asked to evaluate each of potential sources of stress, by their intensity of impacts, on a scale of 1 to 10 and then they ranked them on an individual stress scale. Statistical analysis was performed using the software package SPSS version 10.0. Mann Whitney U test was used to compare the stress response rankings between males and females with $P<0.05$ as a level of statistical significance.

Results

A total of 201 students filled in questionnaires and 194 of them completed questionnaires in an appropriate way usable for research purposes, the response rate was 97.02%. In the sample there were 98 males (50.5%) and 96 females (49.5%), presented in Table 1.

Ten most frequently cited sources of stress, as shown in Table 2 , were:

1. *Death of a family member*, 2. *Serious illness of a family member*, 3. *Misfortune of my loved one*, 4. *Lies and deception by people who are close to me*, 5. *Unwanted pregnancy*, 6. *Disagreement with parents*, 7. *Partner's infidelity*, 8. *Permanent*

Table 1. Sample characteristics by gender and year of study

Year of study	Total number of students	Students included in research		
		Males+Females	Males	Females
Third	107 (53.3%)	103 (53.1%)	52 (26.8 %)	51 (26.3%)
Fourth	94 (46.7%)	91 (46.9%)	46 (23.7%)	45 (23.2%)
Total	201 (100.0%)	194 (100.0%)	98 (50.5%)	96 (49.5%)

loss of a friend, 9. *Separation from a loved one*, 10. *Financial problems, economic crisis.* The situation *Limited time for recreation and social activities* was ranked at the 11th place. Starting from fifth place in the rank, stress events are ranked in different order, depending on the gender.The first 11 ranked situations derived from non-academic sources of stress. They mainly derived from the family, from contacts with important persons (parents, partner, friends, relatives) and social-economic problems. Average values of perceived intensity of almost all stress events were higher in females than

Table 2. Stress situation ratings and perceived intensity of stress reaction in students ($\bar{x}$ ±SD)

Stressors /Stress event	Males+Females		Males		Females		Comparison M/F*	
	Rating	Intensity	Rating	Intensity	Rating	Intensity	Z	P
Death of a family member	1	9.51±1.84	1	9.53±1.80	1	9.48±1.89	0.49	n.s.
Serious illness of a family member	2	8.91±1.61	2	8.86±1.24	2	8.96±1.94	1.55	n.s.
Misfortune of my loved one	3	7.61±2.20	3	7.12±2.00	3	8.10±2.31	2.88	<0.004
Lies and deception by people who are close to me	4	7.15±2.36	4	6.69±2.60	4	7.63±2.01	1.79	n.s.
Unwanted pregnancy	5	6.64±3.00	5	6.35±2.86	6	6.94±3.15	1.28	n.s.
Disagreement with parents	6	6.41±2.74	8	5.76±2.68	5	7.08±2.66	2.49	<0.013
Partner's infidelity	7	6.21±2.99	9	5.69±3.08	7	6.73±2.83	1.66	n.s
Permanent loss of a friend	8	6.12±2.54	6	6.00±2.33	10	6.25±2.76	0.75	n.s
Separation from a loved one	9	6.09±2.67	10	5.63±2.66	8	6.56±2.62	1.85	n.s
Financial problems, economic crisis	10	5.65±2.50	12	5.31±2.41	11	6.00±2.58	1.32	n.s
Limited time for recreation and social activities	11	5.62±2.41	11	5.43±2.57	13	5.81±2.26	0.55	n.s
Exams	12	5.49±2.67	18	4.69±2.54	9	6.31±2.57	3.05	<0.002
Failing the year of study	13	5.48±2.69	14	5.02±2.33	12	5.96±2.97	1.63	n.s
Big economic loss	14	5.30±2.51	13	5.06±2.26	17	5.54±2.74	0.87	n.s
Losing of youth (hypothetical)	15	5.27±2.86	16	4.84±3.09	14	5.71±2.56	1.57	n.s
Inadequate communication and support by staff	16	5.22±2.43	17	4.78±2.40	15	5.67±2.40	1.74	n.s
Fight with someone	17	5.21±2.98	7	5.78±2.67	23	4.63±3.18	1.89	n.s
Excessive workload	18	5.08±2.23	15	4.88±2.17	19	5.29±2.30	0.68	n.s
Separation from family	19	4.91±2.88	20	4.24±2.65	16	5.58±2.97	2.25	<0.024
Belief in own work efficiency	20	4.81±2.81	21	4.22±2.74	18	5.42±2.78	2.13	<0.033
Worry that I am not able to meet all demands of study and practice	21	4.79±2.50	19	4.33±2.53	20	5.25±2.42	1.78	n.s
Feeling that I am not secure enough in my environment	22	4.51±2.92	23	4.19±2.77	22	4.83±3.07	0.98	n.s
Request for perfect performance in work with clients	23	4.50±2.23	24	4.17±2.15	21	4.83±2.28	1.32	n.s
Unsupportive environment during practical work	24	4.32±2.41	22	4.19±2.37	27	4.45±2.47	0.41	n.s
Organization of study and practical work by faculty	25	4.14±2.24	27	3.76±2.15	24	4.54±2.28	1.71	n.s
Literature availability for exam preparation	26	4.12±2.43	26	3.80±2.19	26	4.46±2.63	1.08	n.s
Being overweight	27	4.04±3.21	28	3.73±3.28	28	4.35±3.15	1.03	n.s
Teachers and staff behavior toward students	28	4.03±2.39	29	3.55±2.19	25	4.52±2.51	1.95	n.s
Administrative jobs at the faculty	29	3.49±2.62	30	3.47±2.81	29	3.52±2.43	0.23	n.s
Watching the game when my favorite team loses	30	3.35±2.87	25	4.14±2.87	30	2.54±2.66	3.36	<0.001
Total		6.25±1.33		6.19±1.36		6.31±1.30	0.20	n.s

**Mann-Whitney U test*

in males. Significant differences were found in the following situations: Misfortune of my loved one ($p<0.004$), Disagreement with parents ($p<0.013$), and Separation from family ($p<0.024$).In the group of academic sources of stress, the highest ranked were Exams, at the 12th place in general. There were differences in its ranking according to the gender of respondents. In females, this stressor was at the 9th place, and for males at the 18th place, and average stress intensity values were 6.31 and 4.69 ($p<0.002$). Next in rank were other academic sources of stress: Failing the year of study (13th place), Inadequate communication and support by staff during professional training (16th place), Worry that I am not able to meet all demands of study and practice (21st place), Request for perfect performance in working with clients (23rd place), Unsupportive environment during practical work (24th place), Organization of study and practical work by the faculty (25th place), Availability of literature for exam preparation (26th place), Teachers' and staff behavior toward students (28th place) and Administrative jobs at the faculty (29th place). The average intensity values of the majority of stress sources were higher in females than in males, except for Fight with someone (in males at 7th place in the rank, in females at 23rd place in the rank) and Watching the game when my favorite team loses (in males at 25th place, the average value of intensity was 4.14; in females at 30th place in rank, the average value of intensity was 2.54, $p<0.001$). Females trusted in their own work efficiency less than males did. The situation Belief in own work efficiency in females was at 18th place in rank, with the average value of stress intensity 5.42, while in males it was on the 20th place, with the average value of stress intensity 4.22, $p<0.001$. The gender differences in the responses are shown graphically in Figure 1.

There were no statistically significant differences depending on the year of study.

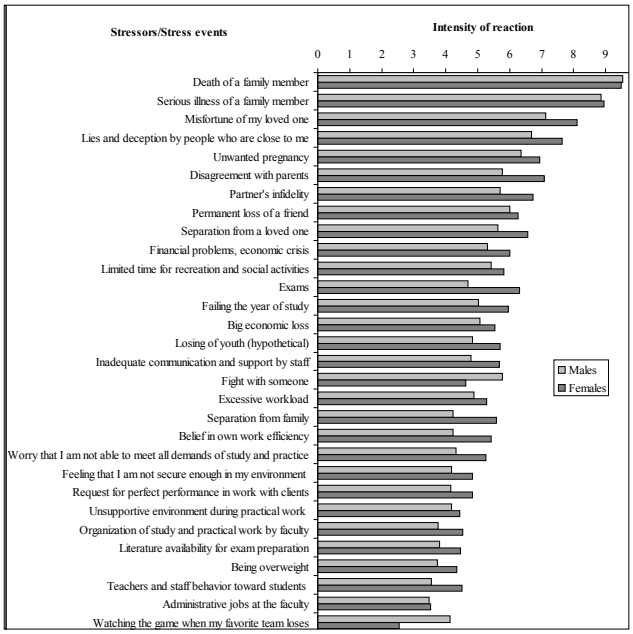


Chart 1. Stress events and perceived intensity of stress reaction in students, both genders

Discussion

This is the first study on perception of stress events and the impact of gender differences in perception of stress in the population of students of the Faculty of Security, University of Belgrade, Department of Human and social resource management. The first ten ranked situations derived from the contact with family and loved ones (parents, partner, friends, relatives). The first two ranking stress events, *Death of a family member* and *Serious illness of a family member,* are a universal stressor, also highly ranked among all nations, people of different ages, gender and education [21, 22]. Most other situations were characteristic for university students, and were classified into a group of academic and non academic sources of stress.

Stress events ranked 3rd to 11th stemmed from relationships with family members, partners, friends and social environment: *Misfortune of my loved one*, *Lies and deception by people who are close to me*, *Unwanted pregnancy*, *Disagreement with parents*, *Partner's infidelity, Permanent loss of a friend, Separation from a loved one, Financial problems, economic crisis and Limited time for recreation and social activities*. Sreeramareddy pointed out that the most frequently cited sources of psychosocial stress for students were separation from family and living in the dorms, parents' high expectations, extensive curriculum, and lack of time and facilities for having fun [23] .

Emotional relationship related problems were highly ranked in our study, as well as in the study of Muirhead and Locker, where 60% of students reported to being under stress because of problems in relations with the opposite sex. [24]

Students of Faculty of security have to meet the challenges of high academic demands, which, along with interpersonal, intrapersonal, and professional requirements may constitute significant sources of stress. The most frequent sources of academic stress in our study were Exams (at 12th place), Failing the year of study (at 13th place), Inadequate communication and support by staff during professional practice (16th place), Excessive workload (18th place), Worry that I am not able to meet all demands of study and practice (21st place), Request for perfect performance in working with clients (23rd place), Unsupportive environment during practical work (24th place), Organization of study and practical work by faculty (25th place), Literature availability for exam preparation (26th place), Teachers' and staff behavior toward students (28th place) and Administrative jobs at the faculty (29th place). In similar studies, these academic sources of stress are often cited as the most important. [4, 16, 23, 25] Moffat pointed out that the main stressors for students were more likely to be related to professional training, in terms of individual learning progress during the year, and performance and availability of literature, than to the student's personal problems. [26] Beside these stress events, results derived from available studies described in the literature indicated that for students, high intensity stress was associated with the following situations: a request for perfect performance in working with clients, excessive workload, belief in own work efficiency. [3] These stressors were also found to be important stress sources in students we focused on in our study. Academic sources of stress were highly ranked at the stress events scale among students of the faculties for future professionals responsible for the human resources care and social services, as well as future health care workers, and it was confirmed in similar studies in Serbia, Bosnia and Herzegovina and Western societies. [27, 28, 3, 23, 24] In our study, students evaluated academic stress as a significant source of stress, but non-academic sources of stress took up the first 11 places on stressful life events scale, largely resulting from the stressors derived from family and social environment, or associated with socio-economic factors. The explanation may be that students have chosen to be future professional human and social resources managers, so they are more focused on individual, family and social environment, and therefore react more intensely to the sources of stress derived from these areas. Also, life in the country with socio-economic transition and instability for almost twenty years, when, according to Maslow's hierarchy of needs, the motivation for survival (personal or family one) is increased, and incentives for self-actualization through academic training are reduced. [29, 30] In future studies, there should be a survey in order to clarify which of these explanations is right. Also, as a result of socio-economic crisis, the situation Financial problems and economic crisis is ranked at the high 10th place at the student's stress scale. Similar results of the influence of socio-demographic factors were found in study by El-Gilany, Amr and Hammad. [2] In countries where a long-term psychosocial stress conditions persisted, in the context of lack of personal security and economic equality, including psychological, economic, social and political stresses of everyday life, a strong sense of frustration with mental health related consequences were registered in young and educated people, as well as in the general population.[26, 31, 32] Gavrilović et al founded that posttraumatic stress reactions were presented in a significant percentage of medical students in both genders, a year after the bombing of Serbia by NATO, in 1999, and gender differences in the intensity of these reactions were found. [33] We also found gender differences in our study, in the ranking of stressful situations, as well as differences in the average values of intensity of individual stressors. Female gender was a significant predictor of higher intensity of reaction to stress in some studies. [25, 34] Females evaluated almost all stress events with higher intensity than males, and significant differences depending on the gender of the respondents were found in the following situations: Misfortune of my loved one, Disagreement with parents, Separation from family. In a group of academic sources of stress, the situation Exams was at female's rank at the 9th place, and in males at the 18th place, and statistically significant gender differences were found. Females were able to express their feelings more easily, including those associated with stressful situations. [17] Also, compared to males, they express a higher degree of empathy for clients. [8] The average values of intensity of the majority of stress events are higher in females than in males, except for a situation Fight with someone and

Watching the game when my favorite team loses, which are typically roles that males are socialized for. Females considered themselves to be less effective at work than males, and the situation Belief in own work efficiency females estimated as a higher intensity stress situation than in males. Blanch et al, in the literature review on gender differences in terms of self-confidence, find that females had lower levels of self-confidence, which could also be one of the reasons why their stress responses were more intense than in male students.[35] Gender-specific access in programs for cognitive-behavioral stress management are based on these findings.[36, 37]

Contribution of the study is that certain stressful events were defined by the future helper professionals as highly significant stressors, which are specific to the population of university students, and that the derived student's scale of stress contained many stress events which are not presented on the standard adult's stress scales. Statistically significant gender differences were found in the perception of certain stress events, as well as differences in ranking of stress events by female and male students. The results represent a starting point for designing of health promotion and stress management programs, as well as early disease detection in university students, primarily for the purpose of promoting and maintaining mental health of this population. [14, 38] Efforts for distress reducing should be part of a broader effort to improve the quality of university students' life in general, which can also increase aspects of their professionalism.

References

1. *Grandy TG, Westerman GH, Combs CE, Turner CH. Perceptions of stress among third-year dental students. J Dent Educ 1989; 53(12): 718-21.*

2. *El-Gilany A, Amr M, Hammad S. Perceived stress among male medical students in Egypt and Saudi Arabia : Effect of sociodemographic factors. Ann Saudi Med 2008; 28: 442-8*

3. *Polychronopoulou A, Divaris K. Dental students' perceived sources of stress: a multi-country study. J Dent Educ 2009; 73(5): 631-9.*

4. *Rajab LD. Perceived sources of stress among dental students.at the University of Jordan. J Dent Educ 2001; 65(3): 232-41.*

5. *Luo Y, Wang H. Correlation research on psychological health impact on nursing students against stress, coping way and social support. Nurse Educ Today 2009; 29(1): 5-8.*

6. *Tully A. Stress, sources of stress and ways of coping among psychiatric nursing students. J Psychiatr Ment Health Nurs 2004; 11(1): 43-7.*

7. *Dyrbye LN, Thomas MR, Shanafelt TD. Systematic review of depression, anxiety, and other indicators of psychological distress among U.S. and Canadian medical students. Acad Med 2006; 81(4): 354-73.*

8. *Liebkind K, Eränen L. Attitudes of future human service professionals: the effects of victim and helper qualities. J Soc Psychol. 2001; 141(4): 457-75.*

9. *Dyrbye LN, Thomas MR, Huntington JL, Lawson KL, Novotny PJ, Sloan JA, Shanafelt TD. Personal life events and medical students burnout: a multicenter study. Acad Med 2006; 81(4): 374-84.*

10. *Thomas MR, Dyrbye LN, Huntington JL, Lawson KL, Novotny PJ, Sloan JA, Shanafelt TD. How do distress and well-being relate to medical student empathy? A multicenter study. J Gen Intern Med 2007; 22(2): 177-83.*

11. *Paschali A and George Tsitsas G. Stress and life satisfaction among university students-a pilot study. Ann Gen Psychiatry 2010; 9(Suppl 1): S96*

12. *Niemi PM, Vainiomäki PT. Medical students' distress-quality, continuity and gender differences during a six-year medical programme. Med Teach 2006; 28(2): 101-2.*

13. *Kjeldstadli K, Tyssen R, Finset A, Hem E, Gude T, Gronvold NT , Ekeberg O and Vaglum P . Life satisfaction and resilience in medical school – a six-year longitudinal, nationwide and comparative study. BMC Medical Education 2006; 6:4*

14. *Dunn LB, Iglewicz A, Moutier C. A conceptual model of medical student well-being: promoting resilience and preventing burnout. Acad Psychiatry 2008; 32(1): 44-53.*

15. *Višnjic A, Stojanović M, Radulović O, Milosavljević N. Utilisation factor in using mental health services for Niš University students. Acta Fac Med Naiss 2007; 24(3): 101-5*

16. *Jović S. Public mental health in the concept of health promotion in Republic of Serbia. Proceedings of the 41th International scientific meeting: Days of preventive medicine; 2007 Sept 24-27; Nis, Serbia. Nis: Institute of public health; 2008. (In Serbian)*

17. *Dutta AP, Pyles MA, Miederhoff PA. Stress in health professions students: myth or reality? A review of the existing literature. J Natl Black Nurses Assoc 2005; 16(1): 63-8.*

18. *Pau A, Rowland ML, Naidoo S, AbdulKadir R, Makrvinka E, Moraru R, Huang B, Croucher R. Emotional intelligence and perceived stress in dental undergraduates: a multinational survey. J Dent Educ 2007; 71(2): 197-204.*

19. *Ivon Bothmer MI, Fridlund B. Gender differences in health habits and in motivation for a healthy lifestile among Swedish university students. Nurs Health Sci 2005; 7(2): 107-18.*

20. *Silver RC, Holman EA, McIntosh DN, Poulin M, Gil-Rivas V. Nationwide longitudinal study of psychological responses to September 11. JAMA 2002; 288(10): 1235-44.*

21. *Holmes TH, Rahe RH. The social readjustment rating scale. J Psychosom Res 1967;11(2): 213-8.*

22. *Viner R. Putting stress in life: Hans Selye and the making of stress theory. Soc Stud Sci 1999; 29(3): 391-410.*

23. *Sreeramareddy CT, Shankar PR, Binu VS, Mukhopadhyay C, Ray B, Menezes RG. Psychological morbidity, sources of stress and coping strategies among undergraduate medical student of Nepal. BMC Med Educ 2007; 2; 7: 26*

24. *Muirhead V, Locker D. Canadian dental students' perceptions of stress. J Can Dent Assoc 2007; 73(4); 323-6.*

25. *Peker I, Alkurt MT, Usta MG, Turkbay T. The evalation of perceived sources of stress and stress levels among Turkish dental students. Int Dent J 2009; 59(2): 103-11.*

26. *Panter-Brick C, Eggerman M, Mojadidi A, McDade TW. Social stressors, mental health, and psychological stress in an urban elite of young Afghans in Kabul. Am J Hum Biol 2008; 20(6): 627-41.*

27. *Jović S, Simonović Lj, Zdravković J. Stressful events in youth and stress-scale. In: Proceedings of the 30th Scientific meeting with international participation Days of preventive medicine; 1996 Sept 25-27; Nish, Serbia; 1996.p. 51. (In Serbian).*

28. *Jović S, Aranđelović M, Milošević Z, Nikolić M, Petrović B, Nikolić D. Sources of stress in medical students and gender-based differences in stress perception. MD - Medical data, 2011; 3(1), 37-42.*

29. *Maslow, A. (1970) Motivation and Personality. New York: Harper and Row*

30. *http://asunews.asu.edu/20100819_maslowspyramid Arisona State University 19.Aug 2011*

31. *Hasić S, Kiseljaković E, Jadrić R, Zecević B, Avdagić N, Nakas-Ićindić E, Radovanović J, Winterhalter-Jadrić M. Influence of long term stress exposure on somatisation symptoms outcome. Bosn J Basic Med Sci 2004; 4(4): 28-31.*

32. *Klarić M, Klarić B, Stevanović A, Grković J, Jonovska S. Psychological consequences o war trauma and postwar social stressors in women in Bosnia and Herzegovina. Croat Med J 2007; 48(2): 167-76.*

33. *Gavrilovic J, Lecic-Tosevski D, Knezevic G, Priebe S. Predictors of posttraumatic stress in civilians 1 year after air attacks: a study of Yugoslavian students. J Nerv Ment Dis 2002; 190(4): 257-62.*

34. *Naidoo S, Pau A. Emotional inteligence and perceived stress. SADJ 2008; 63(3): 148-51.*

35. *Blanch DC, Hall JA, Roter DL, Frankel RM. Medical student gender and issues of confidence. Patient Educ Couns 2008; 72(3): 374-81.*

36. *Hampel P, Jahr A, Backhaus O. Gender-specific stress management training at school. Prax Kinderpsychol Kinderpsychiatr 2008; 57(1): 20-38. (In German)*

37. *Flynn SM, Schipper LJ, Roach AR, Segerstrom SC. Gender differences in delayed-type hypersensitivity response: effects of stress and coping in first-year law students. Brain Behav Immun. 2009; 23(5):672-6. Epub 2009 Jan 4. 2011*

38. *Elliot DL, Goldberg L, Toffler WL. Health promotion and early disease detection among medical school faculty. Prev Med 1994; 23(2): 253-6.*

Corresponding Author
Sladjana J. Jovic,
Medical Faculty, Universitu of Nis,
Nis,
Serbia,
E-mail: sljovic@yahoo.com

Prevention and treatment of atopic dermatitis in newborn infants and children -clinical study

Svetlana Stefanovic[1], Nada Macvanin[1], Dragana Bogicevic[2], Tatjana Radunovic Gojkovic[3], Srdan Kisic[4], Nenad Macvanin[5], Goran Galetic[3]

[1] Medical faculty, Novi Sad, Serbia,
[2] Medical faculty, Beograd, Serbia,
[3] IZZZDIO Vojvodine Novi Sad, Serbia,
[5] Zavod za zdravstvenu zaštitu radnika, Novi Sad, Serbia,
[6] Visoka strukovna škola za preduzetništvo, Beograd, Serbia.

