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Dimension coefficient yielded by Rasch model to measure scale validity: An example using the patient experience diagnostic tool for England hospitals

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Abstract

Background: Dimensionality must be determined before adding item scores to represent the overall performance of a measure. The aim of this study is to help researchers identify the dimension tendency for a scale's validity toward a common entity. This in turn will improve inspecting aberrant responses for each item with individual itemby-item box plots of disclosure for patient views on healthcare service quality.

Methods: We used the Rasch rating scale model to analyse the 2009 English inpatient questionnaire data regarding patient satisfactory perception, which were collected from 162 hospitals, examined unidimensionality, and developed a visual plot in Excel that depicts the satisfaction level of each hospital across questions and monitors aberrant responses with Rasch standardised residual for each item and outfit statistics for individual hospitals.

Results: We found that (1) the Rasch_residual principal component analysis is able to check dimensionality. The dimension coefficient defined as the extent of dimensionality should report to readers. The five key domains of the 2009 English adult inpatient questionnaire data regarding patient experience measure a common entity and earn a dimension coefficient of 0.88, and (2) itemby-item chart plots along with Rasch's fit statistics (i.e., standardised residual and outfit statistics) can help organisations accomplish large improvements on a small number of key areas.

Conclusion: Without removing misfit questions, we found that the 20-item inpatient ques-

tionnaire measured the same construct across types of hospitals. The visual chart plot in Excel provides an exemplary comparison of quality of healthcare for individual hospitals. The Rasch analysis allows intra- (using standardised residuals for each item) and inter- (using outfit statistics across hospitals) hospital performances to be easily, quickly and clearly compared.

Key words: unidimensionality, principle component analysis, Rasch model, National Health Service

Introduction

Most item response theory (IRT) models assume a single domain (unidimensionality for academics), that is, all items in a test measure the same latent trait [1,2]. The domain score represents the average of the item scores when unidimensionality is held. Thus, dimensionality must be determined before adding item scores to represent the performance of a measure.

Unidimensionality matters

Many methods have been proposed to assess the unidimensionality assumption [3]. For example, linear factor [4,5] and nonlinear[6] analyses or tests have been suggested. Principal component analysis (PCA) is another widely used method, in which the number of eigenvalues (EGV) greater than one [7] or scree plots [8] are used to determine the number of dimensions. Parallel analysis (PA) [9] is one of the most recommended methods of dealing with the number-of-factors-to-retain problem [10,11], but is not available in commonly used statistical packages [12] and not reveal the extent of dimensionality for each domain.

The use of Rasch analysis to assess unidimensionality has been the subject of much discussion in the literature [13-16]. Tennant and Pallant's study [17] found that Rasch fit statistics cannot detect unidimensionality when two dimensions have equal item length and moderate correlations. They supported Richard Smith's [18] recommendation that exploratory factor analysis (EFA), especially using PA, should be undertaken to ensure the dimensionality of study data. However, Zwick and Velicer [19] argured that PA exhibits a tendency to over-extract the number of factors. Furthermore, Silverstein [11] argued that PA frequently overestimates one factor. The search for a set of criteria that effectively detects unidimensionality is underway and continuously proceeds forward. The first purpose of the current study is to develop a way to explore the extent of dimensionality that examines the dimension tendency of a scale.

Unidimensionality determined before adding item scores

The patient experience diagnostic tool was developed by the Department of Health in England (DHE). It helps National Health Service (NHS) organisations better understand and interpret the patient experience data of adult inpatient surveys [20, 21]. The tool includes 20 questions within five key domains of patient experience. The scores on these questions were summed to denote the performance of individual NHS trusts. There is currently no evidence that the 20 questions of the diagnostic tool form a single construct. Before developing a way to explore the extent of dimensionality, it is required to inspect whether the five key domains of the England adult inpatient surveys measure a common entity.

Report card evaluating hospital performance of patient experience

Questions on questionnaires are often analysed and presented individually, one item at a time (e.g., item-by-item box plots of disclosure, as shown in published papers [21,22]). The box plots for a hospital only exhibit a juxtaposed comparison that allows for easy differentiation of the performance on each question across hospitals. Nevertheless, the comparisons between different institutions must be interpreted with caution because the performance on each question may be influenced by many factors, such as the healthcare financing system, the healthcare delivery system, and the provider's unique institutional scale and culture. Each hospital has its own distinct traits and SWOT (i.e., strength, weakness, opportunity and threat) pattern.

The item-by-item box plots incorporated with the model's residual statistics can be expected to disclose the hospital's SWOT. **The second purpose of this study** is to apply Rasch's Fit statistic [23] to the patient experience diagnostic tool (developed by DHE) to help NHS interpret the itemby-item box plot of disclosure in patient experience data of adult inpatient surveys, and to aid organisations accomplish large improvements by focusing on a relatively small number of key areas and to examine the SWOT of individual hospitals.

Methods

Data collection

The England National Patient Survey Programme, co-ordinated by the Care Quality Commission, gathers feedback annually from patients on different aspects of their experience of the care that they have received, across a variety of services/ settings (including Inpatients, Outpatients, Emergency care, etc.).

The inpatient questionnaire contains 72 patient experience questions, of which 32 are measurable indicators. The Department of Health has developed toolkits to help NHS (England National Health service) organisations better understand and interpret their patient experience data [24]. These toolkits include 1) a patient experience 'First Steps' diagnostic tool and 2) a tool for measuring 'Public confidence in local NHS'. The former survey includes 20 questions chosen to represent five patient experience domains. It includes the following 5 key domains: access & waiting, safe; high quality, coordinated care; better information, more choice; building closer relationships; clean, comfortable, friendly place to be. The latter tool has 12 questions regarding the 3 key domains of focus on the staff member attitude, patient dignity

privacy and both compassion and organisation's facility that learn from patient's experience.

With permission, we downloaded datasheets from the England National Patient Survey Programme. A total of 162 hospitals completed the inpatient questionnaire survey in 2009, forming a 162×20 rectangle metric (shortly for Inpatient-20) with responses from 0 (worst) to 100 (excellent). The data have been organised by NHS from more than 100 thousand patient ratings of the 162 hospitals' performance. We transformed the 20 questions by dividing 10 from a raw score of 0-100 into 0-9 ordinal categories. After removing those categories without any response, a 0-7 point rating scale was constructed. From these eight categories, the Rasch rating scale model [25] was applied using WIN-STEPS software [26] to yield a respective interval logit score for individual hospitals. This score is used for comparisons within and among hospitals. The summation scores must work on the premise that all items are absolutely or nearly to unidimensionality. That is, dimensionality must be determined before adding item scores to represent the overall performance of a measure [27,28]. If unidimensionality is held, a coefficient of a scale interpreting the extent of unidimensionality is required to report.

Study 1

1. Checking dimensions and item fit using Rasch analysis

The dimensionality of the Inpatient-20 was evaluated with two methods. One method was the exploratory factor analysis with a parallel analysis on the raw scores [9, 17]. The other method was a principal component analysis on the Rasch residuals [29, 30]. The first method was performed to determine the number of dimensions in the Inpatient-20. The second method was then performed to confirm the unidimensionality of the Inpatient-20 that were examined in the first method. The eigenvalue of the first residual factor (named contrast by WINSTEPS) was less than 3 and the percentage of variance attributable to the first contrast out of total variance was less than 5% [26, 31], signifying unidimensionality in the second method. Through the Rasch analysis, the raw scores are transformed to interval measures with the logit (log odds) unit [23,32,33].

Rasch analysis has been used to develop concerning the validity of the scale in many published papers [2, 31]. The weighted (infit) and unweighted (outfit) mean-square errors can be used to assess item and person fit [34]. A mean-square error between 0.50 and 1.50 indicates an acceptable model-data fit [26].

To examine the measure invariance using EV Smith's approach [31], we compared the results of hospital performances estimated with the entire20 scale and its counterpart subcale (i.e., such itms with a negative loading chosen by Rasch residual PCA). A statistically significant *t*-test (> 5%) using formula 1 would indicate the level of the performance differs depending on which items are included in the calibration. This would indicate multidimensionality [31]. Otherwise, once data fit the Rasch model (to construct a unidimensional measurement), then analysis of any subset of items should produce equivalent measures.

$$t = (b_{s} - b_{c}) / SQRT(SE_{bs}^{2} + SE_{bc}^{2}) , \dots (1)$$

Where b_s and b_c is the hospital measure adjusted for a mean equal to zero from the analyses of all 20 items and the counterpart subscale. Both of SE_{bs} and SE_{bc} are the respective standard errors of the hospital measures.

2. A way to report the dimension tendency of a scale

We developed a dimension coefficient (DC) to represent the unidimensional (validity) tendency of a scale via geometric representations of multidimensionality[35]. DC is a ratio for an area under the curve of random data eigenvalues after deducting the area of deviations from the residual eigenvalues illustrated in formula 2 and Figure 1.

The area under the curve of random data eigenvalues is yielded by a series of artrapezoid (laddershaped) calculations with the heights of adjacent eigenvalues on Axle Y and the width of one unit on Axle X, (see formula 3). The area of deviations between eigenvalues of random data and residuals is referred to formula 4.

$$Area_{random} = \sum_{i=1}^{n-1} (Height_{i} + Height_{i+1}) \times 1 \div 2,$$
(2)

$$Area_{deviation} = \sum_{i=1}^{n-1} \left(\begin{bmatrix} (|Height_{raw,i} - Height_{random,i}|) + \\ + (|Height_{raw,i+1} - Height_{random,i+1}|) \times 1 \div 2 \end{bmatrix},$$
(4)



Figure 1. Calculation of the dimension coefficient for residuals of general raw data (left) and unidimensional simulation data (right) Note. A ratio of that under curve area of random data EGVs deducting the area of deviations from residual EGVs.

Where *n* is the item length. The eigenvalues of random data were obtained from the PA Engine programme on website [36]. Raw score eigenvalues were yielded by the statistical package of SPSS 15.0(SPSS Inc., Chicago) through a PCA routine using the data of residual Z-scores (interacted by items and persons from the Winsteps output file of Xfile).

Study 2

Item-by-item box plots with residual Z-score focusing on key questions

The Rasch model [23] is a latent trait model that imposes a probabilistic relationship between the level of latent trait (referred to as satisfaction level for a hospital in this study) and the questions used for measurement (referred to as item difficulty). The easy question earns a high summation score. In contrast, the harder one includes a low score. A visual representation of item-by-item box plots will be demonstrated using Rasch analysis with Z-score (standardised residual) and outfit statistics to inspect aberrant responses for each item that focuses on a small number of key areas for improvement.

Results

Study 1

Item fit and dimensionality of the Inpatient-20

A total of 20 questions (shown in Table 1) did not meet the model's requirements well (i.e., the first 3 items with outfit MNSQ beyond 1.5). Nevertheless, the exploratory factor analysis with parallel analysis on the raw scores identified one domain (in the left panel of Figure 2). The principal component analysis on Rasch residuals yielded an eigenvalue of 2.3(< 3.0) for the first residual factor. The unexplained variances of which was 0.9%(< 5%), indicating the Inpatient-20 can be treated as unidimensional [26,31,32].