Abstract

The latest data from clinical trials and research (evidence based) suggest that further development of the skin within the first two years of life, including children's skins ratio of larger surface area relative to body weight than adults, and greater vulnerability when exposed to harmful effects from the environment.The specifics of children's skin are: 1.increased susceptibility to contact dermatitis due to irritation 2. increased susceptibility to atopic dermatitisTypically, there is a positive history in parents and close relatives for atopy. Atopy is defined as the tendency of the body to react to normal, harmless factors from the environment in a form of allergic reaction which creates specific Ig E antibodies.Most common atopic diseases are eczema and contact dermatitis. Skin allergies can be exanthema or urticaria as a reaction to food, insect bites, hot-cold, pressure, and inhalation allergens - bronchitis, asthma, allergic conjunctivitis et rhinitisDiagnosis is based on history, physical examination, clinical symptoms and laboratory findings.Because of the reasons listed above, one of the main issues of contemporary children's dermatology is whether proper skin care from birth can reduce the prevalence of atopic dermatitis, or at least reduce the severity of the condition? Should more attention be given to healthy baby skin? Does the protection of children's healthy skin become a new paradigm?

Aim of this prospective clinical study was to investigate the effect of Dermalex Repair cream (manufacturers Chefaro Ireland Ltd, Ireland, registered as a medical device class IIa in Serbia, the solution 04-1084/10) on children's skin as therapeutic and preventive measure.

Materials and methods -The prospective clinical study was voluntary throughout June and July 2011 It included 50 children under 3 months of age from the territory of Autonomic Province of Vojvodina. with clinical signs of atopic dermatitis.

Two coherent sets were formed. The first group P, consisted of newborns up to 4 weeks of life with seborrhea syndrome and in whom Dermalex Repair Cream was used for preventive purposes. The second group T, was made up of children aged 4-8 weeks with clinically expressed eczema where Dermalex Repair Cream was used for therapeutic purposes.Control examinations were carried out at regular time intervals, four times in total, at regular intervals of one week and on each examination the skin condition was scored 0-5. One point was given for each of the following symptoms- redness, damp, itching, excoriations, and crusts.The obtained results were processed using statistical methods

Conclusion The results of our prospective clinical study have shown that there is a favorable therapeutic and preventive effect of local skin care with Dermalex Repair cream. Dermalex Repair cream can be recommended for daily skin care in children with an atopic predisposition from the moment they are born.

Key words: dermatitis,prevention,therapy

Introduction

The skin covers the outer surface of the body, the natural openings (eyelids, mouth, genitals) becomes the corresponding mucosa. The skin is almost 16% of body weight and its thickness varies from 0.5 mm on the eyelids to 3.0 mm on the palms and soles in adults.The basic functions of the skin are maintaining body temperature and defense of harmful penetrating substances. The skin can

also receive information about the environment through the senses of touch (pain, heat, cold). There are multiple and important functions that the skin has in maintaining homeostasis of the body, it is extremely important to keep the skin healthy so it can continuously fulfill all of its functions

Skin is a separate entity in a child. Although the anatomical terms are not much different from adult skin, the child's skin is thinner, the stratum cornea and epidermis are thinner and the skin cells are smaller in size. Skin problems that occur early in childhood are very specific. Research shows that children's skin, although more hydrated, is actually more prone to water loss at a faster rate, which challenges the current opinion on the full development of the protective functions of the skin immediately after birth. The latest data from clinical trials and research (evidence based) suggest that further development of the skin within the first two years of life, including children's skins ratio of larger surface area relative to body weight than adults, and greater vulnerability when exposed to harmful effects from the environment.The specifics of children's skin are:

- increased susceptibility to contact dermatitis due to irritation
- increased susceptibility to atopic dermatitis

Atopic dermatitis has a special place in pediatric practice due to the following reasons:

- incidence of disease in childhood is high - about 10% of all children suffer from eczema
- usually occurs in the first two years of life, beginning from the second month of life
- the first sign of susceptibility to eczema in the first weeks of life is seborrhea dermatitis, scaly skin on the forehead and inner corners of eyebrows / or rough, dry skin on the cheeks, the area behind the ear and the outer parts of the extremities.

Typically, there is a positive history in parents and close relatives for atopy. Atopy is defined as the tendency of the body to react to normal, harmless factors from the environment in a form of allergic reaction which creates specific Ig E antibodies.Most common atopic diseases are eczema and contact dermatitis. Skin allergies can be exanthema or urticaria as a reaction to food, insect bites, hot-cold, pressure, and inhalation allergens - bronchitis, asthma, hay fever, and allergic conjunctivitis.

Atopy

Clinical signs of an allergic reaction first appear on the skin if there isn't adequate prevention. In clinically expressed forms there is a progression of allergic reactions of the skin in the digestive tract, cow's milk allergy to proteins, gluten (Celiac disease) and the respiratory system (recurrent bronchitis and asthma).More than half of children with atopic dermatitis will develop asthma or hay fever, later they can develop into chronic diseases with sequels that alter the quality of life.Family history is an important factor which can help prevent the occurrence of atopic eczema. Complete treatment of atopic eczema with continuous skin care application and avoidance of environmental influence can significantly improve the child's care.In medical literature it is known that predisposed children, breast feeding and late introduction of allergenic foods such as citrus fruit, egg, fish, honey, nuts, preservatives and additives, the critical use of antibiotics especially in the first year of life, preservation of probiotic microflora, the presence of antioxidants such as vitamin C and manganese in diet, avoiding exposure to tobacco smoke, maintaining the normal flora of the skin and mucous membranes, may delay or significantly reduce the appearance of atopic disease in children with a genetic predisposition. This implies the importance of preventive measures. **Diagnosis** is based on history, physical examination, clinical symptoms and laboratory findings.

The clinical picture

The skin is dry, rough and coarse. The leading symptoms are erythematic skin, itching, damp skin, excoriations and crusts on the skin.Although the disease is mild in most cases and can be successfully prevented and treated. However, parents and children alike are displeased when there is a lack of scheduled health education and health care. Due to continuous itching the child is constantly crying, scratching, unhappy, and the family is misbalan-

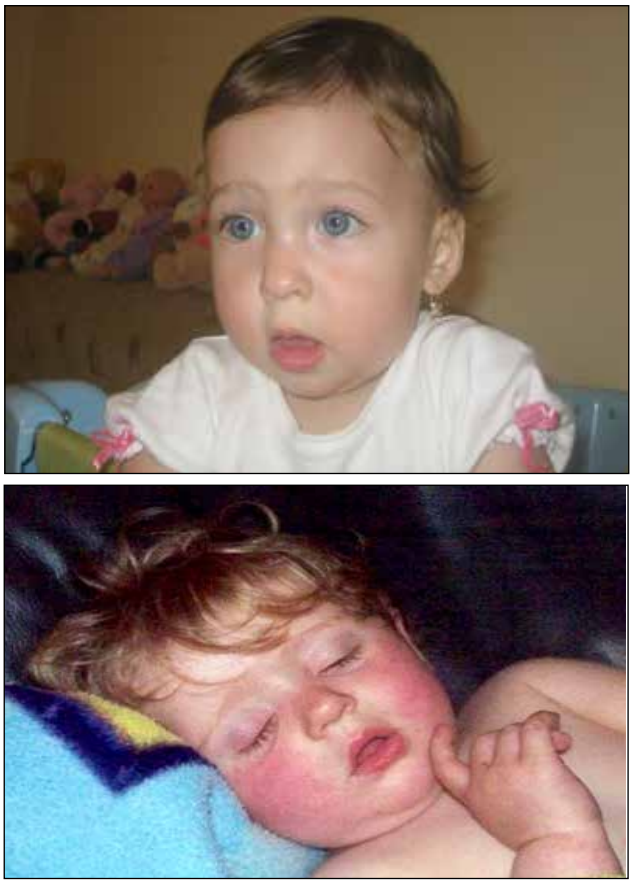


Image A & B. The clinical picture

ced, considering the disease is chronic it requires changes in previous life habits, and occasionally there is a need for professional psychological help. Distribution of atopic eczema varies depending on the age of the child:

Infants: face-cheeks, backside, outsides of the limbs, the region under diapers.

Young children: no changes on the face, lesions cover the extensor surfaces of the extremities.

Children: the skin folds - elbow and behind the knee pits, neck, ankle and wrist joints.

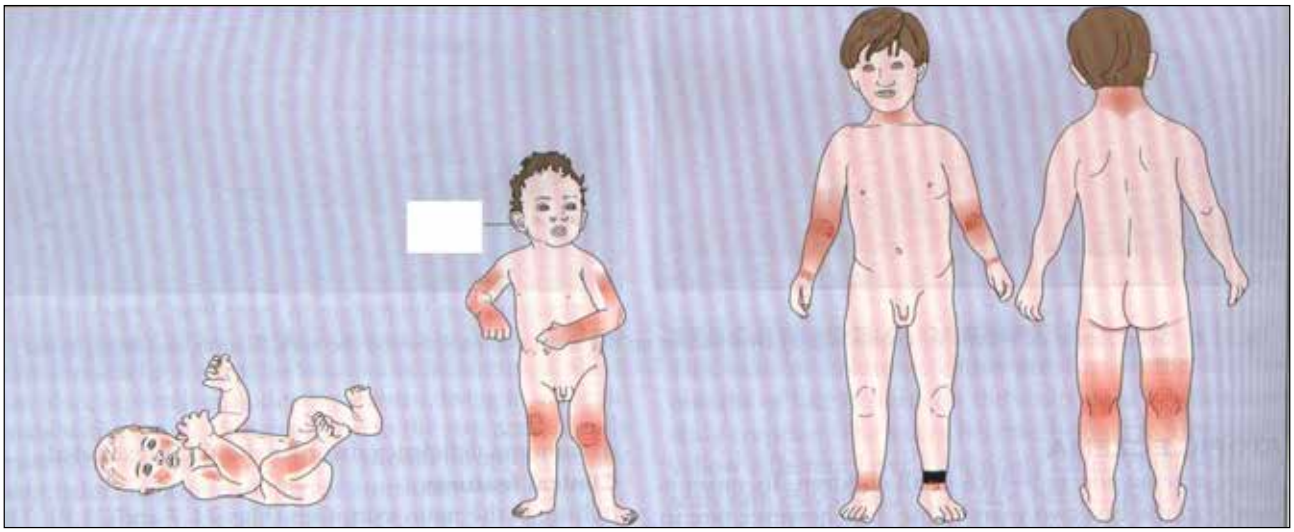
The laboratory findings

- elevated levels of total IgE in plasma
- levels of specific IgE to certain allergens in plasma
- positive skin tests to different types of allergens

Prevention

Preventive measures include compliance with the following principles

- local skin care of the body - the necessity of the use of hypoallergenic products intended for very young children in the form of oil baths
- avoid skin contact with allergens synthetics, nylon, wool, dust, grass, pollen
- avoidance of external factors such as heat and humidity – changing the diapers every 3 hours while regulating the hygiene of the skin region covered with diapers with water and oil baths
- diet - avoiding allergenic matter intake by lactating mothers
- late introduction of high allergenic substances such as egg, fish, honey in infants
- Frequent swabs of the nasal cavity and eyes in seek of Staphylococcus aureus and



frequent fecal analysis in search of Candida because these agents are very often factors for the occurrence of atopic eczema in young children and immediate local treatment with proper medicament

Therapy

Local corticosteroids often have the best results for eczema.Mild corticosteroids 1% hydrocortisone hydroxide applied twice a day is very effective. Local side effects can be skin thinning. Moderately strong corticosteroids have an essential role in the treatment of severe forms of atopic eczema but there use must be minimized because of the potential systemic side effects. In cases of major changes and expressed eczematous itching, at night apply occlusive dressings or impregnated tar paste or diluted corticosteroid creams.Antihistamines-H 1-histamine antagonist in the form of syrup used to calm the itch should only be used at night. Antibiotics are for mild infections in combination with hydrocortisone used locally, but it must be taken into account the possible resistance, so they should be applied short term. Only in the event of serious systemic infections antibiotics are applied. Antiviral drugs are rarely implemented, only for complications such as occurrence of herpes virus infection of eczema, when acyclovir is used.Because of the reasons listed above, one of the main issues of contemporary children's dermatology is whether proper skin care from birth can reduce the prevalence of atopic dermatitis, or at least reduce the severity of the condition? Should more attention be given to healthy baby skin? Does the protection of children's healthy skin become a new paradigm?The fact is that children's skin care is rooted in the culture, not in science, and every nationality has a different approach. Guides to children skin care expand from "less is better" to "active preventive health care of children's skin". Certainly we know that practical recommendations should be based on scientific research and medical evidence.

The aim of the study

Searching for the best way to nurture children's skin and prevent the occurrence of damage, we based our study at newborns and young infants until the age of 3 months, through evidence of the effect of preventive measures - local skin care with nutritive and protective e.g. skin repair cream(Dermalex Repair Cream-manufacturers Chefaro Ireland Ltd, Ireland, registered as a medical device class IIa in Serbia, the solution 04-1084/10), avoidance of contact with allergens and external factors as humidity and heat and therapeutic measures as local treatment with corticosteroids creams and treatment of rhinitis and conjunctivitis caused by Staphylococcus aureus and diarrhea caused by Candida.

Materials and methods

The prospective clinical study included fifty (50) newborns and infants with clinical signs of atopic dermatitis. The clinical study was voluntary throughout June and July 2011. The sample consisted of children from the territory of AP Vojvodina. Two coherent sets were formed. The first group P consisted of newborns up to 4 weeks of life with seborrhea syndrome and in whom preventive measures were used. The second group T, was made up of children aged 4-8 weeks with clinically expressed eczema where therapeutic procedures were obtained. Control examinations were carried out at regular time intervals, every seven days, four times in total, when the skin condition was scored 0-5. One point was given for each of the following symptoms- redness, damp, itching, excoriations, and crusts.The obtained results were processed using statistical methods.

Results and Discussion

According to the gender distribution, 31 were male (in group P-16, in the group T- 15) and 19 females (group P 9, the group T 10) which is consistent with literature - allergies are slightly more common in men.Based on the detailed medical history, the positive family history of genetic atopy susceptibility from the mother was 60% and the father, 40% of test subjects. The atopy reactions were mostly in the form of bronchitis and asthma in childhood, while 10% of parents had manifestations of allergic reactions such as runny nose and contact eczema.The data correlates with the literature, if one parent has atopic constitution, the chance that a child inherits this constitution is 30% and 42% if inherited from the mother and 60% occurrence if both parents are atopic. The basis lies in a number of major and minor genes, which are located at V, VI.VII, XI, XII, XIV, XVI chromosomes.The first

group P, consisted of 25 children, with an average age of 21 days, born at term with an average gestational age of 39.2 weeks with the lowest gestational age 37 3/7 and the highest 41. 2/7 weeks. The average body weight of 3475 grams, the average body length of 52 cm. All the children were exclusively breastfeed. The second group T, is made up of 25 children average age 43.92 days and most were represented by children 6 weeks old, 3 of the children were 32 days old, 4 children were 38 days old, five children were 40 days old, 10 children were 45 days old, 4 children were 50 days old. The average body weight was 4750 g and the average body length was 56 cm. Most of the children were breastfeed and five children, 20 %, were on milk formula. Breastfeeding is significantly reduced in the second month of life in group with clinically expressed dermatitis -it may be the reason of eczema as cow milk protein are highly allergenic and can easily provoke allergic reaction especially in children with positive family history of allergy.In the group P the average score of skin health was 1 because only mild redness was noted and slight desquamation of the area in the inner corners of eyebrows and scalp. As signs of seborrhea The advice was given that children should be bathed in oil baths, and that the affected skin should be applied with protective and repair cream every night after bathing. At check-up, 7 days later, the score was 0 -clinical examination revealed that seborrhea syndrome was no longer present and the entire skin returned to its physiologic state and it remains so during the whole period of 4 weeks while our clinical study was carries out. In group T the average score of skin health was 4. All children had redness, damp, itchy and some even had excoriations and/or crusts. As these are signs of expressed dermatitis, we gave advice for treatment

- Hygiene - bathing in oil baths.
- Problem skin should be treated with skin repair cream two times a day.
- Administration of probiotic that has Lactobacillus rhamnosus and Bifidobacterium BB CG-12.
- The lactating mother should restrict her diet and not eat: fish, eggs, citrus fruits, strawberries, raspberries, tomatoes, parsley, parsnip, concentrated herbs for cooking, industrial products, chocolate, walnuts, hazelnuts, and peanuts.
- Alteration of the baby's diet – restriction of lemonade if already introduced into the nutrition.
- In children with a score of 4 and 5, a local treatment of injured skin with combined cream (a mild corticosteroid + antibiotic+ panthenol + solution acidi borici 3%) - made by the pharmacist , two times per day

The first check up after 7 days of treatment showed that in 17 children, 68%, were almost cured with skin health score only present 1 for local redness of skin, 12% (3children) had skin health score 2 for redness and itching, 20% of children had score 3: redness, damp and itching. None of them was in worse or equal skin condition comparing with the onset of therapy. In the second check up 14 days after treatment, 22 children had a score of 1 which is mild hyperemia of the skin without other accompanying symptoms and 3 children had a score of 0, therefore treatment was successful. Excoriations and crusts were not present in any of the children thus corticosteroid treatment was fully ceased. After 21 days of the therapy, the skin of all patients was excellent with a score O and they all were under only preventive measures and advised, to gradually reintroduce foods that were restricted to lactating mothers with clinical monitoring of possible exacerbation of eczema but it did not occur in any case.

Conclusion

Maternal nutrition is of great importance as a possible factor in provoking the expression of atopic constitution of the child in the form of eczema and should always be altered in breastfeeding mothers as the treatment of eczema in newborns. Taking probiotics is important in preventing bowel wall defect permeability, which consequently controls the absorption of allergens.The magnitude of local skin care allows the regeneration of the skin barrier which prevents inflammation and decreases the symptoms of eczema; such as redness, damp, itchy, scratching, which leads to excoriations and crusts. The strengthening of the skin and its protective function helps repair the damage and inflammation of eczema symptoms. Re-

gularly use of skin repair cream and probiotics is fully recommended in newborns and toddlers with even slight signs of dermatitis, especially in children with positive family history toward allergies. The results of our prospective clinical study have shown that the best way to nurture children's skin and prevent the occurrence of eczema are adequate local skin care, diet excluding allergenic food and every days regular use of skin repair cream and probiotics

References

1. *Alanne S; Nermes M; Söderlund R; Laitinen K Quality of life in infants with atopic dermatitis and healthy infants: a follow-up from birth to 24 monthsActa Paediatr. 2011; 100(8):e65-70 (ISSN: 1651-2227)*

2. *Flohr C; Yeo L Atopic dermatitis and the hygiene hypothesis revisited. Curr Probl Dermatol. 2011; 41:1-34 (ISSN: 1662-2944)*

3. *Lipozencić J; Pastar Z; Kulisić SM; Pavić I Immunologic aspects of atopic dermatitis.Acta Dermatovenerol Croat. 2009; 17(3):226-34 (ISSN: 1330-027X)*

4. *Elias PM; Schmuth M Abnormal skin barrier in the etiopathogenesis of atopic dermatitis. Curr Opin Allergy Clin Immunol. 2009; 9(5): 437-46 (ISSN: 1473-6322)*

5. *Chrostowska-Plak D; Salomon J; Reich A; Szepietowski JC Clinical aspects of itch in adult atopic dermatitis patients Acta Derm Venereol. 2009; 89(4):379-83 (ISSN: 1651-2057)*

6. *Katayama I; Kohno Y; Akiyama K; Ikezawa Z; Kondo N; Tamaki K; Kouro O Japanese guideline for atopic dermatitis Allergol Int. 2011; 60(2): 205-20 (ISSN: 1440-1592)*

Corresponding Author
Svetlana Stefanovic,
Medical faculty,
Novi Sad,
Serbia,
E-mail: healthmedjournal@gmail.com

Pictorial representation of body shape in breast cancer patients

Afsaneh Tabande[1], Sima Besharat[2], Mahsa Besharat[3]

[1] Golestan University of Medical Sciences, Golestan, Iran,
[2] Golestan Research Center of Gastroentrology and Hepatology, Golestan University of Medical Sciences Golestan, Iran,
[3] Golestan Research Center of Gastroentrology and Hepatology, Golestan University of Medical Sciences Golestan, Iran.

Abstract

Background: It has been suggested that body fatness in earlier life of a woman could be inversely related to breast cancer risk. Pictorial perception of body size could be used as a tool to assume the fat distribution in the past years.

Aim: This study was conducted to measure the body image of patients with breast cancer in Golestan province, Northeast of Iran.

Methods and materials: In this cross-sectional study, cases of breast cancer were derived from the population based cancer registry system of Golestan Province (N=127), between 2004 and 2006. A demographic questionnaire was completed through interview. A set of drawings (pictogram) ranging from very lean to obese was used to assess the individual's perception of their body size at three different periods of life (before menarch, up to the diagnosis of breast cancer, and up to menopause if applicable). Pictogram scores 1, 2, and 3 assigned to normal participants; pictogram score 4 for overweight subjects, and pictogram scores equal or higher than 5 for obese ones. Coded data were entered into computer and analyzed using SPSS-16 (SPSS Inc., Chicago, IL, USA).

Results: Mean age (±SD) of these patients was 47.6 (±10.31) years with a range of 28-80 years. Numbers of overweight and obese individuals increased during the different periods of life.