Figure 2. Parallel analysis to determine number of dimensions comparing eigenvalues of raw scores (left) and residuals (right) with counterparts of random data

Table 1.	Item difficulty	and outfit M	INSQ for 20	questions from	the inpatient	questionnaire
	<i>JJ J</i>		~ /	1 2	1	1

Inpatient-20 Questions	Delta	Outfit
Access and waiting		
1: Was your admission date changed by the hospital?	-10.12	1.54
2: How do you feel about the length of time you were on the waiting list before admission to hospital?	-3.46	1.99
3: When you arrived at the hospital, did you feel you had to wait a long time to get to a bed on a ward?	-0.83	2.18
Safe, high quality, coordinated care		
4: Sometimes, a member of staff will say one thing and another will say something quite different?	-0.55	0.54
5: On the day you left the hospital, was your discharge delayed for any reason?	7.34	1.18
6*: Did a member of staff tell you about any danger signals you should watch for after you went home?	12.65	0.90
Better information, more choice		
7: Were you involved as much as you wanted to be in decisions made about your care and treatment?	4.11	0.31
8: Did a staff member explain the purpose of the medications you were taking home in a way that you could understand?	-2.88	0.76
*: Did a member of staff tell you about medication side effects to watch for when you went home?	14.42	0.99
Building relationships		
10: When you had important questions to ask the doctor, did you get answers that you could understand?	-1.88	0.51
11: Did doctors talk in front of you as if you weren't there?	-3.50	0.74
12: When you had important questions to ask a nurse, did you get answers that you could understand?	-1.32	0.48
13: Did nurses talk in front of you as if you weren't there?	-5.80	0.74
Clean, comfortable, friendly place to be		
14: Were you ever bothered by noise at night from other patients?	8.63	1.00
15: Were you ever bothered by noise at night from hospital staff?	-0.29	0.77
16: In your opinion, how clean was the hospital room or ward that you were in?	-5.84	0.85
17*: How would you rate the hospital food?	11.03	1.32
18: Were you given enough privacy when being examined or treated?	-11.30	0.69
19: Overall, did you feel you were treated with respect and dignity while you were in the hospital?	-7.44	0.41
20: Do you think the hospital staff did everything they could to help control your pain?	-2.97	0.54
Overall	0.00	0.92

Note. Delta denotes item overall difficulty in a unit of log odds; The 7 threshold difficulties are -15.3, -9.69, -5.19, -1.82, 3.2, 9.66, and 19.15 with a monotonously increasing.

* represents the most difficult items

The additional analysis using EV Smith's approach revealed no significant number of hospital measure pairs falling outside the 95% confidence for the Inpatient-20 scale (=0.0% or 0/162 pairs), indicating that Inpatient-20 would be unidimensional with a Rasch reliability[37] of 0.88 and a dimension coefficient of 0.881 shown in the right panel of Figure 2.

Item fit and dimensionality of the Inpatient-18

After removing two misfit items (#2, How do you feel about the length of time you were on the waiting list before admission to hospital?; #3, When you arrived at the hospital, did you feel you had to wait a long time to get to a bed on a ward?), a total of 18 items (MNSQ<1.5) met the model's require-

ments rather well. The dimension coefficient for the Inpatient-18 reached to 0.883 (Figure 3). The Rasch reliability also slightly increased to 0.89. The PCA on Rasch residuals and measure equivalence using EV Smith's approach yielded similar results as those in the Inpatient-20, as under Rasch model conditions, indicating those two misfit items provided such a trivial effect on the Inpatient-20.

Study 2

Question properties

The three questions that hospitals had the most difficulty in receiving high patient satisfaction scores were as follows: question 6 (Did a member of staff tell you about medication side effects to watch for when you went home?), question 3 (Did a member of staff tell you about any danger signals you should watch for after you went home?) and question 17 (How would you rate the hospital food?). Hospitals had the least difficulty with question 18 (Were you given enough privacy when being examined or treated?). The mean and standard deviation of questions were 0.00 and 7.20, respectively. All of questions were widely dispersed. The question difficulties were well spread out across the hospitals, as hospitals' performance ranged from 1.35 to 12.74 (M=5.30, SD=1.93) lower than the most difficult question with 12.65 logits, such that the 20 questions earn a high Rasch person separation reliability (near to 0.90).



Figure 3. The Inpatient-18 scale generates a dimension coefficient of 0.88

Item-by-item box plots with residual Z-score focusing on key questions

Figure 4 shows item-by-item box plots for a particular hospital. On the right-hand side of the figure, the outlier residual Z-scores are shown, indicating that such questions responding to this hospital violating model's expectation are required for a further discussion. When the observed score is far apart from the expected response, it will lead the

hospital's outlier residual Z-scores beyond the criterion of 1.96 (p<.05) when Rasch model is well fitted (including those two assumptions of unidimensionality and local independence). Examining these residual Z-scores can help organisations accomplish large improvements by focusing on a relatively small number of key areas. The item-byitem box plot can also reveal the SWOT for individual hospitals, like the KIDMAP diagram used for patient experience diagnostic tool reported in a previous paper [21,22], which indicates whether performance was significantly over or under the model's expectation. With these residual Z-scores, the item-by-item box plot merits a better function for detecting response abnormalities.



Figure 4. Hospital RBV with bar charts across inpatient items performed in 2009 Note. Z-score=(observed – expected)/SD, over expectation while positive, otherwise under expectation

Discussion

Key findings

The two purposes of the current study were fulfilled, including 1) developing a dimension coefficient for a scale to report the extent of unidimensionality and verifying the five key domains of England adult inpatient surveys measure a common entity, and 2) applying Rasch's Fit statistic to the patient experience diagnostic tool to help organisations accomplish large improvements by focusing on a relatively small number of key areas.

What this research adds to what is already known

Tennant and Pallant's study [17] suggested that both PA and percentage of individual *t*-tests outside range \pm 1.96 (95% CI) [38] should be incorporated into Rasch Fit statistics. We propose a dimension coefficient for a scale that could be similar to Cohen's d as an effect size of tendency toward dimensionality of data, for instance, small (0.2 to 0.3), medium (around 0.5) and large (0.8 to 1.0) [39]. This statistic could be regularly reported as Cronbach's alpha in research papers. There is no agreed upon method for assessing unidimensionality that shold not be viewed as a dichotomous yes or no decision, but rather as a continuum [40]. Therefore, a dimension coefficient ranged from 0 to 1 is required to represent the tendency for a scale's validity toward a common entity.

What is the implication and what should be changed

Any scale should be examined against important criteria, such as dimensionality, item fit, person fit, appropriateness of threshold levels, and invariance (or so-called differential item functioning [40]). Many methods have been proposed for assessing the unidimensionality assumption [1,3,41-43]. However, the major drawback of them is the absence of an objective criterion based on the extent of unidimensionality that can be determined, namely without a common coefficient to measure the dimension tendency. Though it is so difficult to have a clear cut point for determining dimensionality [1], it may be possible, from our study, to use dimension coefficient as an effect size to report the dimension tendency (e.g., DC more than 0.95 can be treated as a perfect unidimensionality shown in the right panel of Figure 1). For instance, we see the paper [44] without reporting the extent of unidimensionality, but just using outfit MNSQ less than 1.7 as the criterion of unidimensionality to meet the model-data-fit. We can anticipate that the higher dimension coefficient, the narrower range (e.g., adjusting the criterion of outfit MNSQ 1.7 to 1.5 or less) should be set for the fit MNSQ of items in a study, and the more possible it lets the residuals' EGVs look like those counterparts of random data, see the left panel of Figure 3.

Strength of this study

A factor analysis on the residuals of Rasch-transformed scores should report the dimension extent of the study scale to readers as regularly as Cronbach's alpha in research papers. That might not be sufficient to determine dimensionality merely reporting such a description like that the first and second factors accounted for only 12.3% and 8.3% of the residual variance, respectively in a paper [45]. It is definitely necessary to report the quality of questionnaire with a dimension coefficient, which is an explained proportion compared to the benchmark of 100% unidimensionality using random data (Figure 1 to 3) and is an important piece of evidence given to verify no dominant factors in residuals. The reason for using random data eigenvalues is referred to Humphreys and Montanelli [46] statement (the Kaiser rule[7] is only true for very large correlation matrices). They propose that criterion eigenvalue thresholds be estimated by simulation studies based on random data formed into matrices of relevant sizes, like that we plot 95%CIs of random data in Figure 1 and 2 by the PA Engine programme on website [36].

An Excel module was incorporated with Winsteps software by using BATCH=YES command not only for checking unidimensionality and providing a dimension coefficient for a scale regarding its validity, but for plotting item-by-item box plots with residual Z-score as well. It can be downloaded in the additional file 1 for interested readers to practice. Accordingly, the Excel module incorporated with Winsteps can be feasible, applicable and simple for use, especially for them who are not professional researches familiar to utilizing statistical packages. Accordingly, it is easy to generate a dimension coefficient for a scale to report the extent of unidimensionality and available from the authors upon request.

Application for Excel module

With exception to Rasch PCA method and dimension coefficient, we used Rasch measurement to construct an interval logic scale for patient satisfaction on hospital performance, utilised fit statistics to detect aberrant response patterns, and developed a visual representation of item-byitem box plots of disclosure for patient views on hospital service quality, which may be understood easier, faster and clearer than the traditional Rasch model's KIDMAP diagram published in a previous paper [21,22]. All of them have been integrated into the Excel-VBA module, through which Excel module of item-by-item box plots can simultaneously execute Rasch WINSTEP software to yield reports. The use of the Excel module is convenient and necessary for general hospital staff members not only in determining unidimensionality for questionnaire data, but also for inspecting question misfit integrated in a scale. Readers who are interested in assessing dimensionality with the Rasch model can download it for practice. It must be noted that the Excel module must be placed in the same folder as the examples for WINSTEPS.

In this study, we demonstrated two methods (EFA with PA and Rasch PCA, Figure 2) and a coefficient of unidimensional validity for a scale. That might respond to the question about the standard format for reporting Rasch analysis in publications [47].

Limitations of the study

It is important to have a questionnaire approach that provides feedback for improving health service. More work is needed to further improve the disclosure of an effective feedback system in healthcare settings. In the present study, we demonstrated how an Excel module can be used to compare patient perception on healthcare service using the Rasch model's outfit MNSQ and standardised residual. Users may need some background knowledge to interpret the item-by-item chart plot properly.

As for the England inpatient survey, we obtained the summary scores for each hospital. There may be some bias when transforming raw data from patient views for each hospital on each question. We have not conducted differential item functioning (DIF) [40] analysis to determine interaction effects on items between groups as well as appropriateness of threshold levels to verify average measures advance monotonically within each category[48]. Future studies on this matter are encouraged to conduct DIF analysis on types of hospital in England and to optimise rating scale category effectiveness.

There are many jargons and abbreviations with regards to Rasch model in this article, such as CAT, contrast, DIF, DC, EGV, MNSQ, Outfit, PCA, Rasch residual, unidimensionality, etc.. More work is needed to further understand the relationship among them in an attempt to be properly applied to clinical settings. Accordingly, users may need some background knowledge to interpret unidimensionality and the dimension coefficient properly.