Conclusion: Results showed that before menarch, most of these patients assumed their body as normal, but increasing the age, numbers of normal weight patients decreased, and in menopausal state, obesity was the most prevalent score.

Key words: Pictogram, breast cancer, body fatness

Introduction

Anthropometric indices such as weight, height, waist circumstances and body mass index (BMI) are among the proposed prognostic factors in certain cancers like breast cancer which have been discussed to have a strong relationship with. From one hand, there has been growing concerns about the effect of obesity and metabolic syndrome on the health status of the population all over the world recently, and on the other hand, diagnosed cases of breast cancer are increasing in developed and developing countries which is among the first five causes of death from cancers. [1] BMI is the most frequent index to evaluate the fat distribution in the body, assumed as the underlying mechanism of linkage between obesity and cancer mortality. [1] It has been suggested that body fatness in earlier life of a woman could be inversely related to breast cancer risk, though maybe a much earlier screening tool should be considered against this first killer in females. [2]Studies showed that increasing body weight after the age of 20 years could increase the risk of post-menopausal breast tumors. [3] Although, some studies showed that tallness could increase the risk regardless the menopausal status and fatness increase the risk after menopause. [4]

But in cross-sectional studies, where we have patients with cancer at a defined period of time, measuring BMI could not be specific to predict the outcome, so if we don't have the trend of anthropometric indices, this type of study could be confusing.This study was conducted to evaluate the perception of patients with breast cancer about their body images during the different phases of the life, in Golestan province, Northeast of Iran.

Subjects and methods

In this cross-sectional study, pathological confirmed cases of breast cancer were derived from the population based cancer registry system of Golestan Province, Northeast of Iran (N=300), between 2004 and 2006. This population-based cancer registry gathers data relating to patients affected by various kinds of cancers from all pathology offices, medical laboratories, hospitals, local health offices, clinics, and physician offices.

After excluding repeated data, incomplete addresses, dead persons and those who moved to a different location, 127 cases were left. A demographic questionnaire was completed through interview by trained personnel from Golestan Health Network. The questionnaire included data regards to the age, residency, ethnicity, marital status, profession, educational level, and risk factors which were discussed in previous studies such as age at menarche, menopause and first pregnancy, number of children, and number of abortions.

A set of drawings (pictogram) ranging from very lean to obese, designed by Stunkard et al [5] was used to assess the individual's perception of their body size at three different periods of life (before menarch, up to the diagnosis of breast cancer, and up to menopause if applicable). They were asked to select the most similar figure to their body image. Pictogram was scored 1-9 (Fig. 1). As Keshtkar et al reported [6] pictogram scores 1, 2, and 3 could be assigned to normal participants; pictogram score 4 for overweight subjects, and finally pictogram scores equal or higher than 5 for obese ones.

Coded data were entered into computer and analyzed using SPSS-16 (SPSS Inc., Chicago, IL, USA).

Results

Mean age (±SD) of these patients was 47.6 (±10.31) years with a range of 28-80 years. Mean (±SD) age at marriage was 20 (±5) years, age at menarch was 13.33 (±1.36) years, age at menopause was 45.8 (±6.12) years and age at the first pregnancy was 20.95 (±4.9) years. Their breast feeding durations was 67 (±48.63) months at the average. Eighty one were living in urban areas.Four of them (3.1%) were single, 108 (85%) were housewives and others (15%) were working outdoors, 68.5% were graduated, 23 had a history of cancer in their first degree relatives and 13 in their second degree relatives.

As shown in table 1, numbers of overweight and obese individuals increased during the different periods of life.

Discussion

There has been reported an inverse association between Body Mass Index (BMI) and the risk of breast cancer in pre-menopausal women. Michels et al observed that BMI at the age of 18 years is the strongest predictor of breast cancer risk. [7] But as it was said before, when we are visiting a case of breast cancer, it is so difficult to assume her BMI at the previous stages of life. Thus we need an alternative method to investigate this important predictor. So several studies are done to compare other measurements like visual pictogram with BMI and revealed to an acceptable way of predicting BMI by an imaging perception. [5-6]

So, we used this 9-level scale to ask our breast cancer patients about their body size during 3 notable phases: before menarch, before cancer and up to menopause (if applicable). Results showed

Figure 1. Nine level pictogram of women.

Table 1. Breast cancer patients' perception of their body size in different periods of life

Period of life	Before menarch	Up to cancer	Up to menopause
Score 1-3 (Normal)	109	53	31
Score 4 (Overweight)	10	33	26
Score≥ 5 (Obese)	6	44	35

that before the age of menarch, most of these patients assumed their body as a normal weight person, but after that when the age started to increase and the hormonal status changed, numbers of normal weight patients decreased, and in those at a menopausal state obesity was the most prevalent score that was chosen.Baer et al showed that greater body fatness at young ages, particularly during adolescence, was associated with a substantial decrease in breast cancer risk, both in pre and post menopausal women. [2] Increased body weight and obesity is shown to be an important and potentially avoidable predictor of fatal breast cancer in US women. [8-9] In a recent study from Los Angeles, it was reported that women with breast cancer were more likely to be obese than women without breast cancer. The association between obesity and breast cancer was significant only among African-American women and was especially significant among postmenopausal African-American women. [10]

A practical method of preventive programs for cancer could be decreasing the risk by weight control in women after the age of 20-years, in addition to other confirmed risk factors. We should encourage more physical activity and decrease fat consuming in females, as it is approved to be an effective way in preventing/ delaying breast cancer risk.

References

1. *Yang CY, Peng CY, Liu YC, Chen WZ, Chiou WK. Surface anthropometric indices in obesity-related metabolic diseases and cancers. Chang Gung Med J. 2011;34(1).*

2. *Baer HJ, Tworoger SS, Hankinson SE, Willett WC. Body fatness at young ages and risk of breast cancer throughout life. American journal of epidemiology. 2010;171(11):1183.*

3. *Suzuki R, Iwasaki M, Inoue M, Sasazuki S, Sawada N, Yamaji T, et al. Body weight at age 20 years, subsequent weight change and breast cancer risk defined by estrogen and progesterone receptor status—the Japan public health center-based prospective study. International Journal of Cancer. 2010.*

4. *Ahlgren M, Melbye M, Wohlfahrt J, Sørensen TIA. Growth patterns and the risk of breast cancer in women. New England Journal of Medicine. 2004;351(16):1619-26.*

5. *Stunkard AJ, Sørensen T, Schulsinger F. Use of the Danish Adoption Register for the study of obesity and thinness. Research publications-Association for Research in Nervous and Mental Disease. 1983;60:115.*

6. *Keshtkar AA, Semnani S, Pourshams A, Khademi H, Roshandel G, Boffetta P, et al. Pictogram use was validated for estimating individual's body mass index. Journal of clinical epidemiology. 2010;63(6):655-9.*

7. *Michels KB, Terry KL, Willett WC. Longitudinal study on the role of body size in premenopausal breast cancer. Archives of internal medicine. 2006;166(21):2395.*

8. *Petrelli JM, Calle EE, Rodriguez C, Thun MJ. Body mass index, height, and postmenopausal breast cancer mortality in a prospective cohort of US women. Cancer Causes and Control. 2002;13(4):325-32.*

9. *Huang Z, Hankinson SE, Colditz GA, Stampfer MJ, Hunter DJ, Manson JAE, et al. Dual effects of weight and weight gain on breast cancer risk. JAMA: the journal of the American Medical Association. 1997;278(17):1407.*

10. *Sarkissyan M, Wu Y, Vadgama JV. Obesity is associated with breast cancer in African-American women but not hispanic women in South Los Angeles. Cancer. 2011;117(16):3814-23.*

Corresponding author
Sima Besharat,
3rd floor, Shahid Nabavi polyclinic,
4th Azar alley, 5-Azar St,
Gorgan city,
Golestan province,
Iran,
E-mail: besharat@goums.ac.ir

Quality of life persons with medulla spinalis lesions - pilot study

Sanja Trgovcevic[1], Goran Nedovic[2], Dragana Kljajic[3], Fadilj Eminovic[2], Jadranka Urosevic[3]

[1] Faculty of Political Sciences, University of Belgrade, Belgrade, Serbia,
[2] Faculty of Special Education and Rehabilitation, University of Belgrade, Belgrade, Serbia,
[3] Medical College of Professional Studies, Cupria, Serbia.

Abstract

Introduction. During the past decades, the medical progress has led to the improvement of survival rates in persons who have experienced SCI, but in return the focus from a survival has moved to a lifetime monitoring of the quality of life. The ultimate goal of rehabilitation after the spinal cord injury is the optimization of the remaining functions and achievement of acceptable quality of life.

The aim of the research. Presentation of the obtained results of the perceived quality of life in persons with spinal cord injury and the differences between groups in relation to the lesion level.

Method. The sample consisted of 43 participants of both genders, aged 18-65 years, living on the territory of the R. Serbia. The first group included 23 participants diagnosed with paraplegia and the other included 21 participants diagnosed with quadriplegia.

Instruments of research. The clinical and sociodemographic data were collected by a specially constructed questionnaire *General sociodemographic questionnaire*, and for the purpose of the quality of life evaluation *The Spinal Cord Injury Quality of Life Questionnaire - SCI QL-23* was used. The analysis of variance (ANOVA) was used for determination of the difference between the variables.

Conclusion: Out of four, which were included by the QL-23, in three areas no statistically significant difference between participants with paraplegia and tetraplegiawas found. The difference was identified only at the level of functioning ($P<0.001$). The research results show that the injury level makes no significant difference in the perception of mood and depressive emotions, independence or autonomy loss, and global quality of life.

Key words: spinal cord injury, paraplegia, tetraplegia, quality of life

Introduction

In the essence of human personality, regardless of the epoch, status, education, religion or race, lays a unique desire to live a life fulfilled with pleasure. The terms associated with pleasure, prosperity, fulfillment and happiness are closely related to the concept of quality of life (QL). Terminology determination is not simple and we can say that there are as many definitions as there are tests, considering that many factors, such as material, spiritual, social and above all health factors, contribute to the overall quality of life, individually or in a mutual interaction. The unique definition of quality of life does not exist, so the terms well-being and health status are being used as synonyms for the quality of life, although they represent only few aspects of more comprehensive concept. One of the leading factors in the assessment is the physical well-being, although there are also other numerous factors. Usually they imply a standard of living, education, employment, social status, housing conditions, satisfaction at work, harmonious family relationships, etc., and have an impact on the living conditions of the society, group or individual.

The World Health Organization defined the quality of life in 1993 as the individuals' perception of their position in life, in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and interests. It is presented as a wide-ranging concept which includes: physical health, psychological status, financial independence and level of independence, social relationships and relationship to salient features of environment [(1)]. Later on, the World Health Organization amends the existing definitions saying that the quality of life is a state of complete physical, mental and social well-being and represents multidimensional concept that includes both physical and psychosocial aspects

[2]. Only few events in life can dramatically change a person's lifestyle like spinal cord injury. During the past decades, the medical progress, technological innovation and better living conditions have led to the improvement of survival rates in persons who have experienced SCI [3]. The annual incidence of spinal cord injury in the USA is 40 cases per million people, which represents a 12 000 of new cases each year [4]. In European countries it varies from 12.1 injured per million people in the Netherlands, to 57.8 injured per million people in Portugal, so that the average incidence made on a total of 415.7 million people in Europe is 17.2 per million people [5], while in Serbia and Montenegro that rate is around 12.1 injured per million people [6]. The most dramatic results were detected in the data related to age structure, where the significant increase in injuries was noted among people aged 15-29 years, and older than 65 years, probably due to falls and non-traumatic causes of injury [7]. Data from 2011 show that since 2005 the highest number of spinal-cord injuries occurred in motor vehicle accidents (40.4%) and the road traffic injuries present enormous health, social and economic burden [8,9]. In the next most common cause falls are included, and on the third place violence (primarily gunshot wounds) is placed [4].

There are numerous relevant tests for assessing the quality of life of persons with spinal cord injury which are based on the examination of the various aspects of life and the effects of rehabilitation [10]. The ultimate goal of rehabilitation after spinal cord injury is the achievement of acceptable quality of life and it must be aimed at the limitation of the complications, the optimization of the remaining functions and the improvement of quality of life through all aspects [11].

Barker et al. performed a study that was based on the relation between the quality of life of persons with SCI and those without injury, as well as on the comparison of the quality of life to the components of impairment (activities, limitations, etc..). The authors state that there is a lower rate of QL for persons with SCI, as well as the increasing need for more effective rehabilitation services, resolving the common problems and the employment [12].

An extensive study about the quality of persons with SCI was performed in Australia and Sweden during 2004. The most important predictors of QL perception in the Australia and Sweden were: mood, social and physical functioning, and problems regarding the consequences of the injury. One of the authors' conclusions was that our knowledge in this field might be increased by the participants who are experts in some areas such as maintenance of the social interaction role, emotional well-being, etc. [13].

There are different variations of the quality of life in relation to the demographic conditions, and the data collected vary from country to country [14]. However, most of the studies have shown that the quality of life of persons who have experienced SCI is not equivalent to their peers, while the factors alone that determine it remain undetected [15].

Although a large number of studies examine the factors related to the quality of life, there are few that answer the question which personal or environmental factors are crucial in the improvement of quality of life and subjective well-being. Personal factors such as gender, age, time of injury, level of impairment, show weak correlations with the level of quality of life. Health, the sphincter control and the functional independence level show a more modest correlation, while variables such as mobility, incomes, marital status, pain, secondary complications and self-efficacy show significant correlation with the level of quality of life [16].

The main objective of this study was to present the obtained results of the perceived quality of life in persons with spinal cord injury. The second objective was to determine the differences between the obtained results, and the third was to present the most powerful predictors of the perceived quality of life among the SCI groups. The research hypothesis is that persons with injuries of lower neurological segment, or a higher level of functional capacity, have a higher perceived quality of life in all segments of the QL-23 test.

Methods

The sample consisted of 43 participants of both genders, aged 18-65 years, living on the territory of the R. Serbia. The time elapsed from the spinal cord injury was limited to less than one year, and participants had been treated for at least six months in one of the department for spinal cord

injury. The first group of participants included 23 persons diagnosed with thoracic, lumbar and sacral spinal cord injury (paraplegia), and the other included 21 participants with the neck (cervical) spinal cord injury (tetraplegia).

The criteria for the formation of groups were: age between 18-65 years, diagnosis of paraplegia or tetraplegia, no brain injury, without significant congenital disorders and psychiatric diseases.

The independent variables were: gender, age, educational level, marital status, employment and place of residence. The dependent variable consisted of the quality of life, while the control variables were: time of injury, cause of injury, level of injury, completeness of injury and treatment.

Research instruments

The clinical and socio-demographic data were collected by a specially designed questionnaire General socio-demographic questionnaire, and for the purpose of the quality of life evaluation The Spinal Cord Injury Quality of Life Questionnaire - SCI QL-23 was used[13, 17, 18]. QL-23 is derived from an extensive battery of general and specific questionnaires used in the Studies of persons with SCI. The scientific QL-23 consists of 23 statements/questions, of which 22 contain three variables of physical, mental and social functioning: The Functioning (FUNC) includes 10 items (question from 1a to 1j) related to the physical and social limitations. It originates from the Swedish version [19], SIP-the Sickness Impact Profile[20]. The FUNC covers functional limitations in the area of mobility, self care, movement and social interaction. The questions were previously constructed, in appropriate difficulty degree (according to the weighting system of SIP), so that the participants should only confirm a particular item in accordance with their health. The Mood (MOOD-Mood State)-depression and anxiety, includes 6 items (questions from 2a to 2f) derived from the Swedish version of[21] the Hospital Anxiety and Depression Scale (HAD)[22]. These items are aimed at the confirmation of anxiety and depression symptoms, and the scale provides a possibility of four levels assessment. The problems related to the injury (PROB-problems re. injury) - the experience of the independence loss and other issues related to the injury, include 6 items (from 3a to 3f) derived from a list of specific questionnaires[23] which describe the perception of physical dependence, complications and social stigma associated with a specific injuries. The global quality of life (GQOL-Global Quality of Life) - assesses total rating of the life situations, and includes one question from the Quality of Life Questionnaire-Core 30 (item no. 4) of the European Organization for Research and Treatment of Cancer[24].

The research results

Table no. 1 shows the socio demographic characteristics of participants with spinal cord lesion. According to the results presented in the table, there is no statistically significant differences between participants by all presented items, except in relation to marital status, where a statistically significant difference ($P<0.05$) between participants with tetraplegia (quadriplegia) and paraplegia is founddue to the fact that participants diagnosed with paraplegia were more likely married (12:3). Table no 2. shows the test results obtained by QL-23, in relation to functionality, mood, independence and global quality of life. According to the results presented in the table, participants with quadriplegia and paraplegia are statistically equal on the MOOD scale, the PROBE scale and the GQOL scale, while on the FUNC scale, a group of participants diagnosed with quadriplegia achieved the arithmetic mean of 73.37 (std. 20.8), whereas a group of participants diagnosed with paraplegia achieved the arithmetic mean of 44.06 (std.29.1) which have caused the occurrence of statistically significant differences on the P-level ($p<0.001$).

Table no. 3 shows the correlation between the dependent GQOL variables and independent and control variables. Based on the results obtained, the statistically significant differences were found in participants with paraplegia according to the cause of injury ($P<0.05$) and the presence of pain ($P<0.05$). In participants with tetraplegia (quadriplegia) the statistically significant differences were found between GQOL and completeness of injury, spending time with friends, hobbies and sports activities ($P <0.05$). Discussion about the results:

The assessment of quality of life of persons with SCI is indisputable and scientifically justifi-

Table 1. The socio-demographic characteristics of participants

Characteristics	Group		Total (n=44)	The differences between groups (P-level)
	Tetraplegia (n=21)	Paraplegia (n=23)		
Marital status Married Not married	3 (14.3%) 18 (85.7%)	12 (52.2%) 11 (47.8%)	15 (34.1%) 29 (65.9%)	P<0.05
Children No Yes	16 (76.2%) 5 (23.8)	12 (52.2%) 11 (47.8%)	28 (63.6%) 16 (36.4%)	NS
Employment Unemployed On a sick leave Retired Employed	6 (28.6%) 1 (4.8%) 14 (66.7%) 0	5 (21.7%) 4 (17.4%) 13 (56.5%) 1 (4.3%)	11 (25%) 5 (11.4%) 27 (61.4%) 1 (2.3%)	NS
Education Primary school High school College University	3 (14.3%) 13 (61.9%) 3 (14.3%) 2 (9.5%)	3 (13.0%) 14 (60.9%) 3 (13%) 3 (13%)	6 (13.6%) 27 (61.4%) 6 (13.6%) 5 (11.4%)	NS
Place of residence Hospital or clinic Nursing Home/Institution Property	5 (23.8%) 7 (33.3%) 9 (42.9%)	10 (43.5%) 5 (21.7%) 8 (34.8)	15 (34.1%) 12 (27.3%) 17 (38.6%)	NS
Incomes Below average The average Above average	13 (61.9%) 8 (38.1%) 0	14 (60.9%) 8 34.8%) 1 (4.3%)	27 (61.4%) 16 (36.4%) 1 (2.3%)	NS

ed. The overall assessment of severity and level of disability, deterioration or improvement, may be provided by physicians and other medical professionals. However, information about the quality of life is provided by the people with disabilities themselves, because all people express themselves differently in a different circumstances and a different time of their life. The aim of this study was to determine the difference in the quality of life of persons with SCI in relation to the lesion level. The importance of this study is in identification of the factors that determine the quality of life level in a relation to the neurological injury level.

QL-23 consists of four scales. On the FUNC scale, which refers to the physical and social dysfunction, the statistically significant differences between participants with tetraplegia (quadriplegia) and paraplegia were found (P<0.001). This result could have been expected since the lesion level defines the level and type of impairment, and the participants with lower spinal cord lesions showed better results in the functioning in comparison to the participants with cervical spine injuries.

On the MOOD scale, which refers to the mood and depression, no statistically significant differences among participants were found. In a study from 2005 [13] the results obtained by the mentioned scale showed that the level of mood and depression differed in relation to the country of origin (P<0.0001). According to the results of survey conducted on participants from a population of tetraplegia and paraplegia, the level of lesion had no effect on the occurrence of depression and mood swings. On the PROB scale, which refers to the perceived autonomy or independence loss, no statistically significant difference among par-

Table 2. The functionality, mood, independence and global quality of life

Variables	Tetraplegia (n=21)	Paraplegia (n=23)	P- level
FUNC scale - physical and social dysfunction: (lower score indicates better performance)	73.37 (20.8)	44.06 (29.1)	P<0.001
MOOD scale - mood and depression (lower score indicates better performance)	31.21 (16.1)	36.23 (25.1)	NS
PROB scale - perceived autonomy or independence loss: (higher score indicates better performance)	60.85 (21.5)	59.66 (21.9)	NS
GQOL scale - global quality of life: (higher score indicates better performance)	54.76 (19.8)	50.00 (21.9)	NS

ANOVA model of the determination of the statistically significant differences between arithmetic means of the examined groups
**The mean results obtained are listed (standard deviation)*
***NS-non significant*

Table 3. Correlations between GQOL and socio-demographic variables

Independent variables	Tetraplegia (n=21)		Paraplegia (n=23)	
	r	P-level	r	P-level
Gender	NS	NS	NS	NS
Time ofinjury	NS	NS	NS	NS
Cause of injury	NS	NS	r=0.487	P<0.05
Level of injury	NS	NS	NS	NS
Completeness of injury	r=0.48	P<0.05	NS	NS
Pain	NS	NS	r=(-) 0.462	P<0.05
Marital status	NS	NS	NS	NS
Education	NS	NS	NS	NS
Employment	NS	NS	NS	NS
Spending time with friends	r=0.519	P<0.05	NS	NS
Hobby	r=0.531	P<0.05	NS	NS
Sport	r=0.533	P<0.05	NS	NS

r- Pearson's correlation coefficient
NS-non significant

ticipants from both groups was found which is in accordance with the results obtained from the research [13, 15].