Further studies and suggestions

The dimension coefficient provides a deeper insight on the tendency toward unidimensionality. Researchers can report it along with Rasch reliability and Fit statistics to reveal the properties of questionnaires, especially for validating the questionnaire construct. As for the item-by-item chart plot using the Rasch residual for each hospital, it can inspect patients' perception of hospital performance on a specified question. With that, aberrant responses on the items of "easier but with a significantly high score" or "harder but with a significantly low score" deserve more attention in an attempt to improve hospitals' service performance. The Z-scores in Figure 4 provide an opportunity for a hospital to examine its strengths and weaknesses through self-comparison rather than comparisons with others. Focusing efforts on those questions of "easier but with a significantly high score" can upgrade the overall performance level of a hospital. Future studies should collect data regarding hospital outfit MNSQ greater than 2.0 [48] to understand potential differences in types of hospitals.

We can refer to the PA Engine programme on website [36] for getting the 95% eigenvalues of random data through which the 95% confidence interval [49] of the dimension coefficient can be produced by the formula 1 to 3. The 20 questions examined in this paper can be added to a static questionnaire as a daily routine for examining the healthcare quality of a hospital due to its dimensionality. Item banks (all items congruent to unidimensionality) can be created for a touch screen (e.g., iPad) version of computer adaptive testing (CAT) to reduce patient burden in responding to questions [50,51] in future studies.

Rating scales have been widely used in the healthcare industry. For example, patients are asked to rate the intensity of their pain on a 5-point scale (mild, discomforting, distressing, horrible, excruciating). Within the context of Rasch measurement and item response theory (IRT), the rating scale model [25] has been widely used to fit responses of rating scales [52]. The problem we face is whether there is an indicator ranged from 0 to 1 that can stand for the extent of the validity toward unidimensionality, such as GFI, NFI and CFI in a confirmatory approach, or Cronbach's α commonly used as a measure of the internal consistency or reliability of a psychometric test score for a sample of examinees. There are a variety of reasons for researchers to undertake further study on dimesion coefficient to measure scale validity.

Conclusions

The England Picker Institute Europe annually discloses reports of patients' experience with a particular provider at a specific point by an item-by-item approach with box plots. In this study, we applied the Rasch analysis to programme an Excel-VBA module to help readers to understand further the hidden characteristics of individual hospitals using standardised residual for each item and outfit statistics across hospitals. Furthermore, we quantified the tendency toward unidimensionality using the dimension coefficient of a scale to incorporate Rasch reliability to reveal the quality of questionnaire data.

List of abbreviations

Alpha: Cronbach's α CAT: computer adaptive testing DC: dimension coefficient DIF: differential item functioning EGV: eigenvalue EFA: exploratory factor analysis IRT: item response theory MNSQ: mean square error NHS: National Health Services PA: parallel analysis PCA: principal component analysis VBA: visual basic for application

Authors' contributions

MT and TW collected all data, generated the database, designed and performed the statistical analysis and wrote the manuscript. TW and WW contributed to the development of the study design and advised on the performance of the statistical analysis. The analysis and results were discussed by all authors together. WW, MT and TW contributed to the Excel programming, helped to interpret the results and helped to draft the manuscript. All authors read and approved the final manuscript.

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Charismatic leadership: impulse factor for initiative-oriented health care personnel in the Turkish public hospitals

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Abstract

Background and purpose: Organizations in the health care sector in Turkey parallel to the world are undergoing broad structural reforms. As with most broad reforms employee commitment and support from hospital staff members are need to successfully implement these changes. Our claim is that hospital managers who seek commitment rather compliance are required to meet these challenges. We tested this claim by studying the relationship of charismatic leadership which is thought to emerge in times of stress and crisis, and is an antecedent of follower performance-stimulation and follower initiative-oriented behaviors. Since charisma is also thought influence followers' discretionary behavior in organizations as it creates sense of self efficacy and confidence coupled with performance-stimulation we examined if employee' job autonomy and stress in the workplace enhanced followers' initiative-oriented behavior.

Methodology: We sampled 402 members of medical staff (physicians, medical technicians and nurses) in four Turkish public hospitals by using a questionnaire. Structural Equation Modeling (SEM) was used to test hypothesized relationships between charismatic leadership, stress, job autonomy and initiative-oriented behavior. *Results:* We found a significant and positive relationship between charismatic leadership and initiative-oriented behavior. Stress produced a significant negative relationship with initiative-oriented behavior. However, the interaction between charismatic leadership and job autonomy was not significant. We concluded that charismatic leadership is the strongest predictor of initiative-oriented behavior followed by strain.

Key words: Charismatic leadership, initiativeoriented behavior, job autonomy, stress, Turkish hospitals

Introduction

Problem Statement

The Turkish health system is in transition and as a part of the Government's Health Transformation Program (HTP), institutional and organizational reforms are underway that aim to make the health system more effective by improving governance, efficiency, purchaser / provider satisfaction and long-term fiscal sustainability. Key elements of the HTP include: i) establishing The Ministry of Health as a planning and supervising authority; ii) uniting all citizens of Turkey under a single public health insurance institution through implementation of the Universal Health Insurance; iii) expanding the delivery of health care and making it more easily accessible and user-friendly; iv) improving the motivation of health personnel and equipping them with enhanced knowledge and skills; v) setting up educational and scientific institutions to support the system; vi) securing quality and accreditation systems to encourage effective and quality health care services; vii) implementing rational drug use and management of medical materials and devices, and viii) providing access to reliable information for decision-making, through the establishment of an effective Health Information System [1]. Within the last few years during which the HTP was implemented, Turkey has witnessed a period of health policy changes. This program in progress aim to rapidly mobilize health system change and transform its priorities [2].

To face these changes and challenges, medical staff in all hierarchical levels in hospitals need to actively participate in this transformation process. Thus, there is a growing need for initiative-oriented behavior in the hospitals. In this study, we assume that charismatic leadership, employees' job autonomy and stress in the hospital setting may be available to enhance medical staff's initiative oriented behavior. The impact of charismatic leadership on initiative-oriented behavior was investigated in the German hospital context by the study of Boerner and Dütschke [3]. And they hypothesized that both employee's job autonomy and stress in the workplace will moderate the positive relationship between charismatic leadership and followers' initiative oriented behavior. Results of their study were used to develop our study's model.

Study Aims

The purpose of this study was to examine the relationship between charismatic leadership and follower initiative-oriented behavior, employee' job autonomy and stress in the workplace. Additionally, this study aims to compare and contrast the findings of German colleagues study [3] in the Turkish context and highlight the differences within the cultural context of Turkey. The study was guided by the following research questions: (a) What is the effect of charismatic leadership on initiative-oriented behavior in the Turkish hospital context? (b) What is the effect of health employees' job autonomy on initiative-oriented behavior?

Significance of the study

The fact that this study is the replication of the same study in Germany, it provides cross cultural implications for leadership practices in different national context but same sector i.e. healthcare. This study also provides new information to Turkish hospital managers who think about ways to further followers' initiative-oriented behavior.

Conceptual Framework

The study is framed by the following concepts: Charismatic leadership, initiative-oriented behavior, job autonomy, and job stress which are described in the following paragraphs.

Charismatic leadership

Alexander the Great, Joan of Arc, Mahatma Gandhi, Martin Luther King. Charisma is the one distinct characteristic or quality that they all have in common. Charismatic leader, according to Zaleznik [4], arouses strong positive emotion and influences belief and behavior of followers. They have such management qualities that can empower employees and facilitate co-operation, creativity and innovation among them by instilling a sense of purpose [5]. The most common definition of charisma is a strong attractive personal quality, a trait that makes other people like that person and be attracted to him/her. "This special personality characteristics gives a person superhuman or exceptional powers and reserved for a few, is of divine origin, and results in the person being treated as the leader" [6]. Weber as a sociologist was mainly interested in the forces of authority in the society and how these forces changed over time. He identified three types of authority systems i.e. traditional, legal-rational and charismatic. The basis of authority in the charismatic authority system comes from society's belief in the exemplary characteristics of the leader that is super human qualities or powers of divine origin which set them apart from the ordinary men. There has been a line of criticism over Weber's conceptualization of charisma with respect to the locus of charismatic leadership that is charisma primarily the result of the situation or social context facing the leader, the leader's extraordinary qualities, or the strong relationship between charismatic leaders and followers. Hence, there is contrasting views on the issue and it is still an ongoing discussion about how much charismatic leadership is a function of the situation, the qualities of the leader, the relationships certain leaders have with followers or combination of these three perspectives [7].

Charismatic leadership theory often defined in a way similar to transformational leadership, has been quite popular all the times since its inception [6]. Although there is paucity of knowledge about the processes by which leaders/followers interact to have an impact on social changes [8], it has been proved that charismatic leaders unlike non-charismatic leaders adopt certain behaviors to effect their followers to respond in a certain way to generate social change that is charismatic leaders have the capacity to build strong emotional attachments with followers and in return as a reciprocal behavior get the followers' effort to meet organizational or societal challenges. They are described as passionate, driven individuals with magnetic personalities who are able to paint a compelling vision of the future [7]. According to House [9], charismatic leaders are dominant, selfconfident, have strong moral values and a desire to influence others. Coupled with such personality characteristics, they display certain types of behaviors i.e. strong role models, show competence, articulate goals, communicate high expectations, express confidence and arouse motives.

The main interest of this study is to focus on the characteristic of charismatic leaders' communication of high expectations for followers i.e. the motivational underpinnings of charismatic leadership. The reason being the outcome of this behavior is the increase in the followers' sense of competence and self efficacy [10] which as a result improves performance. As another characteristic of charismatic leaders relevant for the purposes of this study is their capacity to stimulate task-relevant motives in followers such as affiliation, power or esteem.

In alignment with Weber, House also thinks that charismatic effects are more likely to occur in situations where followers are in distress as in such stressful situations followers look for leaders who help them out their hardship [6].

Hence, based on the above mentioned motivational underpinnings and situational appropriateness for the requirement of use of charismatic leadership, charismatic leadership transforms followers' self concepts and tries to link the identities of followers to the collective identity of the organization. The way they achieve this is by setting high expectations for followers and supporting them to gain self efficacy [11] and confidence based on intrinsic rewards to view work as part of their identity [12]. Employees who work for transformational or supportive leaders are likely to exhibit organizational citizenship behaviors (OCB) [13].

Charismatic leaders distinguished by key behaviors relevant for this study is their risk taking, and goal articulation. These characteristics of charismatic leaders based on similarity attraction and needs fulfillment attract a set of followers. Hence, the followers having the same set of personal characteristics, beliefs and values follow charismatic leaders [14]. "Followers are purported to model the leader's values and goals, resulting in congruence between the leader's and followers' values and goals" [15].

Based on the current literature on charismatic leadership which complements charismatic leadership with a motivational theory i.e. self-concept related motivations to explain the relationships between leader behaviors and effects on followers to account for the transformational effects of charismatic leaders [12]. The analysis of followers' responses in a socialized charismatic leadership relationship shows that followers are more likely to show selfreliance and autonomy. Thus, there is both socialized and personalized empowerment. The relationship between charismatic leadership and followers' initiative oriented behavior is a sign of the fact that there is socialized empowerment. Follower initiative may encourage the socialized leader to govern in an egalitarian way to recognize followers' needs [16] and increase the intrinsic value of effort i.e. strengthening followers' belief of being counted and making the effort more meaningful as an expression of collective identity [17].

As a summary, charismatic leaders are likely to strengthen hospital employees' identification with the leader, the task, and the group, thus motivate their willingness to proactively embark in taking initiative-oriented behavior.

Hypothesis 1: Charismatic leadership is positively correlated with followers' initiative oriented behavior.

Initiative - oriented behavior

In today's world, work becomes more dynamic and decentralized with new emerging forms of management with minimum surveillance function, personal initiative of employees to identify and solve problems is highly required [18]. Organizations are interested in initiative directed behavior because it increases organizational effectiveness. Initiative like entrepreneurship implies the use of productive, creative and active strategies and overcoming problems in case they occur [19]. Ohly et al. [20] define initiative as "a specific form of employees' proactive behavior at work that focuses on self starting, proactive and persistent goal –directed behavior". It is thus the proactive nature of the behavior that has the potential to change and improve the current status quo rather than passively adapt to present conditions [18]. In hospital settings, there is a downward shift of responsibility and thus employees need to be willing to take initiative without constant close supervision [21]. In addition to the hierarchical organizational structure, the modernization of hospitals need flexible employees who approach work proactively going beyond task requirements and showing personal initiative [22].

Personal initiative is "work behavior characterized by its self starting nature, proactive approach and persistent characteristic in overcoming difficulties that arise in the pursuit of a goal" [23]. Similar to OCB, personal initiative is discretionary in nature [20,21]. However, it is worth noticing that personal initiative is a rather heterogeneous concept that covers organizationally desirable and undesirable behavior i.e. pro-organizational i.e. taking charge and pro-self types of initiative.

Conceptually distinct from personal initiative, individual initiative describes job related behaviors and is a specific type of OCB i.e. "the engagement of employees in task-related behaviors at a level that is so far beyond minimally required or generally expected levels that it takes on a voluntary flavor" [13]. Job autonomy has been proposed to be a correlate and antecedent of initiative. Anticipating future demand and preparing for them or preventing problems are typical goals of initiative. Initiative implies that employees deal with existing hurdles actively and persistently without giving up. Thus, it may also imply rebellious action against the supervisor [24].

In this research, for the purposes of the study, initiative-oriented behavior is defined as the extent to which an employee engages in self-initiating, future-oriented behavior that aims at enhances ongoing change processes at workplace and improving work outcomes.

Job autonomy

There is a great number of definitions of autonomy. Below is a short depiction of the literature on autonomy. Autonomy is "a dynamic process demonstrating various amounts of independent, selfgoverned, not controlled, or not subordinate behaviors and sentiments related to readiness, empowerment ..." [25]. Autonomy as defined by Stamps and Piedmonte [26] is the "the amount of job related independence, initiative, and freedom either permitted or required in daily routine activities".

Yet another definition is "the right of self-government, personal freedom of will and a self governing community" [27]. "Hall's classification of professional autonomy as a structural or attitudinal attribute i.e the worker's freedom to make decisions based on job requirements with the belief that one is free to exercise judgment on what one knows in decision making , forms the foundation for many disciplines". "Consequences of professional autonomy include accountability, empowerment and commitment to the profession" [25].

Autonomy is multi faceted, with multiple layers of interaction that have yet to be explored. Thus, it has to be envisioned more broadly as a tool to enable quality and focus of team-based decision-making [28]. However, there is a change in the definition of autonomy from "autonomy as freedom to practice, independence in nursing and decision making, the ability to self govern" to a recent one as "control over work, initiative, and freedom from bureaucratic restraints" [29]. The new trend of interdependence and shared control in health care also necessitates the use of autonomy at work. The dynamic nature of healthcare systems challenges the management system to find ways to strengthen partnership models and use team-based strategies to support autonomy of employees at health care settings.

Autonomous forms of motivation are the result of psychological needs of satisfaction and autonomy is one of the most crucial needs. The need for autonomy is basic to the emergence of intrinsic motivation (see self-determination theory, e.g. [30]). Based on that theory, the job characteristics model [31] advocates that "job autonomy is the extent to which a job allows freedom, discretion, and independence to schedule work, make decisions, and choose the procedures and methods to perform activities" [32]. Thus, job autonomy can activate intrinsic motivation.

The interprofessional conflict between doctors and nurses over boundaries of authority due to inequalities in the division of labor resulting from the hierarchical structure of management in hospitals is a long disputed issue in complex healthcare work [33]. Many nurses perceive that their autonomy is limited [34]. The patriarchal dominance by the medical professional [35], autocratic characteristics of the medical profession and governing/ controlling nature of nursing leaders [36] coupled with outdated bureaucratic style of management [37] hinders autonomous nursing practice.

Nurse autonomy has been found to promote teamwork as there is a synergy rather than conflict between autonomy and teamwork among nurses. Moreover, the nurses are reported to be more satisfied with their jobs and high tenure intentions [26].

Lack of perceived control at work for nurses leads to dissatisfaction at work. The ample evidence showing the importance of job autonomy to nurses job satisfaction exists in literature [38].

In sum, based on the argument that charismatic leaders stimulate followers' self-efficacy, the desire for job autonomy will be high in such charismatically led employees.

Hypothesis 2: Followers' job autonomy is positively related to followers' initiative-oriented be havior

Job stress

Although there is a great deal of research as to understand the nature of job stress (see Ganster and Schaubroeck [39] for a review), and debate on the definition of stress, the following is a generally agreed definition: "an unpleasant emotional experience associated with elements of fear, dread, anxiety, irritation, annovance, anger, sadness, grief, and depression" [40]. Although, in healthcare settings, work stress to conform to rigorous standards of cost-containment and quality assurance programs can be considered as useful criterion of hospital organizational performance [41], the constantly changing work environment i.e. the hospital settings, is generally considered to be quite stressful and the capacity to meet its demands are one of the primary sources of workplace stress for the nursing profession [42]. Although nursing is closely associated with stress, nurses are not equipped with coping skills and strategies to overcome stress [43]. Cox [44] states three levels of intervention that can be aimed at either individuals or workplaces i.e. firstly reducing or preventing risks and hazards, secondly changing the perception and way individuals respond to stress and how organizations deal with the problems as they arise, and lastly providing aid to those who suffer from stress. The stress experienced by health professionals is known as burnout and characterized by depersonalization, emotional exhaustion and diminishing sense of personal accomplishment resulting in such as absenteeism and turnover [45].

A leadership style that is supportive to the employees can reduce work stress by enhancing employees' sense of accomplishment. Among the major determinants of emotional exhaustion is lack of social support from superiors and colleagues coupled with task autonomy and feedback. Although it is mostly agreed that supervisory leadership behaviors play a crucial role in moderating the negative effects of work stressors, only a few empirical studies document this relationship [41]. Although supervisory roles of managers generally play a crucial role in mitigating or buffering the negative effects of work stressors [46], the empirical studies proving this relationship is limited and moreover, there are limitations to such studies [41]. Under conditions of acute distress such as difficult and challenging tasks in hospitals, the effect of personalized charismatic leader influence on the follower induces blind obedience to the follower [47]. This conflicts with the assumption that charismatic leadership enhances followers' discretionary behavior [48]. Thus, further studies testing this relationship with different contingency variables such as personality characteristics of the followers is required as charisma as a social process requires analysis of leader/follower interactions.

Moreover, healthcare employees will have less time and energy to engage in initiative-oriented behavior as they are more likely investing their time and energy in stress related coping behavior.

Consequently, high levels of strain at workplace will negatively influence the use of followers' initiative-oriented behavior.

Hypothesis 3: Followers' strain is negatively correlated to followers' initiative-oriented behavior.

Materials and Methods

Study Sample

The data for this study were collected by a selfadministered questionnaire method. The survey was distributed to 550 randomly chosen health employees from four public hospitals in Sakarya, Turkey. Four hundred two (402) usable questionnaires (response rate, 73%) were obtained, which is well above the critical sample size of 200 for developing structural equation models [49]. Sampling power was tested and deemed acceptable.

The descriptive characteristics of the study participants are summarized in Table 1. Males composed of 31.8% of the sample and females 68.2%. Of the sample, 73.9% were nurses, 16.7% were medical technicians and remaining 9.5% were physicians. About half of the respondents (51%) were under 30 years of age and another majority (74.2%) of respondents had working experience less than 10 years. Nearly one third of respondents (29.1%) were graduates of high school and another majority (38.6%) had associate degree.

Measures

Charismatic leadership was measured by a scale adapted from the work of Waldman et al. [50]. The scale consisted of seven items assessing a supervisor's behavior (e.g., "provides a vision of what lies ahead" and "makes people feel good to be around him/her"). For these items, Likert-type scale ranging from 1 (strongly disagree) to 5 (strongly agree) was used. Initiative-oriented behavior was determined by a four item scale developed by Staufenbiel and Hartz [51] and modified by Boerner and Dütschke [3]. (e.g., "I keep up with developments in the hospital" and "I try to keep abreast of changes within the hospital"). Initiative-oriented behavior items were scored on a 5-point Likert scale.

Followers' strain was operationalized with four items by Motowidlo et al. [40] and Beehr [52]: (a) "My job makes me feel worn out at the end of the day", (b) "My job is extremely stressful", (c) "When I come home from work, I am often too tired to do anything else", (d) "I feel a great deal of stress because of my job". These items were scored on a 5-point Likert scale.

Translation processes of these three scales involved the following four steps: (1) The scales were first translated into Turkish separately by two bilingual academicians who had doctoral degree in health administration. (2) Then these two different translations of the scales were reviewed by a bilingual assistant professor. By means of his suggestions, differences between the two forward translations were reconciled and achieved a single, provisional Turkish translation. (3) This version was back-translated into English by a sworn translator. (4) The back translated version and the original version of the scales were found to be quite similar. The content validity of the translated version was verified and validated by two experts in the field of management and organization. Additionally, some modifications were made related to some questions to facilitate penetrability of instrument according to suggestions of the experts.

To measure job autonomy, three items from Job Diagnostic Survey developed by Hackman and Oldham [31] and adapted into Turkish by Aşan [53] were used: (a) "How much autonomy is there in your job?..", "The job gives me considerable opportunity for independence and freedom in how I do the work", and (c) "The job not give me a chance to use my personal initiative or judgment in carrying out the work". Job autonomy items were scored on a 7-point Likert scale.

Gender	n	%	Marital Status	n	%
Female	274	68.2	Single	150	37.3
Male	128	31.8	Married	252	62.7
Position	n	%	Duty term (Year)	n	%
Physician	38	9.5	≤5	186	46.3
Nurse	297	73.9	6-10	112	27.9
Medical Technician	67	16.7	≥11	104	25.9
Age	n	%	Level of Education	n	%
≤25	68	16.9	High school	117	29.1
26-30	137	34.1	Associate degree	155	38.6
31-35	96	23.9	Undergraduate	85	21.1
36-40	56	13.9	Postgraduate	45	11.2
≥41	45	11.2			
Total	402	100.0	Total	402	100.0

Table 1. Descriptive Characteristics of the Respondents

Limitations

Use of Likert type self-report measure of personal initiative in predicting behavioral criteria is problematic as "personal initiative is defined on the level of observable, situated action" (see [19,54]). Second, this study has taken place in public hospitals and the questions stay unanswered what if it took place in the private hospitals. The organizational cultures and thereby the leadership styles of the leaders at private and public hospitals remain to be investigated through future studies.