On the GQOL scale, which refers to the global quality of life, participants with quadriplegia and paraplegia have also shown uniformity, that is, no statistically significant difference between participants was found. However, in order to identify predictors of quality of life we have compared the GQOL scale with socio-demographic variables. Participants with quadriplegia showed (table no. 3) that completeness of injury, spending time with friends, having a hobby and engagement in sports activities have an effect on the global quality of life, as opposed to participants with paraplegia to which these factors have no influence. On the GQOL scale the cause of injury and the presence of pain have a significant effect on the perceived quality of life among participants with paraplegia, which is in accordance with the results obtained from the research [16].

Conclusion

Out of four areas included by the QL-23, in three of them no statistically significant difference

between participants with paraplegia and tetraplegia was found. The difference was identified only at the level of functioning, which might be explained by the level of spinal cord injury. Since we have assumed that the lower level of spinal cord lesion implies to a higher level of functioning, we have expected the difference in the self-assessment of quality of life among participants from these two groups. However, the research results have shown that the injury level makes no significant difference in the perception of mood and depression, loss of autonomy or independence, and global quality of life.

Considering the limitations of the study,the following research shoul beconducted with a significantly higher number of participants. The results obtained by this pilot study could be used for further research in the field of rehabilitation and social integration of persons with the spinal cord injury.

Acknowledgment

This paper resulted from a project named *"Socijalna integracija osoba sa povredom kičmene moždine"* approved by the University of Belgrade (06-8097/21, 06.12.2011.)

References

1. *World Health Organization. WHOQOL Focus Group Work. [MNH/PSF/93.4] Geneva 1993.*
2. *World Health Organization. The world health report: life in 21 centry: a vision for all. Geneva 1998. Available from: http://www.who.int/whr/1998/en/whr98_en.pdf*
3. *Koç Z., Avcı IA, Sağlam Z. The use of complementary and alternative medicine by older patients that have chronic diseases. HealthMED 2012; 6 (2): 413-422.*
4. *Spinal cord injury facts and figures at a glance. Publication of the National spinal cord injury statistical center, Birmingham, Alabama 2011. Available from: https: //www.nscisc.uab.edu*
5. *Blumer CE, Quine S. Prevalence of spinal cord injury: an international comparison. Neuroepidemiology 1995; 14: 258–268.*
6. *Babović, D. Živeti uspravno posle povrede kičmene moždine. Beograd; 2010.*
7. *van den Berg MEL, Castellote JM, Mahillo-Fernandez I, de Pedro-Cuesta J. Incidence of spinal cord injury worldwide: a systematic review. Neuroepidemiology 2010; 34: 184-192.*
8. *World Health Organization. Global status report on road safety: time for action. Geneva 2009. Available from:*
9. *http://www.who.int/violence_injury_prevention/road_safety_status/report/cover_and_front_matter_en.pdf.*
10. *Wang SM, Dalal K. Road Traffic Injuries in Shanghai, China. HealthMED 2012; 6 (1): 74-80*
11. *Hill M, Noonan V, Sakakibara B, Miller W. Quality of life instruments and definitions in individuals with spinal cord injury: A systematic review. Spinal Cord 2010; 48(6): 438–450.*
12. *Jang Y, Hsieh CL, Wang YH, Wu YH. A validity study of the WHOQOL-BREF assessment in persons with traumatic spinal cord injury. Archives Physical Medicine and Rehabilitation 2004; 85(11): 1890–1895.*
13. *Barker RN, Kendall MD, Amsters DI, Pershouse KJ, Haines TP, Kuipers P. The relationship between quality of life and disability across the lifespan for people with spinal cord injury. Spinal Cord 2009; 47:149-155.*
14. *Kreuter M, Siösteen A, Erkholm B, Byström U, Brown DJ. Healt and quality of life of persons with spinal cord lesion in Australia and Sweden. Spinal Cord 2005; 43: 123–129.*
15. *Geyh S, Fellinghauer B, Kirchberger I, Post M. Cross-cultural validity of four quality of life scales in persons with spinal cord injury. Health & Quality of Life Outcomes 2010; 8: 94.*
16. *Jain N, Sullivan M, Kazis L, Tun C, Garshick E. Factors associated with health-related quality of life in chronic spinal cord injury.* American Journal of Physical Medicine & Rehabilitation *2007; 86(5): 387–396.*
17. *Mortenson W, Noreau L, Miller W. The relationship between and predictors of quality of life after spinal cord injury at 3 and 15 months after discharge. Spinal Cord 2010; 48(1): 73-79.*
18. *Elfström ML, Kreuter M, Persson LO, Sullivan M. General and condition-specific measures of coping strategies in persons with spinal cord lesion. Psychology, Health & Medicine 2005; 10: 231-242.*
19. *Lundqvist C, Siösteen A, Sullivan L, Blomstrand C, Lind B, Sullivan MM. Spinal cord injuries: a shortened measure of function and mood. Spinal Cord 1997; 35: 17-21.*

20. *Sullivan BM, Ahlme´n M, Archenholtz B, Svensson G. Measuring health in rheumatic disorders by means of a Swedish version of the sickness impact profile. Scandinavian Journal of Rheumatology 1986; 15: 193–200.*

21. *Bergner M, Bobbitt RA, Carter WB, Gilson BS. The sickness impact profile: development and final revision of a health status measure. Medical Care 1981; 19: 787.*

22. *Siosteen A, Lundqvist C, Blomstrand C, Sullivan L, Sullivan M. Sexual ability, activity, attitudes and satisfaction as part of adjustment in spinal cord-injured subjects. Paraplegia 1990; 28: 285–295.*

23. *Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta Psychiatrica Scandinavica 1983; 67: 361–370.*

24. *Lundqvisat C, Sio¨steenh A, Blomstrand C, Lind B, Sullivan M, Sullivan L. Spinal cord injuries. Part 1: Clinical, functional, and emotional status. Spine 1991; 16:78–83.*

25. *Carlsson AM. Assessment of chronic pain. Aspects of reliability and validity of the visual analog scale. Pain 1983; 16: 87.*

Corresponding author
Sanja Trgovcevic,
Faculty of Political Sciences,
University of Belgrade,
Belgrade,
Serbia,
E mail: strgovcevic@yahoo.com

Gender through the eyes of men

Selma Dinc Kahraman, Handan Zincir, Zeliha Kaya

Erciyes University, Faculty of Health Sciences, Talas Kayseri, Turkey

Abstract

The current research investigates men's views of gender who have high and least education level. As different from literature, this study shows that education alters men's views of relations between men and women in marriage but do not alter men's views on equitable approach to women's gender roles in social life and on male and female children. Also it shows that traditional gender models still continue with their parents infusing these models into children. Two groups were formed for the research, one that consists of university graduate males, the other of literate males or males who received basic education from Kayseri. The education level of first group is collage graduate (high education level and other's education level is primary school graduate (least education level). According to this study, the higher men's education level, the higher marriage age. Also it shows that education has positive impact on marriage choice decision and the higher education, the higher marriage of own choice. But this study shows that men's approach to male and female children do not change with education. This study also shows that training about child rearing before marriage and birth needs to be given to parents to alter traditional gender roles and patterns taught from birth onwards.

Key Words; Gender, Men, Gender Roles; Work And Social Life; Marriage And Family Life

Introduction

Sex is a biological term, natural, universal and determined at birth. In contrast to sex, gender is a psychological and cultural concept and can change over time, vary within and between culture and even from family to family (Pruss and Gee 2003; Akın and Demirel 2003). "Gender" concept denotes female and male personality traits, roles and duties designated socially. So in the definition of gender there are assets, expectations, stereotypes and roles about how society sees, perceives, thinks us and about how to behave as female and male and about what society expects from us. These roles denote female and male's personality traits and behaviors which are seen traditionally and culturally appropriate. In our society, while boys are brought up to be more free and to have more privileges than girls, girls generally are brought up with ban such as premarital sexual intercourse (virginity) under pressure and control, in accordance with more conservative traditional role expectation (Duyan 2004; İnanç 2003; Nelson 1997; Özvarış and Akın 1998).

Women's views of daily life, the identification of gender factors, the effect of gender on women's reproductive health are investigated in the studies before 2000 (Hablemitoğlu 1996; Chodorow 1998; Worsley and Worsley 1990;. Nelson 1997; Özvarış and Akın 1998). Gender differences in daily life, economy and psychological factors, the effects of gender on health, women's views of gender took place in the following studies (Prus and Gee 2003; Akın and Demirel 2003;Civil and Yıldız 2010; Esin and Öztürk 2005; Kahraman 2009). The ultimate purpose of this research is to investigate men's views of gender according to men's education level. Many studies investigated gender through the eyes of women. In our study we investigated gender through the eyes of men. So there are two factors in this study, first is the eyes of men and other is education level.

Gender according to turkish culture

The creators of pressure generally are family and social environment. Even if parents are of different level of education and culture, majority of them maintain traditional attitudes and taboos in this regard and also equitable approach towards male and female children, an understanding that must begin at home, is not sufficiently adopted. Traditions are seen as inextricable from their forbidden and shameful identity so they pervade

throughout female children's lives (Brown and et al. 2001; Dejong and et al. 2007; Gezgin 1997; Civil and Yıldız 2010). In the study by Civil and Yıldız (2010), the majority of students agree that there is taboo on sexuality in our society. So this result strengthens the idea that in our society there is a lack of sexual equality and a presence of gender discrimination in which men are powerful, women are weak, shy, not eager to specify her request and everything is seen as men's right (Civil and Yıldız 2010).

As seen, these roles put on female and male in most areas of social life usually cause female to become of secondary importance and lead to the continuation of inequality model which gives male greater value than female by creating a discrimination against female (Esin and Öztürk 2005; Prus and Gee 2003). Uneducated women are married off early and immediately expected to have baby due to roles of "wife" and "motherhood" given by society. So women are accepted and respected in the society (Russo and Pirlott 2006; Sağ 2003). One of the most significant indicators of gender inequality is the difference of literacy rate between male and female. According to data of Institute of Population Research (TNSA-2008), while 33 % of women were uneducated or did not graduate from primary school, this ratio for men is 20%. Also the mean age of mother at first birth is 22.3 and median age at first marriage is 20.8. These results show that the half of women is married at age 20 (Hacettepe 2008). In other study made in Şanlıurfa region by Kahraman it is found that 41.7 % of women were uneducated. Also in the same study the reasons of why women did not continue their education were examined and it is found that 66.4% of women were not allowed by their family because they were female and all the women said that all family decisions were taken by their husbands (Kahraman 2009). Unfortunately this system causes women not to achieve and exercise some women's rights related to education, work, equal opportunities, decision making / freedom of choice, access to health services, equal pay for equal work, equality of social status and thus women have low social status compared to men (Kitiş and Bilgici 2007; Worsley and Worsley 1990; Türmen 2003). According to study in the East and Southeast Region of Turkey women cannot go to hospital without the permission of their husband, consult to male doctor, benefit from family planning and other health services sufficiently. 60.2 % of men in this region accept the fact that men are smarter than women and 56.7 % of men accept the fact that the husband has the right to beat his wife who does not obey him (Kitiş and Bilgici 2007).

As a result of gender role, working and politic are adopted as male occupation, household chores and specific areas related with family are adopted as female occupation in social sphere naturally (Esin and Öztürk 2005; Worsley and Worsley 1990). Women do not work because they need to stay in home because of household chores such as child care, cleaning, ironing, and cooking. Also if women want to work they should obtain their spouse's permission or should leave the management of their income to their spouse. These situations arising from gender roles cause women to be economically dependent on their spouses so women are in poorer position than men (Arpacı and Ersoy 2007). Because of patriarchal traditions in our society, men expect women to be respectful, responsible, patient and honest towards them and when confronted with the situations such as disrespect, irresponsibility, dishonesty within the framework of their own opinions, they approve to use force women to maintain their control and power (Türmen 2003). In the study by Yılmaz and et al. in 2009, gender role expressions such as "Looking after family is women's main task", "Man must always be the head of the household.", "Responsibility of earning livelihood for the family should be given to man" are asked among high school and college students to determine traditional and non-traditional perception of gender roles and it is determined that students adopt the traditional roles. This result is supported with other studies in literature (Keith and Jacqueline 2002; Kimberly and Mahaffy 2002).

So as to ensure equality among women and men in social life and increase women's social status, to make society conscious of gender roles and raise public sensibility are extremely important. Education can be an important tool in this regard. The rise of educational level especially university level alters social gender roles perspectives of individuals from traditional to modern in which gen-

der equality and rightness is in women's favor. To alter society and ensure equality among women and men, firstly society's views on gender roles must be determined (Chodorow 1998; Dikeçligil 1998; Durakbaşa 1998). So in our society majority of who have traditional structure, it is thought that making a study of what meant by gender roles put on male and female especially these in working, family, married and social life through the eyes of men who have different education level and status is extremely important. Besides by determining men's views on gender roles, next generation's views on gender roles can be shaped equitably.

Accordingly, this study was made to determine men's (who have different education level: primary school and college graduate) views of social gender roles especially in working, married and family life.

Hypotheses

Female and male roles are determined according to gender. As men's views of traditional gender roles change, equality among women and men increases. We believe that education is important tool to alter men. So our hypotheses are based on the effect of education on traditional gender roles.

H1: We predict that the higher men's education level, the higher their spouse's education level.

H2: We estimate that the higher men's education level the less the ratio of early marriage.

H3: As men's education level raises, traditional roles disappear and inequality among women and men decreases. Therefore we anticipate that men graduated from primary school will adopt traditional roles with higher ratio when compared to men graduated from college school and we also estimate that the higher men's education level, the higher equality among women and men.

H4: We predict that as men's education level rises, men's approach to male and female children will change and egalitarian approach to male and female children will be employed.

Method

Participant To determine the effect of education on traditional gender role, we chose two groups who had different education level -high and least education level. The education level of first group is collage graduate (high education level) and other's education level is primary school graduate (least education level). In total, 200 men who are married and have male and female children participated to this study. 100 male faculty members who are collage graduate and work in Erciyes University-Kayseri compose the first group. Second group is composed of 100 male employees who are graduated from primary school and work in the old industrial part of Kayseri. Male faculty members were elected by simple random sampling and male employees who work in the old industrial section were elected depending on snowball sampling because we could not obtain full list of male employees.

Procedure We obtained official permits before study. Data were collected with the use of a questionnaire contained 65 questions. Questions in the survey are prepared and based on the most recent studies. The survey was composed of 4 parts and 65 questions in total. Questions of first part were created to identify sociodemographic characteristics (age, work and his wife's work etc.). Questions of second part were created to determine the relations between husband and wife in marriage (Who do housework in your family? How did you marry your wife?). Third section questions were prepared to reveal men's views of women's role (In your view, should men and women have equal participation in politics?) and last section were prepared to identify men's approach to male and female children (In your view, can boy come home late?- In your view, can girl come home late?). After preparation, questionnaire was tested in 20 men and according to this work, questionnaire was corrected. Before the survey, information about study was given to participants and their consents were obtained. Each questionnaire was applied as face- to- face interviews by researchers and it lasted approximately 10-15 minutes.

The type of research the research has been carried out through descriptive survey method to determine men's views of gender roles through the eyes of men who are graduated from primary school (least education level) and college graduate (high education level) (2008).

Evaluation of Data data was evaluated using descriptive statistics. Results were presented as frequency tables (number and percentage) and Chi-square analysis is performed to independent and dependent variables used in study. The level of significance between group means was tested through (5%) 0.05.

Results

Sociodemographic Results

When the ages of participants were examined, it was seen that 47% of employees who work in the old industrial section of Kayseri and 54% of faculty members was between 20 - 40 ages. It was determined that 56% of employees and 99% of faculty members incomes were equal or more than 1.000 TL. The question of which city he had the longest period in was asked to participants and 76% of employees and 41% of faculty members had expressed that he had the longest period in Kayseri. The education level of participant's wives were examined and it was determined that while 55% of employee's wives were primary school graduate, and 79% of faculty member's wives were college graduate. This result supports our predictions for Hypothesis 1. The higher men's education level, the higher their spouse's education level.

Results to gender role views

It is the presented data related to opinions of participants on marriages at Table 1.It was determined that while 17% of employees got married at or under the age of 20, only 4% of faculty members did the same (Hypothesis 2). Likewise the ratio of employee's wives who got married at or under the age of 20 was bigger than the ratio of faculty member's wives who got married at or under the age of 20 (56 %, 16% t= 0.000 p<0.001) (Hypothesis 2, Hypothesis 3). These results support Hypothesis 2, 3 and these show that education increases marriage age and also as men's education level rises, they get alienated from traditional roles. It is seen in Table 1 that while 33% of employees answered the question of how he married his wife as "My own choice", 75% of faculty members answered similarly (Hypothesis 3). This difference is statistically significant (p<0.01). It was determined that the majority of both employees and faculty members answered the question of why marriage is important as "Since marriage is a necessity of life" (Table 1). This difference is also statistically significant (p < 0.01). It was determined that 80 % of employees and 57 % of faculty members marked the option of "To do housework, look after children" when they were asked to tell what they think about the role of women in marriage. This relation is statistically significant (p<0.01) (Hypothesis 3).

When university and primary school graduate males' level of including their wives into decision making process is examined (Table 1), it is found that there is no big difference between employee's and faculty member's answers and this relation is not statistically significant (p<0.01). As seen education alter men but this change is not sufficient to reach modern family life.

When answers of whether you apply violence to your spouse are examined (Table 1), it is found that 17 % of employees (least education level) and 72 % of faculty members (high education level) said "No" (X^2=0.01 p<0.05) (Hypothesis 3). Similarly 68 % of employees and 95 % of faculty members stated that women should work. These results shows men graduated from primary school will adopt traditional roles with higher ratio when compared to men graduated from college school.

Data related to opinions of participants on social life is presented at Table 2. In this context, while 74 % of employees said that men and women should have equal participation in politics, the ratio of faculty members who approved this was 67%. In the same way, 83 % of faculty members and 88% of employees answered "Yes" to the question of whether men and women should be equal in law in your view. The answers of the question of whether woman's salaries can be higher than men's salaries between married couples in your view examined and it was determined that the ratio of employees was higher than the ratio of faculty members (Table 2).

It is observed that there are difference between employee's and faculty member's answers of the question of whether in your view, women can come after men and this relation is statistically significant (p<0,05) (Hypothesis 3). While this

Table 1. Opinions on marriages

Variables	X^2	Employees S	Employees %	Faculty Members S	Faculty Members %
What age did you get married?					
≤ 20		17	17.0	4	4.0
21–30		83	83.0	78	78.0
≥ 31		0	0, 00	18	18.0
When you get married how old was your wife?					
≤ 20		56	56.0	16	16.0
21–30		44	44.0	84	84.0
How did you marry your wife?	0,000	33	33.0	75	75.0
My own choice	p<0.01	48	48.0	10	10.0
Arranged marriage		19	19.0	15	15.0
My family's choice					
Why is marriage important?	0,000	95	95.0	80	81.0
Since marriage is a necessity of life	p<0.01	5	5.0	19	19.0
Since I get to share my life					
What do you think about the role of women in marriage?	0,00	80	80.0	57	57.0
To do housework, look after children	p<0.01	10	10.0	15	15.0
To contribute to family budget		10	10.0	28	28.0
All of					
Do you apply your spouse violence?	0.01	25	25.0	17	17.0
Verbal violence	p<0,05	58	58.0	11	11.0
Physical violence		17	17.0	72	72.0
No					
Do you ask your spouse when deciding something?					
I take my wife's opinion on everything.		60	60.0	74	74.0
I take my wife's opinion only on issues relating to home	0,30				
and to children	p>0,05	17	17.0	13	13.0
I do not ask to my wife and I'll give orders		23	23.0	13	13.0
Should women work?	0,000	68	68.0	95	95.0
Yes she should	p<0.01	32	32.0	5	5.0
No she should not					

result supports Hypothesis 3, the majority of the results in Table 2 show that as men's education level rises, inequality among women and men increases. Data related to opinions of participants on child-rearing is presented at Table 3.

According to this table, roughly the same ratio was determined (25%) in answers of the question that boy can stay with girlfriends at night. However the ratio of faculty members who answered yes the question that girl can stay with girlfriends at night was higher (8%) than the ratio of employees (4%). 45% of faculty members and 50% of employees answered yes to the question that boy can came home late but 23 % of faculty members and 17 % of employees answered yes to the question that girl can came home late. these relations are statistically significant (p<0,05). these result do not support Hypothesis 4. Education may not alter men's approach and traditional gender model are still infused into children by their parents.

Discussion

One of the basic missions of education is to hand on cultural values and to lead society into desirable future. By reducing pressures of tradi-

Table 2. Opinions on social life

Variables	X^2 P	Employee's (%)		Faculty Member's (%)	
		Yes	No	Yes	No
In your view, should men and women have equal participation in politics?	0,40 p>0,05	74.0	26.0	67.0	33.0
In your view, should men and women be equal in law?	0,31 p>0,05	88.0	12.0	83.0	17.0
In your view, should men and women be equal in the religion?	0,004 p<0,05	89.0	11.0	71.0	29.0
In your view have men and women equal in social life?	0,364 p>0,05	65.0	35.0	66.0	34.0
In your view can women's education be higher than men's education between married couples?	0,67 p>0,05	89.0	11.0	92.0	8.0
In your view can women's salaries be higher than men's salaries between married couples?	0,12 p>0,05	50.0	50.0	68.0	32.0
Do you agree that women's hairs are long but their minds are short?	0,029 p<0,05	14.0	76.0	9.0	81.0
Dou you agree that women are virtue of house?	0,24 p>0,05	19.0	81.0	12.0	88.0
In your view can women be free in selecting her marriage partner?	0,81 p>0,05	93.0	7.0	89.0	12.0
In your view can women dishonor men's promise?	0,39 p>0,05	58.0	42.0	41.0	59.0
In your view can women be senior managers?	0,45 p>0,05	84.0	16.0	79.0	21.0
In your view can women vote for their desiring party?	0,33 p>0,05	36.0	64.0	31.0	69.0
In your view can women come after men between married couples?	0,00 p<0,05	28.0	72.0	64.0	36.0
In your view, can women dress as she pleases?	0,68 p>0,05	54.0	46.0	60.0	40.0
In your view can women go without informing your husband where she pleases?	0,48 p>0,05	29.0	71.0	33.0	67.0
In your view are men the head of household?	0,18 p>0,05	72.0	28.0	62.0	38.0
In your view is there a social pressure against women?	0,17 p>0,05	72.0	28.0	83.0	17.0

Table 3. Opinions on child-rearing

Variables	X^2 P	Employee's (%)		Faculty Member's (%)	
		Yes	No	Yes	No
In your view, can boy stay with girlfriends at night?	0,87 p>0,05	25.0	75.0	26.0	74.0
In your view, can boy stay with boyfriends at night?	0,56 p>0,05	54.0	46.0	58.0	42.0
In your view, can boy stay with relatives at night?	0,41 p>0,05	84.0	16.0	88.0	12.0
In your view, can boy come home late?	0,47 p>0,05	50.0	50.0	45.0	55.0
In your view, does boy have a lover?	0,34 p>0,05	69.0	31.0	75.0	25.0
In your view, can boy go to university?	0,40 p>0,05	98.0	2.0	96.0	4.0
In your view, can boy go to university only in the city which you live?	0,00 p<0.01	27.0	73.0	5.0	95.0
In your view, can girl stay with boyfriends at night?	0,23 p>0,05	4.0	96.0	8.0	92.0
In your view, can girl stay with girlfriends at night?	0,04 p<0,05	30.0	70.0	50.0	50.0
In your view, can girl stay with relatives at night?	0,25 p>0,05	71.0	29.0	78.0	22.0
In your view, can girl come home late?	0,28 p>0,05	17.0	83.0	23.0	77.0
In your view, does girl have a lover?	0,08 p>0,05	42.0	58.0	54.0	46.0
In your view, can girl go to university?	0,03 p<0,05	93.0	7.0	99.0	1.0
In your view, can girl go to university only in the city which you live?	0.01 p<0,05	27.0	73.0	9.0	91.0

tionalist and conservative societies, to ensure a freedom and intellectual environment and to prepare him/her for innovation and change are also possible with education (Sağ 2003). According to the theory of modernization, education which is a criterion of modernization is one of the important elements of person's life style. So the higher level of education the higher possibility of appearance of modern lifestyle. At the same time when the level of education is considered as an indicator of whether family have modern structure, learned gender roles and models are observed more in traditional societies who have low level of education, low level of socio-economic structure (Dermen 2008; Chodorow 1998; Dikeçligil 1998; Kandiyoti 1995; Demirbilek 2007; Leathwood and Read 2010). Accordingly, in this research because of higher education level faculty members are expected to move out of traditional gender roles and models and they are to be affected from social contagion less than employees.

According to this study the ratio of early marriage of women was 36% of all participants' spouse - 56% of employee's spouse and 16% of faculty member's spouse so this result shows that early marriage is still common in our society. However early marriage was very high among employees so education had positive impact on early marriage. This result suggest that as the level of education rises, traditional effects will be less and the age of marriage of men and women will be high, decline of early marriage and marriage in accordance with

individual's desire will be high like in modernized societies.

The ratio of early marriage of women was higher than that of men (Table 1). Women's gender roles may cause this result, because the primary roles of women given by society are as "wife" and "mother" and as keeper of the household (Şahiner 2007). Therefore, in traditional society early marriage of women is considered to be accurate and pressure is created in this respect. According to Arpacı and Ersoy (2007), the ratio of marriage decision given by the parents and family was 57,8 % and the ratio of marriage decision (15,6 %) given by the parents was higher than that of individuals by their own. The ratio of individuals who decided to marry under pressure was 51,1 %. Those making pressure were father with 8,9 %, , mother 2,2 %, father-in-law 2,2 %, mother-in-law 2,2 %, family 33,3 % and traditional position 4,4% (Arpacı and Ersoy 2007). These results are supported with the study by Kahraman in which it was determined that 85 % of women who live in Şanlıurfa center and have low education and socioeconomic level married under the age of 20 and 83.5 % of women married because their father thought it would be suitable (Kahraman 2009).

While Arpacı and Ersoy (2007) determined that the rate of marriage in accordance with individual's desire was only 13.3 % (Arpacı and Ersoy 2007), in this study this ratio was determined as 54% of participants - 33% of employees and 75% of faculty members (Table 1). This result shows a considerable increase in marriage in accordance with individual's desire. The ratio of faculty members who married in accordance with individual's desire was higher than that of employees ($p<0.01$). This result shows that education has positive impact on marriage choice decision and the higher education the higher marriage of own choice. But the rates of arranged marriage and family's choice of marriage which are seen in traditional society were high (46 % of participants).

Gender roles indoctrinate men into the fact that marriage is necessity of life and religion requirement (Keith and Jacqueline 2002; Dikeçligil 1998; Güçlü 1998). Also in this study the result is the same as that of literature. The majority of men in both groups said that they were married since marriage is a necessity of life (Table 1). However the ratio of the answer of "Since I get to share my life" was higher among faculty members (19%) than among employees (5%). This result shows that because of the positive effect of education on the fact that marriage is necessity of life and religion requirement, gender may move from traditional to modern with education.

57% of faculty members and 80% of employees said that the role of women in marriage is to do housework, look after children. This finding supports Parson's gender role differentiation. According to it women specialized in expression roles which are confined to doing homework and looking after children and men specialized in instrumental roles which are confined to providing livelihood in traditional society and these roles are learned within socialization process.

When violence examined 72% of faculty members and 17 % of employees indicated that no "violence was applied to their spouse (Table 1). This result is still very high but at the same time it shows that education is efficient tool to abolish violence against women. In a study by Yılmaz 13.2 % of male college students participated in the suggestion that if women merit, her husband can apply violence against her (Yılmaz and all 2009).

74% of faculty members and 60% of employees said "he takes his wife's opinion on everything". In traditional society decisions are taken by men and women abide by these decisions. This finding is good and significant result in terms of gender equality and women's status in family and society. However employees who never consult to their wife when deciding about something and take their wife's opinion only on issues relating to home and children had the higher ratio than faculty members (Table 1). In a study by Atalay et al (1992) throughout Turkey to determine the basic features of Turkish family structure, they applied questionnaire to 19.210 households, 6.145 from rural and 12.065 from city. In this study, they determined that while decisions were taken together with peers in city, they were taken only with men in rural. Also they determined that in 39.23 % of families lived in city the critical decisions which affect children's future were taken with peers, in 43.09 % of families lived in rural, these were taken with men (Atalay and et all 1992). Hablemitoğlu (1996) made the study on women and their husbands who

lived in 22 village of Kızılcahamam so as to determine women's business model and participation to decisions in rural families. As to results of this, while women took part in agricultural activities such as product marketing, harvesting, preparing soil for planting, hoeing, irrigation, fertilization, transportation, animal care, planting and pruning, the decisions about land purchase- sale, purchase of basic agricultural tools and equipment, use of new technology and new varieties of agricultural products, expenditure of family income were taken with men. Women were involved in these decisions with the family members at the low rate. On the other hand, women can have attended courses related to agricultural activities and household chores and they did not arrange the time of both agricultural activities and household chores. But they stated that women decided only to purchase home chose, apparel, cleaning materials, to determine the need of food. Also they said that men decided to selection of boy and girl's peer, family visits, the evaluation format of vacation days, the number of children, girl and boy's learning process, political party to vote (Hablemitoğlu 1996). At the end of this study, they stated that the higher the education level, the higher ratio of men who think towards to gender equality in the city.

Majority of men in two groups said that women should work but faculty members had higher ratio than employees (95 – 68%). This result also emphasizes the importance of education.

In this research while faculty members are expected to move out of traditional gender roles and models and to be affected from social contagion less than employees surprising, attractive and regrettable results were found in answers of the questions whether men and women should be equal in law, politics, the religions, social life.

In a study on college students by Yılmaz et al,, it is stated that 88.9 % of female students and 63.2 % of male students did not agree with the suggestion that politics is men's job more than women' job and unfortunately 26.4 of male students agreed with this. As for our study, 74% of employees and 67% of faculty members said that women and men should have equal participation in politics. But 31% of faculty members and 36% of employees said that women can vote for their desiring party. These results are surprising and thought provoking because while it is hoped that the more education level the more people who think that women should have equal rights to men, the opposite result is found in this study. Women in Turkey obtained the right to vote and be elected in municipal elections in 1930 and parliamentary elections in 1934. Before this date, the number of country in which women have had the right to vote and be elected is 28 and the number of country in which women have been actually elected to Member of Parliament is 17. So when compared with other countries, Turkey is one of the them in which the ratio that women are participated in politics is the lowest level (Yılmaz and et all 2009; Hablemitoğlu 1996).

It is an attractive and regrettable point that faculty members answered as no to the question of whether women can dishonor men's promise with higher ratio (Table 2).

While the majority of employees answered as yes to the question whether women can come after men between married couples, the majority of faculty members answered as no to same question (Table 2). This result shows that education has positive impact on it. According to a study by Kahraman about women, participants were asked the question whether women should come home before her husband and what the cause of answer is. As a result, 92.2% of women answered as yes stated that women should come home before her husband because women's responsibility is more than men at home and if she does not come before, she neglect her husband and children and women answered as no stated that there is no obligation on women to come early (Kahraman 2009). This result shows that housework is socialized as primary functions of women and women internalize this role because women are largely responsible for housework.

In our study the majority of men agreed with the suggestion that men the head of household (Table 2). Men's education level did not affect this result. In a study by Yılmaz, 56 % of male students agreed with same suggestion. So the similarity between our study and Yılmaz's study indicates that it may be difficult to change men's gender role views to desired level (Yılmaz and et all 2009).

Other attractive and regrettable point in this study is that majority of men in two groups said that there was social pressure against women.

According to a study by Vefikuluçay et al., the majority of participants said that girl and boy should have equal educational rights. However, about one of every three male students participated to the proposition that women should not go out alone to streets in the evening. So this remarkable result indicates that men have traditional gender views (Vefikuluçay and et al 2007). As a result, education level does not change men's approach to male and female children. The fact that traditional gender model is infused into children by their parents still continues now.

Conclusions and recommendations

Women have been exposed to gender discrimination and inequality throughout history. They have always had lower status than men and fewer rights and opportunities than men have had. Undoubtedly, traditional gender roles and socialization process by which these roles were learned have major impact on this situation. The use of gender analysis as a basis in evaluations, monitoring, implementation and development in all areas of health, education and employment to achieve gender equality must be used and empowerment of women and implementation capacity of gender analysis must be increased. Especially men should be incorporated into implementation capacity and opportunities providing women and men equality in every issue should be increased, applied and programs should be developed with this aim.

References

1. *Prus, S.G., Gee E (2003). Gender Differences in The Influence of Economic, Lifestyle and Psychosocial Factors on Later-Life Health, Canadian Journal of Public Health, 94(4), P:306-309*
2. *Leathwood C.; Read B (2010). Gender and The Changing Face of Higher Education. A feminized future?,Gender and Education, 22(1), P; 136 - 137*
3. *Akın A,Demirel S. (2003), Concept of Gender and Effects on Health, R.U. Journal of Medicine Faculty 25 (4), Special Annex, P:73-83*
4. *DuyanV., (2004), Sexual Attitude Scale. Hacettepe University Social Work Collage, Ankara: ABC Printing, p: 2-12*
5. *İnanç N. (2003), Social Gender, 3.International Reproductive Health and Family Planning Congress (Congress Book), Ankara. 20–23 April 2003, 123-125.*
6. *Nelson S. (1997), Women's Sexual Health. Andrews G (Ed.), Women's Sexuality, London: Royal College of Nursing, P:.4-85*
7. *Özvarış Ş.B., Akın A. (1998), Reproductive Health, Health and Society, Women Health, 3-4, 23–26.*
8. *Brown A.D., Jejeebhoy S.J., Shah I., Youth K.M. (2001),Sexual Relations Among Young People in Developing Countries; Evidence From WHO Case Studies Report, Geneva:World Health Organization*
9. *Dejong J., Shepard B., Roudi-Fahimi F., Ashford L. (2007), Young People's Sexual and Reproductive Health The Middle East and North Africa, Population Reference Bureau, 1-7*
10. *Gezgin R. (1997),Women With Statistics,Society and Doctor, 12 (80), 57-67.*
11. *Civil B., Yıldız H (2010). Male Student's Sexual Experiences and Views For Sex Taboo,DEUHYO ED. 3(2),58-65*
12. *Prus S.G., Gee E.(2003).Gender Differences in The Influence of Economic, Lifestyle, and Psychosocial Factors on Later-Life Health, Canadian Journal of Public Health, 94(4) ,306-309,*
13. *Esin M.N., Öztürk N.(2005).Work Life and Women Health, Turkish Medical Association, Journal ofVocational Health and Security, 38-42,*
14. *Russo N.F., Pirlott A (2006), Gender-Based Violence Concepts, Methods and Findings, Ann. N.Y. Acad. Sci. 1087, 178–205,.*
15. *Sağ V (2003). Education and Social Change, C.U. Journal of Social Science, May Volume: 27 No:1 11-25*
16. *Dermen Ç (2008). Patriarchy and Masculinity Relationship in Middle East, C.U. Journal of Social Science, December Volume: 32 No:2, 321-329*
17. *Hacettepe U (2008). Institute of Population Studies, Turkey Demographic and Health Survey (TNSA),*
18. *Kahraman D. S (2009). S.,Social Pressure against Women,1. International Women Health Nursing Congress, 2-4 November İstanbul, Poster Paper,*
19. *Kitiş Y. and Bilgici S.Ş., (2007), A Case of Domestic Violence; Ethical Dilemma Between The Principle of Concealment and The Obligation To Report Violence, Journal of Family, Society, Education and Culture, Year 9, 3 (11), 7-13.*

20. *Worsley A. and Worsley A.J (1990). Women's Views of Women's Roles: A Survey of South Australian Women, Journal of Consumer Studies and Home Economics. 14 3, 229-237.*

21. *Arpacı F. and Ersoy A. F. (2007), Investigation of Effect of Women's Employments on The Quality of Family Life, Journal of Family Education and Culture and Society, Year 9, 3 (11), 41-46.*

22. *Türmen T (2003). Social Gender and Women Health, Gender, Health and Women Book, I. Print, Hacettepe University Publication, 3-14,*

23. *Keith B., Jacqueline S. (2002). Parent and Adolescent Gender Role Attitudes in 1990's Great Britain. Sex Roles 46(7/8): 239–244.*

24. *Kimberly A., Mahaffy K (2002). The Gendering of Adolescents' Childbearing and Educational Plans: Reciprocal Effects and The Influence of Social Context. Sex Roles 46(11/12): 403–417.*

25. *Yılmaz D. V., Zeyneloğlu S., Kocaöz S., Kısa S., Taşkın L., Eroğlu K., (2009),Collage Student's Opinion on Gender Roles,The Journal of International Human Science, 6:1. 775-793*

26. *Chodorow N (1998). Gender Relations and Difference in Psychoanalytic Perspective,ThePoliticy Reader In Gender Studies, Oxford Polity Press,: 41-49.*

27. *Dikeçligil B (1998). The Relationship Between Lifestyle and Income Level, Family Writing, I.Col., BeylüDikeçliğil-AhmetÇiğdem, Ankara: T.R. General Directorate of Family and Social Research Publications, No.5,: 521-536*

28. *Durakbaşa A (1998). Modern Women Identity and Intellectual Men During The Republican Era, A.B.Hacımirzaoğlu (Ed.), Women and Men in 75 Years, İstanbul: History Foundation Publications,:29-50.*

29. *Kandiyoti D (1995). Patriarchal Patterns: Notes for Resolation of The Kingdom of Men in Turkish Society, Ş.Tekeli (Jun), Women Through The Eyes of Women in 1980's Turkey, İstanbul: Contact Press,:367-382.*

30. *Carslon D. (1999). Personality and Role Variables as Predictors of Three Types of Work Family Conflict, Unpublished Researh Paper,*

31. *Demirbilek S. (2007). Investigation of Sociological Aspects of Gender Discrimination: Finance, Politics & Economical Comments Volume: 44 Number:511*

32. *Şahiner G (2007). The Effects of Gender and Violence Against Women On The Utilization of Women's Reproductive Health Services, GülhaneMilitary Medical Academy Institute of Gynecology and Obstetrics Nursing, USA Master's Thesis,. Ankara.*

33. *Güçlü S. Ö (1998). Family Research In Turkey: Problems, Priorities and Solutions, 3. Family Council Proceedings, Ankara: General Directorate of Family and Social Research Publications,*

34. *Atalay B and et all (1992). Turkish Family Structure Research, T.R. Prime Ministry State Planning Organization General Directorate of Social Planning Research Publication, Number.2313. Ankara,*

35. *Hablemitoğlu Ş (1996). Women's Work Models and Participation in Decisions, A.U. Graduate School of Natural and Applied Science, Phd Thesis (Unpublished), Ankara, S. 1-162.*

36. *Vefikuluçay D., Demirel S., Taşkın L., Eroğlu K., (2007). Last Year Student's Views of Gender Roles in Caucasus University, Hacettepe University Journal of Collage of Nursing 14(2): 12–27.*

Corresponding Author
Selma Dinç Kahraman,
Erciyes University,
Faculty of Health Sciences,
Talas Kayseri,
Turkey,
E-mail: selmadinc@mynet.com

F-18 fdg pet/ct imaging in a patient presenting with mediastinal lymphadenopathies: a case of sarcoidosis

Zeki Dostbil[1], Bugra Kaya[2], Oktay Sari[3], Erhan Varoglu[2]

[1] Department of Nuclear Medicine, Faculty of Medicine, Dicle University, Diyarbakır, Turkey,
[2] Department of Nuclear Medicine, Meram Faculty of Medicine, Konya University, Konya, Turkey,
[3] Department of Nuclear Medicine, Selcuklu Faculty of Medicine, Selcuk University, Konya, Turkey,

Abstract

F-18 FDG PET/CT has been used increasingly in evaluation of pulmonary and mediastinal lesions. However, inflammatory and granulomatous disorders may show increased F-18 FDG uptake on PET scanning. So, some benign conditions may cause false-positive results in cancer investigation. In this case, F-18 FDG PET/CT findings were presented in a patient with sarcoidosis who was investigated for primarily suspected malignancy.

Key words: sarcoidosis; F-18 FDG PET/CT; SUVmax

Introduction

2-(18F)-fluoro-2-deoxy-D-glucose (F-18 FDG) positron emission tomography (PET) is a non-invasive imaging technique that displays glucose uptake of the cells throughout of the body. So, local metabolic activity can be revealed easily by this technique. Metabolic imaging with F-18 FDG PET plays important role in management of the oncologic diseases (1). F-18 FDG PET is being used to diagnose, staging and follow-up of cancer patients. This imaging modality differentiate benign from malignant lesions more efficiently than conventional chest CT (2). However, FDG is not a cancer-specific agent. Thus, false positive findings in some benign disorders have been frequently encountered in cases with active inflammation or infection (1,2).

Inflammatory diseases such as sarcoidosis, tuberculosis and Wegener's granulomatosis and some infectious diseases may cause increased F-18 FDG uptake in PET scanning (2,3). In this paper, we reported a case in whom any possible malignancy was investigated by a F-18 FDG PET scanning because of mediastinal lymphadenopathies detected by previous contrast-enhanced CT.

Case Report

Our case was a 67 years old woman with complaint of cough and fever during recent months. Some mediastinal lymph nodes with abnormal size and shape were detected by a contrast-enhanced CT scan. The patient was referred to the Nuclear Medicine Department for F-18-FDG PET/CT scanning to investigate any possible malignancy and metabolic characterisation of the mediastinal lymph nodes. On the F-18 FDG-PET/CT scan, we determined some lymph nodes showing increased F-18 FDG uptake: 11 mm in short-axis diameter in right supraclavicular region (SUVmax: 5,80), 16 mm in diameter in right upper paratracheal (SUVmax: 12,86), and 12 mm in diameter in lower paratracheal region (SUVmax: 5,11). Besides, we observed some lymph nodes in 11 mm in diameter that were not F-18 FDG avid in the aortopulmonary window. In both lungs, there were diffuse ground-glass opacity that did not show increased F-18 FDG accumulation. In splenic hilus, there was a conglomerate lymph node mass showing increased F-18 FDG uptake in size of 58x51x36 mm (SUVmax: 13,08). We also observed several paraaortic lymph nodes at level of the second lumbar vertebra (SUVmax: 5,71). The patient was operated and conglomerate lymph node mass in the splenic hilus was excised. Histopathologic examination revealed a diagnosis of sarcoidosis.