Findings

Test of Validity and Reliability

In order to determine the construct validity of the scales used in this study, factor analysis was used. Prior to performing factor analysis, Kaiser-Meyer-Olkin (KMO) and Barlett's test of sphericity tests were performed, using SPSS, for sampling adequacy. Kaiser-Meyer-Olkin test outcome, which shows the consistency degree for a factor analysis with higher values, was 0.805. As a guideline, if the KMO value is more than 0.5, the factor analysis is acceptable [49]. Significance values for Barlett's test of sphericity, which is used to test if the variables in the population correlation matrix are correlated, showed reliability with the value of

Table 2.	Results	of	Validity	and.	Reliability	Analyses
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Kaiser-Meyer-Olkin Measur	re of Sampling Adequacy			,805				
Approx. Chi-Square								
Bartlett's Test of Sphericity	Df	Df						
	Sig.		,000					
Cronbach Alpha				0,789				
Total Variance Explained				67,677				
	Observed Variable	Factor	Variance Explained	a				
1 Charismatic Leadership		Louding	Lipiuniou					
CL6. Transmits a sense of m	ission	.849						
CL2. I have complete confid	ence in him/her	.846						
CL3. Makes people feel good	d to be around him/her	,836	24.670	0.911				
CL7. Provides a vision of wh	hat lies ahead	,806	,					
CL5. Generates respect		,805						
CL1. Shows determination w	when accomplishing goals	,766	1					
2. Strain								
S4. My job makes me feel w	orn out at the end of the day	,860	17,132	0,865				
S2. My job is extremely stres	ssful	,845						
S3. When I come home from	work, I am often too tired to do anything else	,829						
S1. I feel a great deal of stres	s because of my job	,807						
3. Initiative-oriented Behavio)r							
IOB3. I keep up with develop	pments in the hospital	,850						
IOB2. I attend and participate	e actively in meetings regarding the hospital	,823	15,156	0,802				
IOB1. I try to keep abreast of	f changes within the hospital	,731						
IOB4. I volunteer to take over	,689							
4. Job Autonomy								
JA1. How much autonomy is	830							
your job permit you to decide	,050							
JA2. The job gives me consid	826	10,718	0,627					
freedom in how I do the work								
JA3. The job not give me a c	.524							
in carrying out the work	,021							

p=0.000. The results from both tests indicate that the decision to use factor analysis in this particular case was supported by the data (see Table 2).

In total, 18 items were entered into the analysis and factor loadings > 0.50 were considered significant [55]. As a result of factor analysis, one item with loading of < 0.50 was eliminated from analysis: Item CL4 ("Communicates high performance expectations") from the charismatic leadership scale.

The factor analysis was conducted on the remaining items and is reported in Table 2. As was expected, four-factor model fitted the data. The percentage of total variance explained by the fourfactor model was high (approximately 68%). Only 24.67% of the whole variance was interpreted by the first factor (charismatic leadership), 17.13% of the common variance was explained by the second factor (strain), 15.15% of the common variance explained by the third factor (initiative-oriented behavior) and 10.71% of the common was explained by the fourth (job autonomy) (see Table 2). In factor analysis, an increase in the percent of explained variance yields a stronger factor structure. The percent of explained total variance ranging between 40% and 60% is accepted as adequate in studies based on social sciences [56].

Internal consistency values for each factor were computed using Cronbach's alpha reliability measures. As seen on Table 2, Alpha reliability coefficient of 0.78 was provided from overall instrument. Alpha values which were calculated to assess the reliability of the four study scales, ranged from satisfactory 0.63 to 0.91.

Table 3 presents the mean scores, standard deviations and inter-correlations of all constructs. As can be seen from Table 3, there was a significant positive association between charismatic leadership and initiative-oriented behavior. Additionally, there was a significant but negative association between strain and initiative-oriented behavior. However, job autonomy was not significantly related to initiative-oriented behavior.

Results from Hypotheses Testing

Structural Equation Modeling (SEM) was used to test hypothesized relationships between charismatic leadership, strain, job autonomy and initiative-oriented behavior. SEM is a technique used for specifying and estimating models of linear relationships among variables. Variables in a model may include both measured variables and latent variables [57]. SEM is a standard tool in psycho-

Table 3. Scales Means, Standard Deviations and Correlations

	Mean	SD	1	2	3	4
1. Job Autonomy	4,242	1,302	1			
2. Charismatic Leadership	4,226	1,111	,267**	1		
3. Strain	2,599	1,111	,159**	,020	1	
4. Initiative- oriented Behavior	4,465	0,907	-,027	,308**	-,192**	1

******. Correlation is significant at the 0.01 level (2-tailed).

Table 4.	Fit Measurements	s of Research Model
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Fit Measurements	Estimated Model
CMIN (χ 2)	325.925
Degrees of Freedom (DF)	111
p	0.000
CMIN/DF	2.936
Root Mean Square Error of Approximation (RMSEA)	0.069
Goodness-of-Fit Index (GFI)	0.92
Adjusted Goodness-of-Fit Index (AGFI)	0.89
Comparative Fit Index (CFI)-Delta 1	0.94
Normed Fit Index (NFI)	0.91
Tucker-Lewis Index (TLI))	0.92
Incremental Index of Fit (IFI)- Delta 2	0.94
Parsimony Goodness-of-Fit Index (PGFI)	0.67
Akaike's Information Criterion (AIC)	409.925

logy, sociology, marketing and education for investigating the feasibility of theoretical models [58].

Results of the study by Boerner and Dütschke [3] were used to guide to formulation of this study's model. In the proposed model, charismatic leadership, strain and job autonomy are exogenous independent variables and initiative-oriented behavior is the only endogenous dependent variable.

Before testing structural model, the model was tested by fit measurement indexes to be sure that all causal relationships were sufficient and the structural model was acceptable. Structural equation model can be examined after that the model has a good fit with the data. The various goodness-of-fit statistics are shown in Table 4 and present a good fit between the data and the model. For instance, CMIN/DF value of 2.936 and the values less than 3 are considered to be acceptable values in the literature [59]. Additionally, the goodness-of-fit (GFI) value of 0.92 falls well within the acceptable level and root mean square error of approximation (RMSEA) value of 0.069 falls well within the acceptable range of 0.05-0.08 and exhibits a good level of fit [60,61]. Tucker-Lewis Index (TLI: 0.92) and Incremental Index of Fit (IFI: 0.94) indicated a good fit within the accepted levels [62]. All statistics support the overall measurement quality.

Figure 1 shows the significant structural relationships among the study variables.



Figure 1. Results of Structural Equation Model

According to results of the analysis of the model, there were significant and positive relationships between charismatic leadership and initiative-oriented behavior while strain had a significant and negative association with initiative-oriented behavior. However, interaction between charismatic leadership and job autonomy was not significant. Charismatic leadership (estimated value=0.373, t=5.709) was the strongest predictor of initiative-oriented behavior followed by strain (estimated value=-0.252, t=-3.905). Additionally, charismatic leadership had positive effect on initiative-oriented behavior.

As seen on Table 5, of the three hypothesized relationships, two were statistically significant, that between the charismatic leadership and initiative-oriented behavior (Hypothesis 1), strain and initiative-oriented behavior (Hypothesis 3). Thus, H_1 and H_3 were supported by these results. However, H_2 was rejected, as the hypothesized relationship between job autonomy and initiative-oriented behavior was not statistically significant.

Conclusions

In this study, health employees' perception of charismatic leadership, strain and job autonomy was assessed for impact on their initiative-oriented behavior. The results of this study indicate that charismatic leadership has a positive influence on initiative oriented behavior and job strain has a negative influence on initiated oriented behavior. However, unlike the stated hypothesis, there is no relationship between job autonomy and initiative oriented behavior.

The finding that charismatic leadership was positively associated with employees' initiative behavior in the hospital context is consistent with the results of the study conducted by Boerner and Dütschke [3]. Their investigation revealed that the positive effect that charismatic leaders have on followers' initiative-oriented behavior in the German hospitals. According to this finding, if hospital managers want to foster their followers' initiative-oriented behavior they should choose a charismatic leadership style. There is evidence that charismatic leader behaviors may well generalize across cultures [63]. Bass [64] states that "charismatics appear in societies with traditions of support for them and expectations about their emergence". Thus, effective charismatic leadership may emerge in some cultures and not in some other cultures. On the other hand, Bass [65] asserts that charismatic/transformational leadership may be universal. There is also emphasis that transformational/charismatic leadership will be reported as facilitating outstanding leadership. Thus the results of this study can well be generalized in similar hospitals settings in other countries.

The unpredictability of the future, ambiguity and swift changes in the business environment are stipulating challenges for organizations and forcing leaders to take proactive actions [66]. The situation in the healthcare settings are even more complex and challenging of all contexts, both in terms of the actors involved i.e. highly specialized workforce and the patients, and the volatility of the environment in which various interpretations and constructions of leadership are negotiated and enacted. There emergence of charismatic leadership may find new interpretations in the healthcare setting. The healthcare settings depicted as complex, in crisis or chaotic require leaders to co-create contexts to which they have to respond. Hence, although charismatic leaders can strengthen hospital employees' identification with the leader, the task and the group, thus motivate them to engage in proactive initiative oriented behavior, the policy domain of healthcare systems is a strong factor in shaping leadership interventions and may relate to important problems about leadership engagement at all levels.

For the year 2003 to today, a series of changes and innovations were put into implementation in order to qualify health services provision in accor-

			1		1	
Hypothesized Paths				S.E.	t	Hypothesis
Charismatic Leadership	\rightarrow	Initiative-oriented Behavior*	,373	,045	5,709	H ₁ Accepted
Job Autonomy	\rightarrow	Initiative-oriented Behavior**	-,051	,095	-,816	H, Rejected
Strain	\rightarrow	Initiative-oriented Behavior*	-,252	,049	-3,905	H ₃ Accepted

Table 5. Results of Hypotheses Testing

*p<0.01, **p>0.05

dance with modern standards and in order to render them more efficient, effective and accessible in Turkish health care system [2]. These changes in the health care require that hospital workforce actively participate in the change process. There is an increasing need for self-initiative and future-oriented behavior in the hospitals. Doctors, nurses and other health employees should behave in an initiativeoriented manner that aims at stand for undergoing change process in their work environment.

Charismatic leadership can be learned and it can be the subject of management training and development. Several studies have shown that managers at all hierarchical levels can be trained to be charismatic [67]. For example, Frese et al. [68] demonstrated that action training to enhance some aspects of charismatic leadership was successful. In addition, Dvir et al. [69] revealed that a general training promoted charismatic leadership. Therefore, leadership training efforts are very important and hospitals should support the leadership training programs.

Another important finding is that followers' strain had a negative effect on their initiative-oriented behavior. Hence, to foster organizational change and support the employees to behave initiative-oriented, hospital managers should reduce employees' level of stress.