Figure 1. (a,b,c,d) F-18 FDG PET, CT, PET/CT fusion and PET MIP images in the patient with sarcoidosis, seen above, respectively. Right supraclavicular (SUVmax: 5,80), right upper paratracheal (SUVmax: 12,86) and conglomerate lymph node

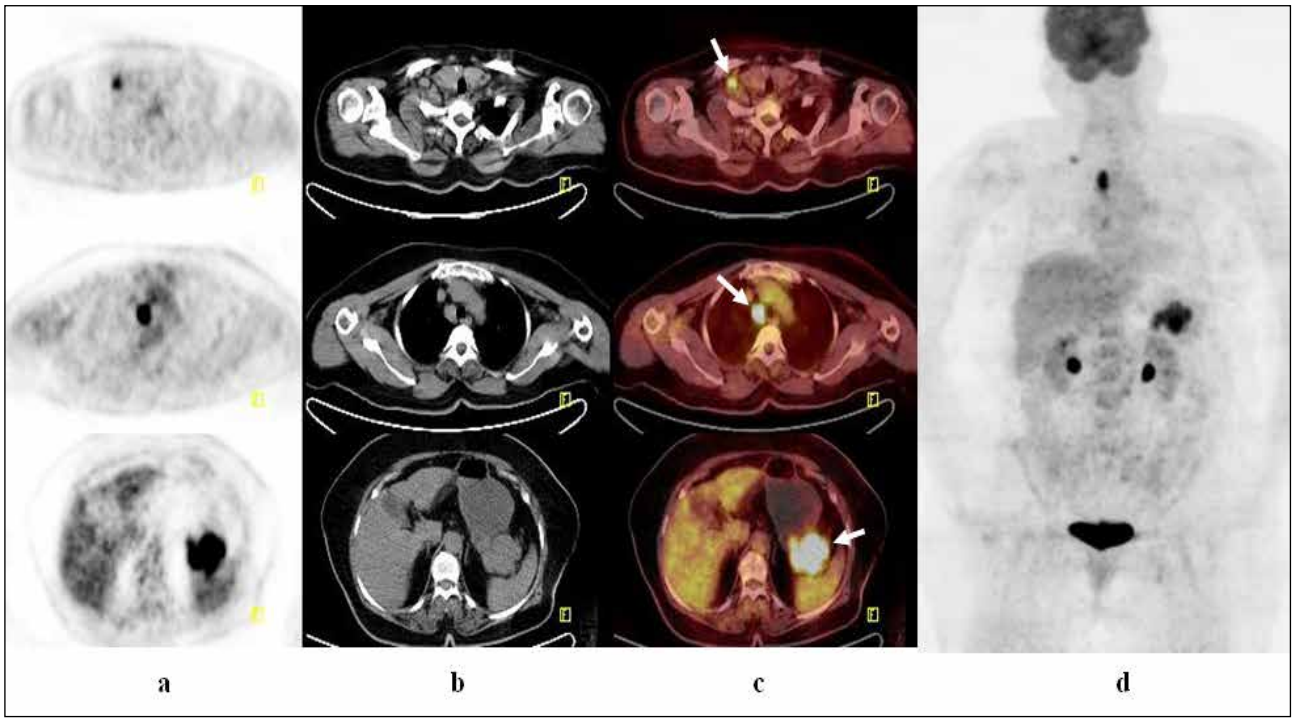


Figure 1. (a,b,c,d) F-18 FDG PET, CT, PET/CT fusion and PET MIP images in the patient with sarcoidosis

mass in splenic hilus (SUVmax: 13,08) showing increased F-18 FDG uptake (white arrows).

Discussion

Sarcoidosis is a chronic multisystem granulomatous disease. It may affect many system, but most commonly presents with thoracic involvement (4). The common presenting symptoms are dyspnea, cough, fever, weight loss, fatigue, and etc (4). In this case, presenting symtoms were cough and fever. Many organs such as skin, eye, bone, liver, spleen, heart, brain, respiratory system, etc. may be affected. The diagnosis is based on the clinical features, radiological findings and noncaseating granulomas shown at histopathologic examination (4). F-18 FDG PET has been proven usefull in detected occult sites of disease in many of the patients (5).

In pulmonary sarcoidosis, the lung parenchyma and mediastinal lymph nodes may be affected. CT appearance of the lung involvement can mimic lymphangitic carcinomatosis, lymphoid interstitial pneumonia, silicosis, and coal workers' pneumoconiosis (4). In our case, there were diffuse ground-glass opacity in both lungs and mediastinal lymph nodes on CT scan.

F-18 FDG PET is valuable for assessment of disease activity, thus plays important role in guiding therapeutic intervention and follow-up of the efficacy of medical treatment in sarcoidosis (4). In active period, there is increased F-18-FDG uptake due to inflammatory and granulomatous processes in lesions. It has been suggested that intensity of F-18-FDG uptake may reflect activity of the disease (2,6). In our case, diffuse ground-glass opacity in both lungs and some of lymphadenopaties did not show F-18-FDG uptake, whereas right supraclavicular region (SUVmax: 5,80), several mediastinal lymph nodes (SUVmax: 12,86 and 5,11), conglomerate lymph node mass in splenic hilus (SUVmax: 13,08) and several paraaortic lymph nodes at level of the second lumbar vertebra (SUVmax: 5,71) demonstrated increased F-18-FDG accumulation. Jain et al. have shown resolution or decrease in the uptake of F-18 FDG after treatment with steroids on repeat F-18 FDG PET scannings (4).

To differentiate benign thoracic pathologies from malignant is difficult. Our case had a complaint of fever and cough for recent months, and contrast-enhanced CT had revealed mediastinal lymadenopathies and diffuse ground-glass opacity in both lungs. Based on these findings, F-18 FDG PET/CT was decided to identify a possible malignancy. On detecting lymph nodes showing increased F-18 FDG uptake in right supraclavicular, mediastinal, splenic and abdominal paraaortic

regions; we also thought likelihood of lymphoma for diagnosis (7). Because, both sarcoidosis and lymphoma affect lymphoid system in the body, and these two disorders may not be differentiated on F-18 FDG PET scanning (8). However, histopathologic examination revealed noncaseating granulomatous reaction. Finally the patient was diagnosed with sarcoidosis. F-18 FDG avidity in benign conditions such as inflammatory and infectious processes should be kept in mind during assessing the F-18 FDG PET/CT scan in cancer investigation.

Corresponding Author
Zeki Dostbil,
Dicle Üniversitesi Tıp Fakültesi,
Nükleer Tıp Anabilim Dalı,
Diyarbakır,
Turkey,
E-mail: zekidostbil@yahoo.com

References

1. *Chang JM, Lee HJ, Goo JM, Lee HY, Lee JJ, Chung JK, Im JG. False positive and false negative FDG-PET scans in various thoracic diseases. Korean J Radiol. 2006; 7(1): 57-69.*

2. *Kostakoglu L, Agress H, Goldsmith SJ. Clinical role of FDG PET in evalutaion of cancer patients. RadioGraphics. 2003; 23: 315-340.*

3. *Almuhaideb A, Syed R, Iordanidou L, Saad Z, Bomanji J. Fluorine-18-fluorodeoxyglucose PET/CT rare finding of a unique multiorgan involvement of Wegener's granulomatosis. Br J Radiol. 2011; 84(1006): 202-4.*

4. *Jain V, Hasselquist S, Delaney MD. PET scanning in sarcoidosis. Ann N Y Acad Sci. 2011; 1228: 46-58.*

5. *Teirstein AS, Machac J, Almeida O, Lu P, Padilla ML, Iannuzzi MC. Results of 188 whole-body fluorodeoxyglucose positron emission tomography scans in 137 patients with sarcoidosis. Chest. 2007; 132(6): 1949-1953.*

6. *Brudin LH, Valind SO, Rhodes CG, Pantin CF, Sweatman M, Jones T, et al. Fluorine-18 deoxyglucose uptake in sarcoidosis measured with positron emission tomography. Eur J Nucl Med. 1994; 21: 297-305.*

7. *Juweid ME. FDG-PET/CT in lymphoma. Methods Mol Biol. 2011; 727: 1-19.*

8. *Kara PÖ, Kara T, Gedik GK, Sarı O, İsmailoğlu M. Pulmoner Sarkoidozlu Bir Hastanın F-18 FDG PET/BT Görüntülemesi. ACU Sağlık Bil Derg. 2011; 4(2): 228-230.*

Importance of adenosine deaminase in rheumatoid arthritis diagnosis and therapeutic effect of applied methotrexate

Nela Zivkovic[1], Boris Djindjic[2], Aleksandar Dimic[3], Jelena Aleksandric[4], Svetlana Milovanovic[4]

[1] Faculty of medicine, University in Nis, Clinic for Endocrinology, Diabetes, and Metabolic Disorders, Serbia,
[2] Faculty of medicine, University in Nis, Institute for Prevention, Treatment and Rehabilitation of Rheumatic and Cardio-vascular Patients "Niska Banja", Serbia,
[3] Faculty of medicine, University in Nis, Serbia,
[5] High Medical School of Profesional Studieses, Cuprija, Serbia.

Abstract

Diagnosis of rheumatoid arthritis (RA) requires detailed clinical examination of the patient, radiological and laboratory analyses. Enzyme adenosine deaminase (ADA) is one of important components for initiation of cell-mediated immune response and observed separately or in a group of test results of the patients with rheumatoid arthritis, which can help diagnosing the disease.

The aim of this research was to determine the importance of adenosine deaminase in early diagnosing of rheumatoid arthritis, and to analyze the influence of methotrexate therapy on catalytic activity of adenosine deaminase with patients in early and late stage of rheumatoid arthritis.

This analysis included 120 patients, 90 of which were patients with rheumatoid arthritis and 30 with degenerative disorder. Within the group of patients with RA, in 30 patients the symptoms appeared in the period of less than one year (early stage of RA), while 60 patients had RA diagnosed for more than one year (late stage of RA). Along with anamnesis and clinical examination (examining the number of tender joints, number of swollen joints and duration of morning stiffness), in all patients laboratory test results were performed (erythrocyte sedimentation in the first hour, hemoglobin, number of red blood cells, number of platelets, rheumatoid factor and C-reactive protein) and enzyme adenosine deaminase was determined.

Values of ADA in control group were significantly lower than in the group of patients with RA ($p<0.001$), where the values of ADA in the group with the early stage of RA were significantly higher than in the group of patients with the late stage of RA ($p<0.001$). There was no significant difference in values of laboratory test results between the group of patients treated with methotrexate (MTX) and the group of patients who did not receive the therapy. However, the level of ADA was significantly lower ($p<0,001$) in patients treated with MTX, both in early and late stages of RA, compared to the patients who did not receive MTX therapy. ADA is enzyme which can be used for diagnosing RA as well as in monitoring the effects of the MTX therapy which leads to reduction of ADA level in these patients, and therefore reduces inflammation.

Key words: Adenosine deaminase, rheumatoid arthritis

Introduction

Rheumatoid arthritis (RA) is inflammatory systemic disease which causes joint damage and loss of the ability to perform everyday activities. This disease appears more often in women than in men, with prevalence of 1% (1). Pathogenesis of RA consists of a sequence of immune and inflammatory reactions where local and systemic effects of inflammation appear through large number of biochemical markers which are, directly or indirectly, included in the progress of this disease (2). Standard laboratory test results of disease progress, sedimentation (SE), C-reactive protein (CRP) and rheumatoid factor (RF) are often used in laboratory analyses, but there is a need for introduction of new parameters which will, in more reliable and faster manner represent the progress of RA.

Adenosine deaminase (ADA) is enzyme included in catabolism of purine bases as well as in

converting adenosine in inosine. Main role of this atypical serine protease is based on preventing the inhibition of T-cell proliferation through adenosine. In many inflammatory and autoimmune diseases, where the immune status is modified, there is a change in catalytic activity of ADA in the serum as cell immunity marker. Previous research imply that ADA is one of important components for initiation of cell-mediated immune response and observed separately or in a group of test results of the patients with rheumatoid arthritis, can be helpful in diagnosing the disease (2). Recently, significant results in the field of drug therapy of RA have been achieved, where the golden standard represents the application of methotrexate (MTX). Low doses of MTX in treatment of this disease were introduced in 1985, and for its proven efficiency, acceptable reliability and low price (3), MTX has become first choice in RA therapy, therefore today MTX is, most often, the first disease-modifying drug prescribed to the patient (4). After absorption, 10% of this drug is converted in 7-hydroxy MTX in the liver, and afterwards both are excreted through kidneys (5,6,7). Several pharmacological mechanisms of MTX effects are explained, including anti inflammation effect mediated by stimulating adenosine receptors (8,9). Namely, MTX causes reduction of ADA level in three ways: first, MTX can directly inhibit ADA, second, MTX inhibits ADA indirectly through aminoimidazole carboxamide ribose-5-phosphate (AICAR) and its metabolites, and third- ADA can be inhibited indirectly to compensate the adenosine reduction. Reduction of ADA causes increase in adenosine level and consequent anti inflammation effect (9).

The aim of research was to determine the importance of adenosine deaminase in early diagnosing rheumatoid arthritis and to analyze the effect of methotrexate therapy on catalytic activity of adenosine deaminase in patients with early and late stage of rheumatoid arthritis.

Methods

Research included 120 patients who were treated at the Clinic for Rheumatology of Institute for Prevention, Treatment and Rehabilitation of Rheumatic and Cardio-vascular Patients in Niska Banja.

The research included two groups of patients:

I group- included 90 patients of both sexes with rheumatoid arthritis. The diagnosis was based on ARA classification (American Rheumatism Association) from 1987. The criteria include: morning stiffness, arthritis in 3 or more joint areas, hand arthritis, symmetrical arthritis, rheumatoid nodules, positive rheumatoid factor and radiologic changes. RA is diagnosed when 4 out of 7 criteria are present, where changes given in criteria 1 to 4 have to prevail for at least 6 weeks.

This group of patients is divided into two subgroups:

- Ia sub-group includes patients with early stage of rheumatoid arthritis (30 patients) – with the symptoms duration less than one year
- IIa sub-group includes patients with late stage of disease (60 patients) with the symptoms prevailing for more than one year
- II group (control group) - includes 30 patients with degenerative spinal disorders (cervical syndrome, lumbal syndrome, or both) without clinical and laboratory test results of rheumatoid arthritis presence.

Patients with chronic inflammatory diseases (connective tissue diseases, other systemic diseases), chronic respiratory, cardiac and renal insufficiency, serious acute diseases, and other related diseases which could modify inflammatory response are excluded from this analysis.

Methods of approach included prospective analysis of anamnesis, clinical and laboratory test results. Age, sex, and duration of disease of all patients are recorded. Clinical examination which includes determination of number of tender joints, swollen joints and duration of morning stiffness in minutes was performed. In all patients, blood for laboratory analysis was obtained from cubital vein early in the morning before breakfast (12 hours period without food) into heparinized vacuum tubes. Blood is processed in general laboratory using standard methods and samples for ADA determination are stored in temperature of +2°C until conducting the analysis.

From blood samples, using standard methods, following results are determined:

- blood test parameters (hemoglobin-Hb, red blood cells-RBC, platelets-Plt, white blood

cells-WBC) in auto analyzer for blood test Haematolog
- erythrocyte sedimentation rate – in the first hour Westergreen method
- C-reactive protein - Latex method with normal value up to 6mg/l
- rheumatoid factor - Latex method with normal up to 20ij/l

Determination methods of adenosine deaminase:

Blood serums are used for examination of catalytic activity of ADA. The serums were acquired through processing blood samples taken from the patients according to the request of the specialist. Peripheral blood was obtained by venipuncture and the serum was separated from blood in centrifugal pump at 3500 rpm in duration of 15 minutes. Obtained serum samples were transported to laboratory of Polyclinic "Human" where the activity of this enzyme was determined. The enzyme is stable for 7 day on temperature from 2 to 4 °C, so container for transport of medical material was used to transport the serum from the Institute to the Polyclinic. Serum samples were transported in micro tubes in volume of 1 ml.

Overall activity of adenosine deaminase in the serum was determined on temperature of 37°C with adenosine as substrate. This method is based on Berthelot reaction, that is, appearance of colored indofenol complex from ammonium which was released from adenosine, quantified by spectrophotometer at 550nm. One ADA unit is defined as the quantity of enzymes necessary for release of 1μmol/min of ammonium from adenosine in standard test conditions. Adenosine deaminase activity is expressed in units per liter.

Statistics

Obtained results are expressed as mean value ± SD. For testing the statistical significance of results Student's t-test and ANOVA test were used. Values of alpha $p<0.05$ were considered as significant. Statistical analysis was performed in programs Excel 7.0 and SPSS 11.0 in Windows 98 operating system, and the results are presented in tables and graphs.

Results

Total number of observed patients was 120, 90 of which were diagnosed with RA and 30 patients were in control group. Thirty patients were in early stage of RA while 60 other patients had late stage of RA. Age and sex ratio of patients in observed groups are presented in Table 1.

Results of statistical analysis indicate that the patients with late stage of RA were significantly older than patients in control group ($p<0.01$). This difference was not observed between patients in early stage of RA and control group. In all groups, women dominated therefore the results indicate existence of sex distribution in observed groups.

Study results indicate that the values of morning stiffness, number of tender joints and number of swollen joints in control group were significantly lower than the values in groups with RA. Furthermore, there was no significant difference in values between the group with early stage of RA and the group with late stage of RA (Table 2). Values of ADA were significantly different in observed groups. Post Hoc analysis indicates that the values of ADA in control group was significantly lower than the values in the groups of patients with RA ($p<0.001$), where the values of ADA in the group with late stage of RA were significantly lower than the values in the group with early stage of RA ($p<0.001$) (Table 3). Results of statistical analysis do not indicate significant difference in laboratory tests between patients receiving MTX therapy and patients who were not treated with MTX. However, the level of ADA was significantly lower ($p<0,001$)

Table 1. General characteristics of patients

Group	Number of patients	female (n / %)	male (n / %)	age (years)
late stage of RA	60	54 / 90%	6 / 10%	59.81±
early stage of RA	30	22 / 73.3%	8 /26.6%	56.86±
control group	30	20 / 66.6%	10 /33.3%	49.86±
total	120	96 / 80%	24 / 20%	57.61±

*Data are presented as n/% or mean±SD; **p<0.01 vs. control group; RA- rheumatoid arthritis*

in patients who received MTX, both in early and late stage of RA, compared to patients who were not treated with MTX. Moreover, values of ADA were significantly higher (p<0,001) in patients in early stage of RA who received MTX therapy and who did not, compared to patients with late stage of RA and who received MTX therapy (Table 4).

Discussion

Revised ACR criteria from 1987 are also used nowadays to diagnose RA. However, occasionally difficulties appear in early diagnosing and differential diagnosing RA and other auto immune diseases of connective tissue, impose the need for determination of new markers which would be useful for early diagnosing of the disease as well as in monitoring the efficiency of applied drug in therapy. Inflammation is initial process in RA progress. Persistent inflammation is typical where primary caught peripheral joints become swollen, painful and stiff. The number of tender joints, swollen joints and morning stiffness was significantly larger in patients with RA than in patients with degenerative disorder (Table 2). These results are expected, since morning stiffness longer than 1 hour is diagnostic criteria for RA, and that tender and swollen joints are characteristics of inflammatory diseases such as RA but not for degenerative disorders.

Observed laboratory test results were within normal range and there were no deviations within the groups. The only difference marked was at the level of catalytic activity of ADA between the groups. The majority of researches accentuate the importance of RF and CRP in diagnosing RA (10,11). In this analysis no significant difference in RF between the patients with early stage and late stage of RA was found, which is in accordance with the research conducted by Radunovic et al. who concluded that although positive RF is specific for RA, its presence in other systemic connective tissue disorders not accompanied with arthritis, as well as in chronic infectious diseases, causes doubt in importance of the role of these antibodies for RA (12). Surekha R et al. pointed out the importance of ADA as serum marker compared to traditional CRP and this is in accordance with our results which do not indicate variations at the level of CRP in the groups, while the level of ADA is significantly different (13). Group of researchers (14) observed the levels of both forms of ADA (ADA1 and ADA2) and concluded that serum levels of these isoforms are in good correlation with RA and that this non invasive examination method can be used as biochemical marker of inflammation, as well as that it may surpass standard laboratory parameters of CRP and SE.

During this analysis, statistically important higher values of ADA were registered in patients

Table 2. Clinical results characteristics of patients

Group	Morning stiffness (min)	Number of tender joints	Number of swollen joints
late stage of RA	39.41±	10.6±	2.27±
early stage of RA	20.17±	11.79±	2.97±
control group	3.93±	1.07±	-
total	29.07±	9.67±	2.16±

*Data are presented as mean±SD; *p<0.05 vs. late stage of RA and early stage of RA; RA- rheumatoid arthritis,*

Table 3. Values of ADA in observed groups of patients

	N	ADA (U/L)	95% Confidence Interval forMean	Minimum	Maximum
Late stage of RA	60	13.05±	11.33-14.76	6.00	32.09
Early stage of RA	30	20.42±	18.35-22.49	10.10	30.27
Control group	30	6.19±	5.25-7.13	4.12	9.54
Total	120	14.20±	12.76-15.65	4.12	32.09

*Analysis of variance (F=30.63, p<0.001), Post Hoc-***p<0.001 vs. other groups; RA- rheumatoid arthritis, ADA- adenosine deaminase*

with RA than in control group. Moreover, the level of ADA proved to be significantly higher in early stage than in late stage of the disease. Mean value of ADA in the group of patients in late stage of RA was 13.05±6.58 U/L, in the group of patients with early stage of RA the value of analyzed enzyme was 20.42±5.43, while in the control group the value was 6.191.62. In the majority of previous analyses, the results showed higher values of ADA, thus one group of authors (2) pointed out that in patients with RA the value of ADA was 26.67±8.74 and in the control group - 19.79±5.63. Surekha R et al. (13) also presented high levels of ADA in patients with RA - 59.79±21.09 and in control group the value was 20.71±5.63. This discrepancy in the level of obtained enzyme can be explained by different methods of enzyme analysis, as well as the transport of obtained serum from the Institute laboratory where blood was extracted to the laboratory where ADA was determined, along with the fact that the enzyme is unstable at temperature above 4°C. Beside the discrepancy at the level of enzyme, this analysis confirms the results of mentioned analyses (2,13) which claim that catalytic activity of ADA in serum is higher in the patients with RA. Contrary to our results, Nalesnik et al. (15) obtained almost the same results of values of ADA in patients with RA and control group. Similar results were presented in another research (16), the values of ADA in serum of the patients with RA, osteoarthritis and reactive arthritis were not significantly different, but it stressed the importance of extracting enzyme from synovial fluid of the joint.