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Relationship between physical fitness variables and bone mineral density in Korean elderly women

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Abstract

The purpose of this study was to investigate the relationship between physical fitness variables and bone mineral density (BMD) in Korean elderly women. This study recruited 101 Korean elderly women aged 60-79 years who visited a public health center in Seoul, Korea. In July 2010, their physical fitness parameters were measured at this center: VO, max (mL·kg-1·min-1), sit-ups (reps/ min), grip strength (kg), sit-and-reach (cm), vertical jump (cm), whole body reaction time (msec), single leg stance with eyes open (sec), and vital capacity (L); BMD (g/cm³) was analyzed using central dual energy X-ray absorptiometry at the lumbar spine. Subsequently, the relationship between physical fitness and BMD were assessed using partial correlation analysis adjusted for age and body mass index (BMI). BMD showed a significant positive correlation with the number of sit-ups (r=0.336, p=0.001), grip strength (r=0.703, p <0.001), and vital capacity (r =0.550, p <0.001). However, BMD was not significantly correlated with VO₂max, vertical jump, whole body reaction time, time of single leg stance with eyes open, and the results of the sit-and-reach test (p>0.05). We concluded that BMD showed a significant positive correlation with muscular endurance, muscular strength, and vital capacity in Korean elderly women. However, BMD was not correlated with cardiorespiratory endurance, power, agility, balance, and flexibility.

Key words: bone mineral density, elderly, physical fitness variables

Introduction

Osteoporosis and related fragility fractures caused by falls have become serious public health problems worldwide, and their risk is projected to increase as the population ages (1). According to the World Health Organization (WHO) report, globally, falls are the second leading cause of unintentional injury deaths, causing approximately 424,000 deaths per year. Moreover, 37.3 million falls that are so severe that the patients require medical attention occur every year. Therefore, prevention strategies should place emphasis on training, education, creating safer environments, prioritizing fall-related research, and establishing effective policies to reduce the risk of falls (2).

Osteoporosis is one of reasons for fragility fractures caused by falls. Osteoporosis is a systemic skeletal disease that progresses with age. It is characterized by low bone mass and micro-architectural deterioration of bone tissue that consequently result in an increase in bone fragility and susceptibility to fractures (3). The well-known risk factors of osteoporosis associated with lifestyle and nutrition are nulliparity, prolonged secondary amenorrhea, smoking, excessive alcohol intake, physical inactivity, depression, prolonged immobilization, prolonged parenteral nutrition, and low body weight (4-6).

Recently, several studies have shown that physical fitness criteria such as muscular strength is associated with bone mineral density (BMD) because dynamic mechanical forces that depend on muscular strength act on bone and influence skeletal morphology (7-8).

Based on the principles of exercise prescription, physical fitness is divided into health- and motor-related physical fitness. Health-related physical fitness consists of cardiorespiratory endurance, muscular endurance, muscular strength, and flexibility. On the other hand, motor-related physical fitness consists of power, agility, and balance (9). Although physical fitness has been divided into several categories, previous studies have generally focused on muscular strength during the assessment of an association between physical fitness levels and BMD (10-11).

Muscular strength is certainly a significant risk factor for the prevalence of osteoporosis. However, supplementary studies are needed to characterize the relationship between physical fitness variables, such as cardiorespiratory endurance, muscular endurance, muscular strength, flexibility, power, agility, balance, and vital capacity, and BMD to establish the clinical principles for exercise prescription. Therefore, the purpose of this study was to investigate the relationship between physical fitness variables and BMD in Korean elderly women.

Methods

Subject

This study recruited 101 Korean elderly women aged 60–79 years. These subjects visited the public health center in Yangcheon-gu, Seoul, Korea, in July 2010 for the assessment of physical fitness and BMD. All study procedures were approved by the Human Care and Use Committee of the Institute of Sports Science of Seoul National University, and all subjects provided written consent.

Experimental procedures

The height and weight of the subjects were measured (Inbody 720, Biospace, Seoul, Korea) and their BMI (kg/m²) was calculated from the data obtained.

Physical fitness variables such as cardiorespiratory endurance, muscular endurance, muscular strength, flexibility, power, agility, balance, and vital capacity were measured as follows: VO_2max (mL·kg⁻¹·min⁻¹), sit-ups (repetitions/min), grip strength (kg), sit-and-reach (cm), vertical jump (cm), whole body reaction time (msec), single leg stance with eyes open (sec), and vital capacity (L).

For the measurement of cardiorespiratory endurance (VO₂max), the subjects were required to perform the YMCA submaximal cycle ergometry test (Helmas SH-9600K, Korea). VO₂max was estimated by gradually increasing the exercise intensity, starting from 150 kgm for 3 min as per the YMCA protocol (12). The heart rate of each subject was monitored using a Polar HR monitor system (Polar S610, Finland).

For the measurement of muscular endurance (sit-ups), the subjects were required to lie on the situp board (Helmas SH-9600N, Korea), bend their knees to 90°, grab their neck with both hands, and raise their upper body and bend forward, using only the abdominal muscles. This action was repeated for 1 min, and the number of sit-ups was counted.

For the measurement of muscular strength (grip strength), the subjects were required to turn the control lever of the grip strength dynamometer (Helmas SH-9600D, Korea), which is equipped with a potentiometer control system, and fit it to the second knuckle of their fingers. The maximum strength was measured while the subjects grabbed the dynamometer with force. The measurements were repeated 3 times, and the mean value was recorded.

For the measurement of flexibility (sit-andreach), the subjects were required to sit on the flexibility measuring instrument (Helmas SH-9600G, Korea), spread their heels approximately 5 cm apart, move their heels to the edge, stretch their knees straight, bend their back forward, and naturally move the measuring instrument board forward. The mean score from 3 sit-and-reach trials was recorded.

For the measurement of power (vertical jump), the subjects were required to jump to the greatest possible extent from a vertical jump board (Helmas SH-9600F, Korea). The height was measured in centimeters, and the mean value from 3 trials was recorded.

For the measurement of agility (whole body reaction time) (msec), the subjects were required to stand on a plate (Helmas SH-9600I, Korea) and flex their knees between 120° and 160°. The average duration (msec) from the 3 trials in which the subjects widened both their legs as fast as possible at the sound of a beep was recorded.

For the measurement of balance (single leg stance with eyes open), the subjects were required to stand on 1 foot on the balance measuring instrument (Helmas SH-9600H, Korea), with eyes open, using the preferred leg. We measured the time until the elevated leg touched either the other leg or the ground or until both the hands placed on the waist dropped; the mean result from 3 trials was recorded.

For the measurement of vital capacity, the subjects were required to attach the vital capacity measuring instrument (Helmas SH-9600C, Korea), equipped with a pneumatic sensor, to the mouth. The maximum exhalation volume (liters) was measured after deep inhalation. The physical fitness tests were carried out as per the recommendations in the book Advanced Fitness Assessment and Exercise Prescription (9).

BMD (g/cm³) was measured using dual energy X-ray absorptiometry (DEXA) at the average lumbar spine from L1 to L4; for this purpose the Hologic QDR-1000 DEXA scan system (USA) was used.

Statistical analysis

All the results were expressed as mean \pm standard deviation. The partial correlation coefficient was used to adjust for age and body mass index (BMI) when analyzing the correlation between physical fitness variables and BMD. Statistical significance was set at p < 0.05, and all the analyses were performed using SPSS ver. 12.0 (SPSS, Chicago, IL, USA).

Results

The characteristics of the subjects

The characteristics of the subjects are shown in Table 1. The average age of the subjects was 66.19 \pm 5.22 years, average height was 154.81 \pm 5.71 cm, average weight was 57.50 ± 6.53 kg, average BMI was 24.00 ± 2.50 kg/m², average VO₂max

Table 1. The characteristics of the subjects $(N = 101)$							
	Range	Mean ± SD					
Age (years)	60.00 - 79.00	66.19 ± 5.22					
Height (cm)	143.00 - 169.80	154.81 ± 5.71					
Weight (kg)	44.50 - 79.00	57.50 ± 6.53					
Body mass index (kg/m ²)	18.72 - 28.91	2400 ± 2.50					
VO ₂ max (mL·kg ⁻¹ ·min ⁻¹)	18.40 - 31.90	25.71 ± 2.72					
Sit-ups (repetitions/min)	0.00 - 22.00	8.98 ± 5.05					
Grip strength (kg)	11.30 - 45.20	24.75 ± 5.78					
Sit-and-reach (cm)	1.51 - 6.90	3.50 ± 1.18					
Vertical jump (cm)	5.10 - 31.40	16.65 ± 5.10					
Whole body reaction time (msec)	170.00 - 885.00	392.20 ± 132.95					
Single leg stance with eyes open (sec)	11.05 - 45.70	32.38 ± 7.23					
Vital capacity (L)	1.69 - 4.18	2.73 ± 0.54					
Bone mineral density (g/cm ³)	0.625 - 1.258	0.880 ± 0.151					

was $25.71 \pm 2.72 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$, average number of sit-ups was 8.98 ± 5.05 reps/min, average grip strength was 24.75 ± 5.78 kg, average value of sitand-reach test was 3.50 ± 1.18 cm, average height of vertical jump was 16.65 ± 5.10 cm, average whole body reaction time was 392.20 ± 132.95 msec, average time of single leg stance with eyes open was 32.38 ± 7.23 sec, average vital capacity was 2.73 ± 0.54 L, and average BMD was 0.880 ± 0.151 g/cm³.

The partial correlation coefficients analyses

The partial correlation coefficients that were used to adjust for age and BMI during the analysis of a correlation between physical fitness variables and BMD are shown in Table 2. BMD showed a significant positive correlation with the number of sit-ups (r = 0.336, p = 0.001), grip strength (r =0.703, p < 0.001), and vital capacity (r = 0.550, p < 0.001). However, BMD was not significantly correlated with VO2max, measurement of vertical jump, whole body reaction time, time of single leg stance with eyes open, and measurement of sitand-reach (p > 0.05).

Discussion

This study examined the relationship between physical fitness variables and BMD in Korean elderly women. BMD showed a high positive correlation with muscular endurance, muscular strength, and vital capacity, even after adjustments for age and BMI.

Variables	Bone mineral density (g/cm ³)				
variables	r	<i>p</i> -value			
VO ₂ max (mL·kg ⁻¹ ·min ⁻¹)	0.160	0.114			
Sit-ups (repetitions/min)	0.336	0.001**			
Grip strength (kg)	0.703	<0.001***			
Sit-and-reach (cm)	0.154	0.127			
Vertical jump (cm)	0.102	0.316			
Whole body reaction time (msec)	-0.180	0.074			
Single leg stance with eyes open (sec)	-0.036	0.724			
Vital capacity (L)	0.550	<0.001***			

Table 2. Partial correlation of bone mineral density and physical fitness variables in Korean elderly (N=101)

***p < 0.001, tested by partial correlation analysis after adjusted for age, body mass index

Previous studies have reported that dynamic mechanical force applied by muscle on bone influence skeletal morphology. Thus, muscular strength is surely associated with BMD (7-8). The results of our study also support the findings of previous studies that showed that muscular strength is strongly associated with BMD (r = 0.703).

Interestingly, our study showed that muscular endurance and vital capacity are also correlated with BMD. Several studies have shown that an increase in mechanical strain caused by physical activity (PA) results in bone deposition; however, a decrease in mechanical strain caused by immobility or disability results in bone resorption (13-14).