There is not enough information from literature about ADA activity in early and late stage of arthritis. Research indicates that the level of this enzyme is higher at the beginning of the disease than in the later stages (Table 3), which points to potential importance of ADA in diagnosis.

It is known that reduction of local concentration of adenosine using ADA contributes joint inflammation in RA. MTX, as one of the most effective anti rheumatic drugs, among other things, increases concentration extracellular adenosine at the inflammation area (17,18). Results of this analysis confirm the fact that, in patients with RA who are receiving MTX therapy, the level of ADA is significantly lower than in the patients who are not treated with MTX (Table 4). These results are in accordance with the mechanism of action of MTX through adenosine metabolism, that is, ADA inhibition. Similar results are presented in Riksen et al. (19) research, where it was pointed out that MTX inhibits deamination of adenosine and vasodilatation is induced by adenosine. One group of researchers (15) also presented significant difference between the levels of ADA in patients with RA treated with MTX and in patients who did not receive MTX in their therapy. Early diagnosis of RA is extremely important for starting early, aggressive therapy, in order to prevent the progress of disease, joint damage and therefore lower the rate of functional ability reduction. Despite deca-

Table 4. Values of ADA and analyzed results in RA patients receiving MTX therapy

	I group (late stage of RA)		**II group (early stage of RA)**	
	With MTX	**Without MTX**	**With MTX**	**Without MTX**
	n=39	**n=21**	**n=17**	**n=13**
ADA(U/L)	8.95±2.31 b	21.03±4.49 a	17.55±4.02	24.49±4.55 a
SE (mm/h)	31.41±20.70	27.05±19.22	33.76±24.94	38.75±32.43
Hb (g/L)	130.03±10.03	133.03±15.01	133.00±14.95	131.58±10.75
RBC (T/L)	4.37±0.43	4.42±0.42	4.43±0.49	4.46±0.45
Plt (G/L)	275.00±82.86	268.15±72.17	278.00±56.57	298.17±94.93
WBC (G/L)	7.31±2.08	6.67±2.87	7.71±1.72	7.24±1.95
RF (ij/l)	88.62±131.00	64.80±139.53	57.88±131.19	64.00±149.47
CRP (mg/l)	27.08±52.57	19.20±50.22	22.59±40.00	53.98±76.12

Data are presented as mean±SD; [a]p<0.001 vs. with MTX; [b]p<0.001 vs. II group; RA- rheumatoid arthritis, ADA- adenosine deaminase, SE- erythrocyte sedimentation, Hb- hemoglobin, RBC- red blood cells, Plt- platelets, RF- rheumatoid factor, CRP- C-reactive protein, MTX- methotrexate

dal researching, no unique disease marker was found to be a satisfying criterion for RA diagnosis. ADA represents one of the disease markers which can be helpful in early disease screening. After introduction of MTX in the treatment of patients with RA, ADA acquires another very important role in monitoring the effects of applied drug.

Conclusion

Obtained results imply that ADA is the enzyme useful in diagnosing RA as well as monitoring the effects of MTX therapy which reduces level of ADA in these patients, and therefore, leads to reduction of inflammation.

Reference

1. *Scott DL. Early rheumatoid arthritis. British Medical Bulletin 2007; 81: 97-114.*
2. *Pallinti V, Ganesan N, Anbazhagan M and Rajasekhar G. Serum biochemical markers in rheumatoid arthritis. Indian J Biochem Biophys. 2009; 46(4): 342-344.*
3. *Cronstein BN, Naime D and Ostad E. The antiinflammatory mechanism of methotrexate. J Clin Invest 1993; 92: 2675-2682.*
4. *American College of Rheumatology Subcommittee on Rheumatoid Arthritis Guidelines. Guidelines for the menagement of rheumatoid arthritis: 2002 update. Arthritis Rheum 2002; 46: 328-346.*
5. *Cronstein BN. Going with the flow: methotrexate, adenosine, and blood flow. Ann Rheum Dis 2006; 65: 421-422.*
6. *Tian HT and Cronstein BN. Understanding the mechanisms of action of methotrexate. Bull NYU Hosp Jt Dis 2007; 65(3):168-173.*
7. *Swierkot J and Szechinski J. Methotrexate in rheumatoid arthritis. Pharmacol Rep 2006; 58: 473-492.*
8. *Van Ede AE, Laan RFJM, De Abreu RA, Stegeman ABJ, Van de Pute LBA. Purine enzimes in patients with rheumatoid arthritis treated with methotrexate. Ann Rheum Dis 2002; 61: 1060-1064.*
9. *Cronstein BN. Low-dose methotrexate: A mainstay in the treatment of rheumatoid arthritis. Pharmacol Rev 2005; 57: 163-172.*
10. *Machold KP, Stamm TA, Nell VPK, Pflugbeil S, Aletaha D, Steiner G et al. Very recent onset rheumatoid arthritis: clinical and serological patient characteristics associated with radiographic progression over the first years of disease. Rheumatology 2007; 46(2): 342-349.*
11. *Westwood OMR, Nelson PN and Hay FC. Rheumatoid factors: What's new? Rheumatology 2006; 45: 379-385.*
12. *Radunovic G, Mircetic V i Bukilica M. Rheumatoid factors in diagnosis of rheumatic diseases. Balneoclim 2002; 26(1): 143-152.*
13. *Surekha RH, Madhavi G, Srikanth BMV, Jharna P, Rao URK and Jyothy. Serum ADA and C-reactive protein in rheumatoid arthritis. Int J Hum Genet 2006; 6(3): 195-198.*
14. *Sari RA, Taysi S, Yilmaz O and Bakan N. Correlation of serum levels of adenosine deaminase activity and its isoenzimes with disease activity in rheumatoid arthritis. Clin Exp Rheumatol 2003; 21(1): 87-90.*
15. *Nalesnik M, Mehanovic-Nikolic J, Jandric S. Adenosine deaminase and C-reactive protein in diagnosing and monitoring of rheumatoid arthritis. Med Glas Ljek komore Zenicko-Doboj kantona 2011; 8(1): 163-168.*
16. *Yuksel H, Akoglu TF. Serum and synovial fluid adenosine deaminase activity in patients with rheumatoid arthritis, osteoarthritis and reactive arthritis. Ann Rheum Dis 1988; 47: 492-495.*
17. *Mehanovic-Nikolic J, Lalos-Miljus J, Stajcic-Nalesnik M, Lakic LJ, Bobic Z et al. The diagnostic value of anti-cyclic citrullinated peptide antibodies, adenosine deaminase activity and other potential biomarkers for predicting and monitoring rheumatoid arthritis. JMB 2008; 27(3): 383-388.*
18. *Nakamachi Y, Koshiba M, Nakazawa T, Hatachi S, Saura R, kurosaka M et al. Specific increase in enzimatic activity of adenosine deaminase 1 in rheumatoid synovial fibroblasts. Arthritis Rheum 2003; 48(3): 668-674.*
19. *Riksen NP, Barrera P, Van den Broek PHH, Van Riel PLCM, Smits P et al. Methotrexate modulates the kinetics of adenosine in humans in vivo. Ann Rheum Dis 2006; 65: 465-470.*

Corresponding Author
Nela Zivkovic,
Faculty of medicine,
University in Nis,
Serbia,
E-mail: nela77@open.telekom.rs

Hormonal changes in hirsute women

Besa Gacaferri-Lumezi [1], Natyra Karahoda Gjurgjeala, Violeta Lokaj- Berisha[1], Hatixhe Latifi-Pupovci[1], Ganimete Minci-Bejtu llahu [1]

[1] Department of Physiology and Immunology, Medical Faculty, University of Prishtina, Kosovo

Abstract

Background: Hirsutism is defined as the excessive growth in androgen-sensitive regions.

It usually due to increased androgen production from ovaries or adrenal gland. Idiopathic form is not associated with androgen excess.

Aim of this study was to evaluate women with hirsutism, report the hormone levels in women with hirsutism and correlation with Ferriman-Gallwey score.

Materials and Methods: Prospective study included 66 women with hirsutism and 30 women as control group age of 15-45 years. We measured the levels of hormones with RIA/IRMA methods.

Results: in Laboratory of Endocrinology, Department of Physiology and Immunology, 66 patients with hirsutism were analyzed. The mean age was 20-24 years (37,9%). About 77,3% of patient have positive family history. Amenorrhea was present in 7,6%, dismenorrhea in 13,6%, oligomenorrhea in 48,5% , Galactorrhea was present in 6,1%. The muscular distribution was chainged in 10,6% of patients, hair recession was present in 9,1%. Oily skin was present in 48,5%, acne in 39,4%. There was correlation between oily skin and presence of acne. 25 patients was married, 60% of them infertile. The emotions described like sadness 42,4%, frustration 27,3%, anxiety 24,2 %, indifference 6,1%. Associated disorders had 4 women (6,1%), 1 with diabetes mellitus, 1 with epilepsy and 2 with obesity.

Ferriman-Gallwey score was 9-13 in 51% of patients. Testosterone level was elevated in 16,7% of patients, 17-0H-progesterone was elevated in 6.1%, DHEAS in 9.1%. Gynecology ultrasound was irregular in 18,2% of patients. Prolactinemy was present in 13,6%. PCOS had 10.6% and CAH was present in 6,1% , the other had idiopathic hirsutism.

Conclusion: Hirsutism is symptom rather then disease. It can appeared as the single symptom or it can be a symptom of many other disorders.

Key words: hirsutism, Ferriman-Gallwey score, hormone levels.

Introduction

Hirsutism is defined as the excessive growth in androgen-sensitive regions. (1)To many women, hirsutism is a manifestation of excess androgens. Androgens promote growth and increase thickness of terminal hairs in androgen sensitive regions. Women with androgen sensitive hirsutism are exposed to excess androgens or have higher sensitivity of the receptor to normal levels of androgens. In other cases hirsutism is independent of androgens abnormalities and has genetic characteristics or is caused by medications. Hirsutism affects 2-10% of women aged 18-45 years. Therefore it can be a source of emotional disorders and a sign of significant health disorders.

Hirsutism develops when follicles in androgen sensitive areas begin to thick and dense, pigments terminal hairs compared to vellus non pigmented thin hairs normally found in females in these areas. (1,2) There are different ways of scoring to determine hirsutism and to standardize diagnosis and to evaluate different options of treating the disease. One of the most popular systems is the Ferriman-Gallwey score.(2,3)

Materials and Methods

Patients

Prospective study included 66 women aged 15-45 years, in Laboratory of Endocrinology, Department of Physiology and Immunology, were analyzed for this purpose and 30 health women as a control group. The women checked in because of hair growth in the androgen sensitive areas, menstrual irregularity or infertility.

Clinical evaluation

Evaluation of hirsutism was done according to Ferriman-Gallwey score, grading 11 androgens sensitive parts (upper lip, chin, chest, hand, arm, tight, leg, upper part of back, lower part of back, upper part of abdomen, lower part of abdomen). Grading was done starting with the value 0 (total absence of terminal hair) up to 4 (extended presence of the terminal hair). The value 8 or above 8 is considered as hirsutism.

Laboratory assays and other investigations

Hormones were determined with RIA (Radioimmunoessay) and IRMA (Immunoradiometric assay) methods, in the Laboratory of Endocrinology, Department of Physiology and Immunology , UCCK, Prishtina. Used substances were produced by IMMUNOTECH Company (France).

The levels of serum FSH, LH, estradiole, progesterone, prolactine, cortisole, were measured three time within period (folicular phase, middle phase and luteal phase). The level of testosterone , 17-OH progesterone and DHEAS is measured only once, within period (at the middle of the period). Pelvic ultrasound for ovaries and adrenals were carried in all the patients, X-ray skull, abdominal Magnetic Resonance and abdominal CT were carried out in selected patients only.

Statistical analysis

The collected data were stored in a specially database . Statistical processing was done with Excel Statistic Analyses. Numerical data was presented as index of structure, arithmetic mean, mean +_ SD, as median number (%), standard deviation. To test the hypothesis between the groups, t-test , Mann-Whitney test and Fisher exact test with significant level of $p<0.05$ and $p<0.01$ were used.

Results

Evaluation of hirsutism was done according to Ferriman- Gallwey score, grading 11 androgen sensitive areas. 97% of the examined patients had terminal hair over the upper lip; on chin 90,9%; chest 89,4%; leg 98,5%, thigh 97%; hand 92,9%; arms 31,8%; upper back 6,1%, lower back 24,2% upper abdomen 25,8% and lower abdomen 72,2%.

Score level 1 was mostly found in chest in 60, 6 % of the cases, in lower part of the abdomen 43,9%, in thighs 31,8% and on arms 27,3%. Grading level 4 was found in 2 women on the chin, 7 women on the legs, and on thighs and hands in 3 women or 4,5% of all cases with hirsutsim.

Examined women were diagnosed with hirsutism if the overall grading according to Ferriman-Gallwey score was = 8 or >8. More than half of women that, is 51,5% had the overall grading 9-13, then 31,8% had grading 14-18, 15,2% had grading 19-23 and 1,5% had grading 24-28.

Hormonal changes in large number of women with hirsutism causes also the appearance of acnes in different parts of the body. In our clinical sample 26 women or 39,4% had acne.

32 (or 48,5%) of women with hirsutism had oily skin . We have found that in most cases there is a connection between oily skin and the 24 (or 75%.0%) had acne, wile from the group that didn't have oily skin only 2 (or 5,9%) had acnes. The probability that acne will appear in women with oily skin is 48 times higher than of those with non-oily skin (OR=48.0, 95% CI= 9.33-246.9).

We have obtained the difference with a high statistical significance (p=0.0024) in appearance of acnes according to the age group. Out of 35 women with hirsutism under the age of 25,20 (or 57.1%) had acne, while out of 31 women of age 25 have 5,5 times more chances to get acne than women over the age 25 who also have hirsutism. There is a 95% of certainty that all women with hirsutism over the age of 25 are 1,8 times to 16,9 times grater risk to have acne than those over the age of 25(OR=5.556, 96% ci.822-16.938). In our clinical sample 39.4% of women had acne on face or other parts of the body. 27.3% had acne only on face; face and back 6.1%; face and other parts of the body 1.5%. Thus all women that had acne, they had them at least on the face; 7.6% of them had acne on the back and 6.1% had acne on the face, and on the other parts of the body.

In order to investigate the connection between the hirsutism and level of hormones , the investigation included 66 women with hirsutism and 30 women without hirsutism, as control group. The average age of the women with hirsutism was 25.8

Table 1. Correlation between oily skin and acne

Oily skin		Acne				Total	
		Yes		No			
	N	%	N	N	N	%	
Yes	N	24	92.3	8	20.0	32	48.5
	%	75.0	-	25.0	-	100.0	-
No	N	2	7.7	32	80.0	34	51.5
	%	5.9	-	94.1	-	100.0	-
Total	**N**	**26**	**100.0**	**40**	**100.0**	**66**	**100.0**
	%	**39.4**	**-**	**60.6**	**-**	**100.0**	**-**
Fisher-test		p=0.00001				S	
OR 95% CI		48.0 9.33 - 246.9					

years (SD=7.1, Age range15-45). The average age for the control group was 27,2 years (SD=6.5, age range 19-41). With the t-test we didn't obtain any significant difference (t-test=0.9107. p>0.05) related to the age group for both groups, therefore they could be compared.The level of testosterone is measured only once , within period (at the middle of the period) (tab.2). Testosterone in the group women with hirsutism had abnormal level (increased) in 16.7% of cases, while it was within normal range (within reference values) in 83.3% of the cases. In control group , in all the cases the level was within the normal range. Average level of testosterone of both groups: in the group with hirsutism average level was 2.5nmol/L (SD=2.2 nmol/L); in the control group average level was 1.5 nmol/L (SD= 0.6nmol/L) and with t-test we have obtain a difference with important statistical significance . (t-test = 2.442, p<0.03). Regarding the correlation between the values of the testosterone hormone and the level of hirsutism according to the Ferriman-Gallwey score, we have noticed that correlation is medium and quotient of determination R2 =0.0518 shows that in 5.18% the level of testosterone hormone could influence the overall grading. 4 women (6,1 %) had elevated 17-OH-progesterone level and 6 (9,1%) had elevated levels of DHEAS. Tab. 3, 4. 1 women (1,5%) had elevated FSH in follicular phase, and 3 women (4,5%) in luteal phase. In follicular phase LH was increased in 10 women (15,2%) was elevated, but in middle phase just one (1,5%). Serum prolactine was elevated in 10 women (15,2%) in middle of cycle. Anovulation was present in 23 women (34.8%). PCOS had 7 women (10.6%) with oligomenorrhea, high FSH:LH ratio, without ovulation, increased testosterone, high estrogen levels. CAH was present in 6,1%, the other had idiopathic hirsutism.

Discussion

Increased production of androgens is found in 10-20% of women in fertile age. Increased level of androgens could be ovarian and adrenal origin but also as a consequence of increased level of free androgens that are not connected to the transporting protein (SHBG), increased activity of enzymes (5-alfa reductase) in pilosebaceale unit, increased production of Dehidrotestosterone (DHT) biologically active, increased sensitivity of pilosebaceale unit in DHT. (1,2,,4,5,6,7).

Table 2. The testosterone levels in the middle of cycle

nmol/l	Group				Total	
	Experimental		Control			
	N	%	N	%	N	%
- 3.0	55	83.3	30	100.0	85	88.5
>3.0	11	16.7	-	-	11	11.5
Total	66	100.0	30	100.0	96	100.0
Mean ± SD	2.5 ± 2.2		1.5 ± 0.6		S	
T-test	t = 2.442 p= 0.0165					

Although by most of the women with hirsutism the increase of androgens in serum could be confirmed, quite often women with hirsutism have the level of androgens in normal range, that is an evidence of increased sensitivity of pilosebaceale unit towards androgens. Severe hisutism could be seen by discrete hyperandrogenemy and vice versa, severe increase of the level of androgens does not mean that it will result with hirsutism . This is explained with the fact that hirsutism was induced before with hyperandrogenemy, whereas now the level of androgens is normal, while the confirmation of the high level of androgens in absence of hirsutism may be a consequence of their episodic secretion. (8,9,10,11). Therefore this could explain that 16,7% of women with hirsutism have increased level of testosterone. With the t-test we have obtained difference with an important statistical significance between the group with hirsutism and the control group ($p<0.05$). At the least half of the women with the mild hirsutism (hirsutism from 8-15 according to Ferriman-Gallwey score) and regular period, have idiopathic conditions. (4,5,12,) Our results are similar, at least 51,1% of women with hirsutism have overall grading according to Ferriman-Gallwey score from 9-13, whereas 31.3% have regular menses. Historically this hirsutism in women is could idiopathic hirsutism, but this group includes also the cases with idiopathic hyperandrogenemy which includes the syndrome of polycystic ovaries, atypical and non-classic.(4,5,12,13,14) If the hirsutism is severe (the grade above15) it shows a secondary cause that is followed with the increased of androgens. In these cases ultrasound findings of ovaries and suprarenal glands helpful (and especially magnetic resonance and CT) in order to eliminate the existence of neoplasm (5,15,16,17,), as well as to detect polycystic ovaries.(18)In our study we have not found very high levels of testosterone

Table 3. Value of 17 - OH progesterone

17-OH progesterone (nmol/L)	Group				Total	
	Experimental		Control			
	N	%	N	%	N	%
<0.66 decreased	2	3.0	-	-	2	2.1
0.66-14.0 referent value	60	90.9	30	100.0	90	93.8
>14.0 increased	4	6.1	-	-	4	4.2
Total	**66**	**100.0**	**30**	**100.0**	**96**	**100.0**
Mean ± SD	4.8 ± 4.6		1.4 ± 0.6		S	
T-test	t = 4.021, p = 0.0001					

Table 4. Value of DHEAS

DHEAS (µmol/L)	Group				Total	
	Experimental		Control			
	N	%	N	%	N	%
<0.81 decrease	1	1.5	3	10.0	4	4.2
0.81-9.0 referent value	59	89.4	27	90.0	86	89.6
>9.0 increase	6	9.1	-	-	6	6.3
Total	**66**	**100.0**	**30**	**100.0**	**96**	**100.0**
Mean ± SD	4.6 ± 3.1		2.2 ± 1.0		S	
T-test	t=4.13, p=0.0001					

that could indicate the existence of tumors (values above 7nmol/L or 2.5 times above the upper limit are indications for the existence of tumors), (19) moreover investigations did not detect tumors of ovaries nor of suprarenal glands. If the female is affected by average hirsutism (Ferriman-Gallwey scale over 15) one should look for other signs such as irregular menstrual cycle, the oily skin, acne, hair loss, change of muscular distribution, deepening of voice etc. If we observe oligomenorrhea or amenorrhea in ultrasound, and increased levels of androgens, we can suspect PCOS. Infertility and obesity may exist. The number of women can be found polycystic ovaries without the presence other symptoms, except slight rise in the level of androgens. But in other cases an increase of the ovaries without the presence of cysts may be a form of PCOS. In other words, if women have symptoms and signs of PCOS, of course there are also changes in the ovaries which are not visible. (20, 21, 22, 23). With this may explain the small number of women with polycystic ovaries, but with a change in the level of androgens and the presence of other symptoms. On the other hand the values of testosterone may be normal in PCOS. Even oral contraceptives could decrease the level of testosterone and could hinder the interpretation (it could be good to measure the level of testosterone 3 months after interruption of oral contraceptives). (19, 24)

In conclusion we can say that hirsutism is symptom rather then disease. It can appear as the single symptom or it can be a symptom of many other disorders.

References

1. *Deplewski D, Rosenfield RL,. Role of hormones in pilosebaceus unit development. Endocr Rev 2000; 21: 363-92.*
2. *Ferriman D, Gallwey JD. Clinical assessment of body hair grouth in women.J Clin Endocrinol Metab 1961; 21: 1440-7.*
3. *Goodheart HP. Hirsutism. Women's health in Primary Care.2000; vol.3, 329-337.*
4. *Reingold SB, Rosenfield RL. The relationship of mild hirsutism or acne in women to androgens. Arch Dermatol 1987; 123: 209-212.*
5. *Rosenfield RL. Plasma testosterone binding globulin andodexes of concentration of unbound androgens in normal and hirsute subjects, J Clin Endocrinol Metab 1971; 32: 717-728.*
6. *Wild RA, Umstot ES, Andersen RN, Ranney GB, Givens JR. Androge parameters and their correlation with body weight in one hundred thirty-eight women thought to have hiperandrogenism. Am J Obstet Gynecol 1983: 146: 602-606.*
7. *Azziz R, Sanchez LA, Knochenhauer ES, et al. Androgen excess in women :experience with 1000 consecutive patiens. J Clin Endocrinol Metab 2004; 89: 2453-462.*
8. *Speroff, Glass RH, Kase/NG. Clinical gynecological endocrinology and infertility. 6th edition. Lippincott, William and Wilkins,1999.p. 523-56*
9. *Aydinlik S et al. Lomg-term of signs of androgenisation with a low dosed antiandrogen-estrogen combination. Clin. Trials J 1990; 27: 392-402.*
10. *Berking EW, Holma P, Pyorala T: Effect of oral contraceptive combinations containing Levonorestrel or Degestrel on serum proteins and androgen binding. Scan Clin Lab Invest 1981, 41, s, 663.*
11. *Prelevic G. Klinicka Reproduktivna Endokrinologija,1996; 43: 268-315.*
12. *Carmina E. Prevalence of idiopathic hirsutism. Eur J Endocrinol 1998; 139: 421-3.*
13. *Polson DW, Adams J, Wadsworth J, Franks S, Polycystic ovaries a common finding in normal women. Lnacet 1988; 870-872.*
14. *Glintborg D, Herman AP, Brugoard F, Hangarard J, Hagen C, Andersen M. Significantly higher adrenocorticotropin-stimulated cortisol and 17-hydroxyprogesterone levels in 337 consecutive, premenopausal, Caucasian, hirsute patients compared with healthy controls. JClin Endocrinol Metab 2005; 90: 1347-1353.*
15. *O'Driscol JB, Mamtora H, Higginson J, Pollock A, Kane J, Andertson DC. A prospective study of prevalence of clear-cut endocrine disorders and polycystic ovaries in 350 patiens presenting with hirsutism and androgenic alopecia. Clin Endocrinol (Oxf) 1994; 41: 231-6.*
16. *Lobo RA. Ovarian hyperandrogenism and androgen-producing tumors. Endocrinol Metab Clin North Am 1991; 20: 773-805.*
17. *Ehran DA, Rosenfield RL, Barns RB, Brigell DF, Sheikli Z. Detection of functional ovarian hyperandrogenism in women with androgen excess. N Engl J Med 1992'327-157-62.*

18. *Azziz R. Diagnostic criteria and long-term health risk related to polycycstic ovary syndrome. Fertil Steril 2004; 81: 19-25.*

19. *Derksen J, Nagesser SK, Mlinders AE, Haak HR, Van de Velsk CJ. Identification of virilizing adrenal tumors in hirsute women. N Engl J Med 1994; 331: 968-973.,*

20. *Polson DW, Adams J, Wadsworth J, Franks S Polycystic ovaries – a common finding in normal women. Lancet 1988; 870-872.*

21. *Mechanick J, Dunaif A. 1999. Hirsutism. Trends in endocrinology and metabolism. March/April: 185-188.*

22. *Dunaif A, Givens JR, Haseltine F, Merriam GR.1992. The polycystic ovary syndrome. Cambridge, Massachusetts: Blackwell Scientific.*

23. *Dunaif A. 1997 Insulin resistence and polycystic ovary syndrome mechanisms and implications for pathogenesis. Endocr Rev 1997; 18: 74-800.*

24. *Rosner W. The functions of corticosteroid binding globulin and sex hormone binding globuline :recent advances. Endocr Rev 1990; 11: 80-91.*

Corresponding Author
Besa Gacaferri Lumezi,
Department of Physiology and Immunology,
Medical Faculty,
University of Prishtina,
Kosovo,
E-mail: besa_gacaferri@yahoo.com

Ultrasound assessment of echo structure of the distal uterine segment (DUS) after prior Caesrean Section and subsequent delivery

Ejub Basic[1],Vesna Basic Cetkovic[2], Mirsad Selimovic[3], Admir Rama[1], Selma Begovic[1]

[1] Clinic for Gynaecology and Obstetrics, Clinical Center University of Sarajevo, Bosnia and Herzegovina,
[2] Institute for Transfusiology, Sarajevo, Bosnia and Herzegovina,
[3] Clinic for Urology, Clinical Center University of Sarajevo, Bosnia and Herzegovina.

Abstract

The objective of this scientific article is to determine the ultrasound technique appropriate as a base for determination of the echo structure of the distal uterine segment (DUS), as one of the criteria used to evaluate which pregnant patient priorly delivered by Caesarean Section is to be planned for spontaneous vaginal delivery. The prospective study was carried out and included 108 pregnant women who were priorly delivered by Ceasarean Section. The echo structure of distal uterine segment was measured. Measurements were carried out using 2D and 3D ultrasound technique. The study included: pregnant women once priorly delivered by Caesarean section with unlimited number of prior vaginal deliveries, single (one foetus) pregnancy without fetal anomalies, gestational age of more than 35 weeks, pregnant women less than 40 years of age.

The protocole of the study procedure was explained in detail to each pregnant woman, and the study involved only pregnant women who signed voluntary written approval.

In comparing successfulness of assessment of echo structure of the distal uterine segment there existed significant statistical difference ($p>0.01$) between 2D and 3D techniques i.e. 98% (3D) in comparison to 66% (2D), false positive assessments with 2D ultrasound were 52%, and with 3D were 4%. False negative assessments with 2D ultrasound were 44%, and with 3D ultrasound were 10%.

There existed statistically significant difference in the rates of specificity (0.04), sensitivity (0.05), PPV values (0.01) and NPV (0.01) between 2D and 3D ultrasound image of the echo structure of the distal uterine segment after prior Ceasarean section in favour of 3D method. The study showed that measurement of echo structure of distal uterine segment had practical application in decision making with respect to method of termination of the pregnancy in pregnant women who were priorly delivered by Caesarean section.

Key words: distal uterine segment, echo structure, ultrasound

Introduction

The comparison of women deceased during childbirth revealed that the number of deceased women was six times greater during caesarean delivery in relation to the mortality rates of women during vaginal delivery. (1)

With respect to the caesarean delivery, one must consider and anticipate the increased morbidity rate of women. Above all, this refers to intra and postpartal haemorrhage and infections. In approximately 1% of all caesarean deliveries, the surgical procedure ends in hysterectomy due to atonic uterus, abnormal adherence of the placenta and haemorrhage. The postoperative recovery carries increased risk of infection, particularly in cases of premature rupture of membranes (PROM). Infections are clinically manifested as wound infections, endometritis with uterine subinvolution, postoperative adnexo-parametritis, pelveoperitonitis with dehiscence of uterine sutures, diffuse peritonitis, and even generalised postoperative infection in the form of postpuerperal sepsis. (2)

All these complications increase morbidity and mortality rates of women when caesarean delivery is employed, and this must be taken into obligatory consideration during the process of decision making and indicating the mode of delivery.

The existing risk involves ignorance about the condition of the uterine cicatrix and the danger of uterine dehiscence and uterine rupture.

Antenatal assessment of distal uterine segment (DUS) allows for selection of pregnant women for possible successful vaginal delivery, regardless of the prior caesarean section.

The ultrasound examination of uterine cicatrix includes analysis of various parameters i.e.:

- cicatrix shape
- thickness (thickenning)
- continuity
- outer border of the cicatrix
- echo structure of distal uterine segment (so called Supersonic criteria, Popov et al., 1994)(**20**)

In accordance with this study, the criteria for „satisfactory cicatrix" are: triangular form of lower uterine segment (even beyond outer borders), cicatrix thickness greater than 3.5 mm, the continuity of the cicatrix and the homogenous echo structure. The authors have shown that the supersonic criteria are definitely sufficient for adequate assessment of the distal uterine segment in the current pregnancy. (Popov et al., 1994) Some studies e.g. Asakura et al. (2000) measured only thickness of the lower uterine segment as a predictor of dehiscence of uterine cicatrix. (Asakura H et al., 2000).

The term distal uterine segment, DUS, was introduced into clinical practice by Bundle as early as in 1875.Aschoff defined the superior border of the DUS toward the uterine corpus as ostium internum anatomicum, and lower border toward uterine cervix as ostium internum histologicum. (3)

The distal uterine segment is an anatomical and functional entity created by interaction of several mechanical factors (distension, distraction and intraovulatory pressure). They cause stretching of the isthmus, its elongation and thinning. (4)

The objective of the present study is to determine the ultrasound technique appropriate as a base for determination of the echo structure of the distal uterine segment (DUS), as one of the criteria used to assess and evaluate which pregnant patient priorly delivered by Caesarean Section is to be delivered vaginally.

Subjects and methods

Prospective study was carried out and included 108 pregnant women, at the Clinic for Gynaecology and Obstetrics, Clinical Center University in Sarajevo.

The study included:

- Pregnant women once priorly delivered by Caesarean section with unlimited number of prior vaginal deliveries
- Single (one foetus) pregnancy without fetal anomalies
- Gestational age of more than 35 weeks
- Pregnant women who signed voluntary written approval of participation in the study
- Pregnant women less than 40 years of age
- The protocole of the study procedure was explained in detail to each pregnant woman, and the study involved only pregnant women who signed voluntary written approval.

The system of anonymous connection of the procedures was utilised for the purpose of connecting personal data and biological parameters with secured database, with suitable computer algorhythm containing neither names nor adressess of the patients.

Ultrasound examination was carried out using 2D and 3D ultrasound techniques.

- The twodimensional ultrasound is considered standard (conventional) method and it creates images consisting of the series of thin slides. Only one slide is visible at one point in time.
- 3-D technology offers multisectional possibilities which were so far only available by computer tomography and NMR (**5)**

Every modern 3-D ultrasound probe has built in convex or sector converter which moves in the fan shape mode or by rotation during scanning. When the electromagnetic sensor is attached to the conventional probe, and relative position and orientation for each tomogram is determined, the possibility of carrying out comparative scanning emerges, scanning using free hand or free sliding technique.

For the purpose of examination by tridimensional ultrasound, the tridimensional probe (VoluSon) is necessary, adapted to various tridimen-

Table 1. The structure of distal uterine segment

Echo structure of distal uterine segment	Caesarean section		Vaginal delivery		Total	
	No of women	%	No of women	%	No of women	u %
Inhomogenous	54	90,0	5	10,4	59	54,6
Homogenous	4	6,7	43	89,6	47	43,5
Unknown	2	3,3	0	0,0	2	1,9
Total	**60**	**100**	**48**	**100**	**108**	**100**

sional applications. The principle of the volume scanning is based on fan shaped scanning, so called „fan scan". The twodimensional image in live view serves as a median plane used for orientation within the volume which is to be shown. **(5)**

In order for the volume frame to be set properly onto an object under observation, it is necesssary to determine sector angle, the depth of penetration and shift angle.

„The slow scanning" achieves the best resolution, whereas the „fast scanning" characterised by weaker resolution is utilised for objects in motion. So called „normal scanning" is characterised by medium value of the quality of resolution and scanning duration. **(5)**

3D ultrasound can form slides oriented in any direction enabling in this manner better visualisation. Furthermore, 3D ultrasound enables obstetritian 360º manipulation in all three planes (sagital, transverse and coronal). Thus, the distal uterine segment can be visualised in several different perspectives.

Table 2. The difference in assessment of the homogenous quality of the cicatrix between 2D and 3D ultrasound

	Homogenous echo	Increased echo
2D	20	18
3D	35	3
P	0,05	0,02

Results

The difference in echo structure of the distal uterine segment as dependant on the method of delivery Caesarean section/vaginal delivery – is statistically highly significant. The value of Hi-square test: H_i^2 = 69,449; p<0,001. *Table 1* presents the echo structure of the distal uterine segment in pregnant women delivered by prior Caesarean section and those vaginally delivered. There exists statistically significant difference in assessment of homogenous quality of the cicatrix between 2D and 3D ultrasound. Diagnostic precision in assessment of echo structure of the distal uterine segment was measured by success in assessment of delivery (spontaneous vaginal or caesarean delivery). In comparing successfulness of assessment of echo structure of the distal uterine segment there existed significant statistical difference (p>0.01) between 2D and 3D techniques i.e. 98% (3D) in comparison to 66% (2D) False positive assessments with 2D ultrasound were 52%, and with 3D were 4%. False negative assessments with 2D ultrasound were 44%, and with 3D ultrasound were 10%. There existed statistically significant difference in the rates of specificity (0.04), sensitivity (0.05), PPV values (0.01) and NPV (0.01) between 2D and 3D ultrasound image of echo structure of the distal uterine segment after prior Ceasarean section in favour of 3D method.

Table 3. Assessment of echo structure of the distal uterine segment 2D ultrasound

2 D assessment	Spontaneous	Caesarean delivery
N = 54	22	33
Delivery after assessment	40	44
P	0,05	0,05

Table 4. Assessment of echo structure of the distal uterine segment 3D ultrasound

3 D assessment	Spontaneous	Operative
N = 54	44	10
Delivery after assessment	42	12
P	NS	NS

Table 5. Sensitivity of the method 2D and 3D ultrasound

Sensitivity of the method	2D	3D	p
A/A+C	30/54	52/54	
%	55%	95%	0,05

Table 6. Specificity of the method 2D and 3D ultrasound

Specificity of the method	2D	3D	p
D/B+D	32/54	48/54	
%	53%	83%	0,04

Table 7. Positive predictive value of 2D and 3D ultrasound

PPV methods	2D	3D	p
A/A+B	30/54	50/54	
%	55%	93%	0,09

Table 8. Negative predictive value of 2D and 3D ultrasound

NPV methods	2D	3D	P
A/C+D	31/54	51/54	
%	57%	94%	0,01

Discussion

The distal uterine segment is characterised by thin muscular layer and scarce vascular meshwork, making it a site of choice for surgical incision during surgical delivery, whereas it simultaneously becomes a site of increased risk of uterine rupture.

The pregnancies and deliveries after prior Caesarean section are considered of particularly high risk, due to the scar tissue that additionaly further jeopardises the DUS. (6)

Therefore, the antenatal assessment of the condition of the DUS is a means of decreasing the risk of cicatrix rupture to minimum and ensuring successful vaginal delivery.

Based on the investigation done on 642 subjects, the group of French authors (7) comcluded that the risk of the rupture of the cicatrix was directly dependent on thinning of the DUS as measured at approximately 37 weeks of gestation.

The specificity of 3D ultrasound method was 93% with very high NPV of 94% which enables selection of pregnant women with homogenous echo of the cicatrix. These supersonic criteria (Popov et al., 1994) (8) would be sufficient for the obstetrician to decide to deliver vaginally.

Numerous studies analysed the percentage of successful vaginal deliveries in pregnant women with uterine cicatrix and prior caesarean section. Thus, the study of Nguyena et al. (1992) showed that 72% of women with cicatrix and prior caesarean section can be allowed to go into trial labour for vaginal delivery. Concurrently, the highest percentage of successful vaginal deliveries was noted in pregnant women in which the prior Caesarean section was performed due to fetal breach presentation (86%). In addition, there was no significant influence of the fetal weight (±4000 g) on successfulness of vaginal delivery (73 vs. 76% in birth weight less than 4000 g, Nguyen et al., 1992).

The study of Qureshi et al. (1997) established the «cut-off value» of 2.0 mm, whereby the cicatrix thickness of 2 mm and more was considered as good tissue healing, and the values below were

considered poor tissue healing. The ultrasound method in the study of Qureshi et al. (1997) proved to be highly specific and sensitive (86.7%, 100%, respectively), also both positive and negative predictive values were rather high (86.7, 100%, respectively). This study concluded that the ultrasound presents exceptionally useful in differentiation and dilema with respect to assessment of uterine scarring in pregnant women with prior caesarean section (Qureshi et al., 1997).

The present study showed that 3D ultrasound can assess with high sensitivity the echo structure of the cicatrix on the distal uterine segment and select pregnant women with prior caesarean delivery who could be possibly successfuly delivered vaginally. In this way, numerous complications, in both mother and neonatus, associated with Caesarean section would be avoided.

Conclusion

Based on the results obtained it was concluded that 3D ultrasound method was the method of choice in estimate and evaluation of echo structure of the distal uterine segment in pregnant women priorly delivered by Caesarean section. This method, due to its high specificity and sensitivity, provides assurance to the physician in the process of decision making to deliver vaginally. In this manner, it contributes to decrease in number of Caesarean sections, and consequently

- Decreased risk of tromboembolism
- Decreased hospital stay
- Eeasier and faster postoperative recovery of women
- Decreased need for blood transfusions and blood derivatives.
- Decreased possibility of postpartal fever, wound infection, endometritis
- Decrease in Neonatal Respiratory Distress problems
- Improved cost effectiveness

References

1. *Lydon-Rochelle M, Holt VL, Easterling TR. Martin DP. Risk of uterine rupture during labor among women with a prior cesarean delivery. N Engl J Med 2001; 345: 3-8*
2. *Shipp T, Zelop C, Cohen AP, et al. Postcesarean fever and uterine rupture in a subsequent trial of labor. Am J Obstet Gynecol 2001: 184: S187*
3. *Popov I. The ultrasonic assessment of the cicatrix after a past cesarean section. Akush Ginekol (Sofiia) 1994; 33: 10-12*
4. *Danforth DN, Evanston I, Ivy AC. The Lower uterine segment, Am J Obstet Gynecol, 1949,-57: 831-41*
5. *Cragin EB.Conservatism in obstetrics NY Med J, 1916: 103: 1-3*
6. *Merz E. 3-D ultrasound in Obstetrics and Gynecology, Lippincott Williams&Wilkins Philadelphia, New York-Baltimore, 1998: 3-17.*
7. *Mcchen W, Burke G,CehoeJT, Magani IM True rupture / scar dehiscence in delivery following prior section. Eur J Opstet Gynecol Reprod Biol 1990: 31: 249-54*
8. *Rozenberg P, Goffinet F, Phillippe HJ, Nisand I. Echographic measurement of the inferior uterine segment for assessing the risk of uterine rupture. J Gynecol Obstet Biol Reprod 1997; 26: 513-9*

Corresponding Author
Ejub Basic,
Clinic for Gynaecology and Obstetrics,
Clinical Center University of Sarajevo,
Bosnia and Herzegovina,
E-mail: healthmedjournal@gmail.com

Instructions for the authors

All papers need to be sent to e-mail: healthmedjournal@gmail.com

Every sent article gets its number, and author(s) will be notified if their paper is accepted and what is the number of paper. Every corresponedence will use that number. The paper has to be typed on a standard size paper (format A4), leaving left margins to be at least 3 cm. Ali materials, including tables and references, have to be typed double-spaced, so one page has no more than 2000 alphanumerical characters (30 lines). Sent paper needs to be in the form of triplicate, considering that original one enclosure of the material can be photocopied. Presenting paper depends on its content, but usually it consists of a page title, summary, text references, legends for pictures and pictures. Type your paper in MS Word and send if on a diskette or a CD-ROM.

Title page

Every article has to have a title page with a title of no more than 10 words: name (s), last and first of the author (s), name of the instituion the authors (s) belongs to, abstract with maximum of 45 letters (including space), footnote with acknowledgments, name of the first author or another person with whom correspondence will be maintained.

Abstract

Second page needs to contain paper abstract, 200 words at the most. abstract needs to hold all essential facts of the work-purpose of work, used methods (with specific data, if possible) and basic facts. Abstract must have review of underlined data, ideas and conclusions from text. Abstract has no quoted references. For key words, at the most, need to be placed below the text.

Central part of the article

Authentic papers contain these parts: introduction, goal, methods, results, discussion and conclusion. Introduction is brief and clear review of a problem. Methods are shown so that interested reader is able to repeat described research. Known methods don' t need to be identified, it is cited (referenced). Results need to be shown clearly and legically, and their significance proven by statistical analysis. In discussion, results are interpreted and compared to existing, previously published findings in the same field. Conclusions have to give an answer to author's goal.

References

Quoting references must be in a scale in which they are really used. Quoting most recent literature is recommended. Only published articels (or articles accepted for publishing) can be used as references. Not-published observations and personal notifications need to be in text in brackets. Showing references is as how they appear in text. References cited in tables or pictures are also numbered according to quoting order. Citing paper with six or less authors must have cited names of all authors; if seven or more authors' wrote the paper, the name of the first three authors are cited with a note "et all". If the author is unknown, at the beginning of papers reference, the article is named as "unknown". Titles of the publications are abbreviated in accordance to Index Medicus, but if not listed in the index, whole title of the journal has to be written.

Footnote-comments, explanations, etc., cannot be used in the paper.

Statisticial analysis

Tests used for statistical analysis need to be shown in text and in tables or pictures containing statistical analysis.

Tables and pictures

Tables have to be numbered and shown by their order, so they can be understood without having to read the paper. Every column needs to have title, every measuring unit (SI) has to be clearly marked, preferably in footnotes below the table, in Arabian numbers or symbols. Pictures also have to be numbered as they appear in text. Drawings need to be enclosed on a white paper or tracing paper, while black and white photo have to be printed on a radiant paper. Legends next to pictures and photos have to be written on a separate A4 format paper. All illustrations (pictures, drawings, diagrams) have to be original and on their backs contain illustration number, first author last name, abbreviated title of the paper and picture top. It is appreciated if author marks the place for table or picture. Preferable the pictures format is TIF, quality 300 DPI.

Use of abbreaviations

Use of abbreviations has to be reduced to minimum. Conventional units can be used without their definitions.