An increase in PA is strongly related to muscular endurance. Furthermore, the elderly undergo a phase of rapid physical decline, decrease in anabolic hormone levels, negative psychological changes, and central nervous system degeneration (15-19). We believe that although increase in PA is related to muscular endurance it might be sufficient to stimulate bone formation in the elderly. For this reason, in case of the elderly, muscular endurance level might be a good predictor of BMD levels. However, further well-designed studies are necessary to confirm this.

Legroux-Gérot et al. (2011) reported that lung function tests such as forced expiratory volume in 1 second (FEV₁) as the percentage of predicted FEV₁ (% pred) are correlated with BMD of the spine, hip, and femoral neck because a lower level of lung function adversely affects exercise capacity (20). Out study did not elucidate the mechanism by which lung function affects BMD. However, the results of our study support those of a previous study that showed that lung function is associated with BMD. Further, well-designed studies should be performed in the future to determine the correlation between lung function and BMD.

This study has some limitations. First, it only provides a correlation; it did not provide a cause and effect relationship. Second, because the study participants were recruited from a health promotion center at Yangcheon-gu, Seoul, Korea, they did not represent the entire Korean elderly women population. Third, the number of subjects who participated in this study (N = 101) did not constitute a large sample.

Conclusion

We concluded that BMD showed a significant positive correlation with muscular endurance, muscular strength, and vital capacity in Korean elderly women. However, BMD did not correlate with cardiorespiratory endurance, power, agility, balance, and flexibility.

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Evaluation of Group-Therapy Efficacy by Cognitive-Behavioral Therapy Method for Promoting General Health among Breast Cancer Patients

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Abstract

Purpose: This study performed to evaluate the efficacy of group therapy by cognitive behavior therapy method (CBT) in decreasing psychological disorders in breast cancer patients and their physical health progress. The main goal of this study was to determine the efficacy of group therapy by CBT in decreasing anxiety and depression due to breast cancer and its effect on physical health progress of these patients.

Material & methods: Statistical society of this research was all breast cancer patients between 30 to 50 years old who were under hormone therapy with Tamoxifen and referred to Tooba clinic. Total number of patients was 50 in which 16 of them were selected randomly. Patients were divided into two groups as case and control.

Results: Depression from mild to moderate was diagnosed by questionnaires and clinical interview. 12 sessions of CBT was performed for case group then both groups were examined.

Conclusion: According to covariance analysis the results showed that CBT decreases anxiety and depression and increases health level in patients with cancer. It can decrease clinical symptoms such as nausea, vomiting, sympathetic symptoms and insomnia.

Key words: Anxiety, Depression, Health promotion, cognitive therapy, Breast Neoplasms

Introduction

Although cancer diagnosis is not equal to certain death nowadays, all kinds of cancer are still the cause of 9% of death around the world. Cancer treatment is initiated with invasive methods almost always. Surgery can cause deformity. Radiotherapy and chemotherapy are performed after surgery to reduce malignant cells so the patient is forced to accept long term poisoned drug treatment. Cognitive behaviour therapists may incorporate stories, metaphors and analogies within their daily practice, when assessing suitability for treatment, challenging unhelpful styles of thinking, and addressing maintaining behaviours. The collaborative development of stories can enhance rapport, enable clients to gain a new perspective upon their problems, increase personal impact and clarity of meaning, and reinforce clients' motivation to effect therapeutic change. (1). For this reason cancer diagnosis causes hysterical and emotional problems in patients and their families. Some reasons for this problems are, implied meanings of diagnosis on patient's mind such as: probability of deformity, pain, financial and social issues, dependency, family division, death and also truly happening of some of these problems in patient real life. The most common psychological disorder in these patients is adjustment disorder. This disorder has some ethical subtypes such as adjustment disorder with anxiety, with depression and adjustment disorder with both anxiety and depression. Anxiety and depression can cause negative effects on functional condition, quality of life, admission duration and even treatment results(2, 3) .There are 4 different types of anxiety in cancer patients; situational anxiety or anxiety related to scary prospect of cancer; anxiety related to disease; anxiety related to treatment procedure; exacerbation of preexistent anxiety disorders (phobia, panic attack, GAD, PTSD, and OCD). But in these patients depression diagnosis is a bit harder. Because the neoplastic disease already caused some signs as asthenia, fatigue, impotency, insomnia, concentration and motivation loss (4). Most common factors which cause depression in physical patients are:

Long term treatment, invasive treatments, financial problems and lack of social supports such as insurance etc, social and familial issues, and biophysical changes caused by disease, side effects of drugs and treatment methods(5). Cognitive-behavioral therapy (CBT) is one of treatments that are used as psychological treatment in hard and chronic medical situations. A study on CBT showed effectiveness in cancer patients. This method can correct disease representation during treatment period by reducing fear and anxiety. Patients tried hard to control their doubts and fear in their lives by using CBT, paying attention on avoidable problems and feeling safe about their environment. Rebuild of non-logical cognition to resolve long term stress is effective on regular treatment and also it is effective on reduction anxiety in cancer patients(6, 7).

CBT causes self management in patient, incorporative relationship with health care agents and encouragement of taking active role in treatment. This approach is connected with correlation quiddity, patient-doctor relationship and creating of skill assortments to treat psychological problems(8, 9). CBT can specify that how believes had effects on patient's mind and feelings during admission and also had effects on the cause of treatment rejection in patients by emphasizing on non-efficient thoughts of cancer and evaluation of patient's mood at diagnostic time(10).

CBT is suitable for aiming initiator mechanism, enhancer and maintenance of psychological problems caused by cancer with the help of conceptbased thoughts and treatment methods evaluation. With those help we can prepare patient to tolerate physical treatment period and also we can decrease concerns of relapse. Then our patient will have enough living motivation(11). Enright said: it is logical to say that we don't have any physical or psychological problems that CBT don't have any effect on. Most of CBTs are short term for psycho-social problems treatment and they are defined as limited time interventions. They give patients the power to modulate their feelings about cancer and its effects.

Breast cancer patients experience the same emotional dysfunctions (anxiety, depression). First in this treatment method there are three dimensional models of human with emphasis on reciprocal relationship of cognitive, behavioral, psychological and emotional processes. Then patients accustoms to A-B-C sequences, means belief stimulator event or thought and its emotional consequence and they been helped to recognize their self- derived thoughts and basic beliefs. Patient is educated to register negative cognitions Then patients can modify their negative beliefs with primary reciprocal inhibition methods such as: opposite belief creation, active self-control (self-punishment, self-rewarding), harm and beneficial interpretation and self concept challenge. As a result they can reduce their anxiety and depression about cancer (9).

The goal of this study is the evaluation of group therapy with approach of CBT method to decrease anxiety and depression rate in breast cancer female patients and their general health.

Material and Methods

Our method was a semi experimental method with unmatched control group design with pre and post tests. In this study we observed all female breast cancer patients that were received Tamoxifen in Toba clinic in 2010. Total patients number was 50. Whereas in past studies such as Heimberg and Becker (12)(2002) and Bieling(13) (2006) ideal number for CBT was reported as 5-10. We selected 16 patients simple randomly then we put them into two groups of case (8 patients) and control (8 people). All patients participated in consultation session. Their rate of anxiety and depression was measured by the Hamilton Rating Scale for Anxiety (HRSA), the Hamilton Rating Scale for Depression (HRSD).

The Hamilton Rating Scale for Depression (HRSD), also known as the Hamilton Depression

Rating Scale (HDRS) or abbreviated to HAM-D, is a multiple choice questionnaire that clinicians may use to rate the severity of a patient's major depression(14). he Hamilton Depression Rating Scale has been the gold standard for the assessment of depression for more than 40 years(15).

HRSD measures 24 items such as:

- 1. Depressed Mood,
- 2. Work and Activities,
- 3. Social Withdrawal,
- 4. Genital Symptoms,
- 5. Somatic Symptoms GI,
- 6. Loss of Weight,
- 7. Weight Gain,
- 8. Appetite Increase,
- 9. Increased Eating,
- 10. Carbohydrate Craving,
- 11. Insomnia Early,
- 12. Insomnia Middle,
- 13. Insomnia late,
- 14. Hypersomnia,
- 15. Somatic Symptoms General,
- 16. Fatigability,
- 17. Feelings of Guilt,
- 18. Suicide,
- 19. Anxiety Psychic,
- 20. Anxiety Somatic,
- 21. Hypochondriasis,
- 22. Insight,
- 23. Motor Retardation, and
- 24. Agitation

In this scale each sign scored in 5 point scale. Total score shows depression intensity. Maximum score for each sign is 4 and maximum total score is 96.

Hamilton Rating Scale for Anxiety(16). HRSA is a 14-item clinician-rated scale to assess the severity of anxiety. THE HAMILTON ANXIETY RATING SCALE, This checklist is to assist the physician in evaluating each patient with respect to degree of anxiety and pathological condition-Hamilton Rating Scale for Anxiety measures 14 items such as

1. ANXIOUS MOOD: worries, anticipation of the worst, fearful anticipation, irritability,

2. TENSION: feelings of tension, fatigibility, startle response, moved to tears easily, trembling, feelings of restlessness, inability to relax,

3. FEAR: of dark, of strangers, of being left alone, of animals, of traffic, of crowds,

4. INSOMNIA: difficulty falling asleep, broken sleep, unsatisfying sleep and fatigue on waking, dreams, nightmares, night terrors,

5. INTELLECTUAL (COGNITIVE): difficulty in concentration, poor memory,

6. DEPRESSED MOOD: loss of interest, lack of pleasure in hobbies, depression, early waking, dirunal swing,

7. SOMATIC (MUSCULAR): pains and aches, twitchings, stiffness, myoclonic jerks, grinding of teeth, unstready voice, increased muscular tone,

8. SOMATIC (SENORY): tinnitus (ringing in ears), blurring vision, hot and cold flashes, feelings of weakness, picking sensation,

9. CARDIOVASCULAR SYMPTOMS: rapid pulse, palpitations, pain in chest, throbbing of vessels, fainting feelings, missing beats,

10. RESPIRATORY SYMPTOMS: pressure or constriction in chest, choking feelings, sighing dyspnea,

11. GASTROINTESTINAL SYMPTOMS: difficulty in swallowing, wind, abdominal pain, burnng sensation, abdominal fullness, nausea, vomiting, stomach gurgling/grumbling, looseness of bowels, loss of weight, constipation,

12. GENITOURINARY SYMPTOMS: frequency of urination, urgency of urination, stopped periods, heavy periods, premature ejaculation, loss of libido, impotence,

13. AUTONOMIC SYMPTOMS: dry mouth, flushing, paleness, tendency to sweat, giddiness, tension headache, raising of hair, gooseflesh, and 14. BEHAVIOUR AT INTERVIEW.

In this scale each sign scored in 5 point scale. Total point shows anxiety intensity. Max score for each sign is 4 and max total score is 56.

In researches were performed to evaluate reliability and validity of this scale, correlation coefficient was 0.6 with Beck questionnaire, 0.73 with SCL-90 and 0.77 with clinical evaluation (Black and Herson). Miz, Bowler, Philip and Hoser (1998) were reported correlation of 0.65 between anxiety semiology and anxiety mood. Convergence correlation coefficient of depression mood with this scale is 0.59 and 0.78 and differential correlation coefficient of anxious mood with this scale
is 0.25 and 0.69. Correlation coefficient of HRSA with Beck anxiety questionnaire is 0.51. Reliability of this test was reported by Haghshenas (1990) with reexamination.

Cases participated in 12 sessions of cognitivebehavioral group therapy after determination of anxiety and depression intensity. These sessions were performed by a psychologist based on CBT method twice per week for 2 hours. First psychologist discussed about reciprocal effect on thought, excitation and behavior. Then we introduced wrong beliefs that effect on excitation and behavior by education of automatic, intermittent and basic thoughts and cognition derivation.

Treatment was performed by benefit-harm thoughts determination, education of logical analysis, belief challenge and providing hierarchy of related situation with patient's basic beliefs, education of conceptual change criteria (adversary beliefs, supportive evidences of adversary beliefs), education of Cortico-autonomic inhibition method to control non logical beliefs and their consequences and education of self reward-punishment method. Then clinical interview, depression and anxiety tests of Hamilton were performed for both groups.

Statistical data were analyzed by SPSS-18 and in statistical level parametric tests like covariance were used.

Results

First theory evaluation

Based on results from table 1, group effect was significant because test level amount was lower than significant level (p<0.05) and level of observed F (F= 309.259) was higher than F level of table (F= 4.667) with df= 1 and 13 so cognitive-behavioral therapy is effective on decreasing depression.

	Variation Source	Sum Of Squares	Test Power	Test Level P	Table F	Fischer Test F	Mean Squares	Degree Of Freedom Df	Variance Homogeneity Test	R ² Squad	
1	Fixed Coefficient	2.322	136.0	375.0	667.4	844.0	322.2	1			
2	Group Effect	851.098	000.1	0.000	667.4	259.309	098.851	1	D=0.412	0.050	
3	Pre Test Score Effect	181.284	000.1	000.0	667.4	872.65	284.181	1	(P>0.05)	0.939	
4	Error	35.777					752.2	13			
5	Total	8879.00						16			

 Table 1. Covariance analysis test of theory 1

Results showed average score of depression was the same in both group before therapeutic period but after treatment in case group it was lower than controls and it was significant. Average point was decreased from 26.13 to 19.50. As a result cognitive-behavioral group therapy was effective on depression decreasing. Depression score of patient before therapeutic period is effective on this score after treatment. Also with evaluation of this table statistical power against table of covariance analysis, we can see statistical power increasing caused by group therapy. In fact more statistical power means more effectiveness of cognitive-behavioral group therapy.

	Post T	est	Pre Test			
Group	Standard Deviation	Mean	Standard Deviation	Mean		
Control	338/7	88/24	520/7	63/24		
Case	536/8	50/19	250/9	13/26		
Total	175/8	19/22	180/8	37/25		

Table 1. Descriptive Statistics of Depression Scores

Second theory evaluation

Based on results from table 2, group effect was significant (p<0.05) because F amount observed (66.838) was higher than F amount of table (4.667) so cognitive-behavioral group therapy is effective on post test score and also it is effective on decreasing anxiety score. Pretest score was significant too (p>0.05) because F amount observed (126.763) was higher than F amount of table so pretest anxiety score is effective on this score after therapeutic period.

With evaluation of this table's statistical power against table of covariance analysis we can see statistical power raise caused by group therapy and it means more effectiveness of cognitive-behavioral group therapy on anxiety score.

	Post T	`est	Pre Test			
Group	Standard Deviation	Mean	Standard Deviation	Mean		
Control	071.4	50.19	549.4	88.18		
Case	659.2	25.10	973.2	63.17		
Total	818.5	88.14	768.3	25.18		

Table 2. Descriptive statistics of anxiety scores

Third theory evaluation

General health score in control group was higher than cases pre therapeutic period but post therapeutic period in case group was higher than controls. Of course we observed significant improvement after treatment in case group and mean score of improvement reached to 2.25 from 1.25.

Rate of R" was 0.666 and it was a bit more than resulted amount. According to this high level coefficient, this model is suitable.

Based on results from table 3, group effect was significant (p < 0.05) because observed amount of F (31.497) was higher than F amount of table so cognitive-behavioral group therapy is effective on physical improvement progress.

With evaluation of this table statistical power against table of covariance analysis we can see increase of statistical power caused by group therapy and it means more effectiveness of cognitive-behavioral group therapy on physical improvement progress.

Table 3.	- Descriptive	Analysis	of	Improvement
Progress	Scores			

	Post To	est	Pre Test			
Group Standar Deviation		Mean	Standard Deviation	Mean		
Case	641.0	13.2	463.0	75/1		
Control	707.0	25.2	707.0	25/1		
Total	655.0	19.2	632.0	50/1		

Conclusion

In this study there was a significant difference between case and control groups' scores in depression, anxiety and health level. As a result cognition-behavioral therapy can decrease depression and anxiety and increase physical improvement. This study showed that CBT have a significant effect on depression and anxiety in patients with breast cancer and also it can increase their physical health(4). Patients with cancer experience a high level of anxiety due to disease condition and unpredictable future. Also hopelessness in this group of patients lead to depression maintenance

	Variation Source	Sum Of Squares	Test Power	Test levels	Table F	Fisher's test	Mean Squares	Df	Variance Homogeneity Test	R ² Squad
1	Fixed Coefficient	0.003	0.050	0.973	667.4	0.001	0.003	1		
2	Group Effect	138.552	000.1	0.000	667.4	66.838	138.552	1	D = 0.042	
3	Pre Test Score Effect	262.772	000.1	000.0	667.4	126.763	262.772	1	(P>0.045)	0.939
4	Error	26.984					2.073	13		
5	Total	4048.000						16		

Table 2. Covariance Analysis Test of Theory 2

Table 3.	Covariance	Analysis	Test for	Theory 3

	Variation Source	Sum Of Squares	Test Power	Test Level P	Table F	Fischer Test F	Mean Squares Ms	df	Variance Homogeneity Test	R ² Squad
1	Fixed Coefficient	1.134	0.739	0.015	667.4	7.918	1.134	1		
2	Group Effect	4.513	0.999	0.000	667.4	31.497	4.513	1	D-0.000	
3	Pre Test Score Effect	1.200	0.763	0.013	667.4	8.376	1.200	1	(P>0.000 (P>0.05)	0.666
4	Error	1.863					0.143	13		
5	Total	83.000						16		

so considering the psychological aspects in these patients is very important. Thoughts also effect on excitation and behavior as it can effect on patients' physiology so we should take these psychological disorders into consideration (8). Gielissen (2206) and et al. evaluated the effect of CBT on cancer patients' post therapeutic fatigue and their study showed that fatigue intensity in case group was significantly lower than control group. As a result CBT can help to decrease fatigue in patients with cancer(9). Edelman and et al.(1999) evaluated CBT effect on patients with breast cancer metastasis(8). They performed 8 sessions of CBT and their results showed that CBT can decrease depression and psychiatric disorders as it can increase selfconfidence. Bridge and et al. evaluated two compartments of CBT (relaxation and imagination) effect on patients with breast cancer (1988). 154 patients were selected randomly and were divided in 3 groups: A (control group), B (patients who were undergone only relaxation), C (patients who were undergone both relaxation and imagination). Results showed that group B had a higher level of calmness than control group. Group C had lower anxiety and higher calmness in comparison with group B. these results also showed higher level of improvement in women older than 55 years old. These results show that CBT can help to improve depression and anxiety in patients with cancer.

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Why and when do patients with pulmonary diseases die?

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Abstract

Introduction and Objective: Department of pulmonary medicine is interested in diagnosis and treatment of diseases like chronic obstructive pulmonary disease (COPD), pneumonia, lung cancer that are significant causes of mortality and morbidity worldwide. In this study, we aimed to investigate mortality rate, death causes and death times in patients who were hospitalized in pulmonary diseases clinic.

Methods: File records of patients who died in pulmonary diseases clinic of a university hospital between January 2006 and December 2009 were analysed retrospectively.

Results: It was detected that a total of 3553 patients of whom 2258 (64%) were males and 1295 (36%) were females had been hospitalized and of these patients, 243 patients (162 male-67%, 81 female-33%) had died in our clinic. Four-year mortality was estimated as 6.8%. Mean age was found as 68.4±11.3 years for male patients who died and as 72.5±12.5 years for female patients . Main causes of death, additional diseases and death times of 202 (83%) patients out of 243 were analysed. According to this, while main causes of death were detected as pneumonia (28.2%), COPD (27.2%), malignities of the lung and pleura (18.1%), pulmonary thromboembolism (6.6%) respectively, causes of death could not be determined in 15 (6.2%). An additional disease was detected in 135 out of 202 (56%) patients. The most common additional diseases were detected as cardiac diseases (25.7%), pulmonary diseases (23.3%), hypertension (20.8%). Respiratory failure (RF) was detected in 99 (49%) of dying patients. Twentyfour hours was divided into four equal periods in order to compare death times of the patients (06:00-12:00 h, 12:00-18:00 h, 18:00-00:00 h, 00:00-06:00 h). According to this, more patients with RF were found to have died during sleeping hours (between 00:00-06:00 h) (p=0.049).

In conclusion, pneumonia and COPD are the most common causes of mortality in our clinic. Additionally, the fact that more patients die between 00:00 and 06:00 suggests that staff on duty during these hours should be more carefull. Nevertheless, further miscallenous studies are needed to investigate the causes of death of patients with RF in this time period.

Key words: Mortality, respiratory failure, death time

Introduction

Diseases like COPD, pneumonia, lung cancer that leads to high mortality and morbidity worldwide are among the conditions taking place in speciality area of pulmonary diseases. According to data of World Health Organization (WHO), while COPD is the fifth leading cause of death worldwide in 2002, it is estimated to be the third leading cause of death in 2030 unless measures are not taken (1). Lung cancer accounts for 12.8% of cancer cases and 17.8% of cancer-related deaths worldwide (2).

At present, while infectious diseases-related deaths are gradually reducing due to common use of antibiotics and effective vaccination policies, pneumonias are still causes of high morbidity and mortality. Pneumonia is the sixth leading cause of death in UK and USA and the first leading cause of infection-related deaths (3). In our country, lower respiratory tractus infections are the fifth leading cause of death (4.2%) (4).

Clinics of Pulmonary Diseases in our hospital has a total of 37 beds of which 2 for tuberculosis, 4 for intensive care intermediate unit, 6 for allergy patients and 25 for general patients. In this study, we aimed to investigate mortality rate, causes of death and time of death of the patients who were hospitalized in our clinic between January 2006 and December 2009.

Methods

Records of the patients who died in the course of their treatment in the clinic of pulmonary diseases of our hospital between January 2006 and December 2009 were analysed retrospectively. Data of demographic features, diagnosis, additional diseases, causes and time of death were recorded from the files. Whether the patients had RF or not was evaluated with arterial blood gas analysis obtained in room air after their hospitalization. According to this, PaO2<60mmHg and/or PaCO2>50mmHg was defined as 'RF'. The patients who observed cardiopulmonary arrest however a asystole (flatline on electrocardiography) obtained despite effective cardiopulmonary resuscitation during their hospitalization were accepted as 'exitus' and this time was recorded as hour of death. The 24-hour period was divided into four equal parts in order to compare hour of deaths (06:00-12:00 h, 12:00-18:00 h, 18:00-00:00 h, 00:00-06:00 h).

SPSS (Statistical Package for Social Sciences) for Windows 15.0 was used for statistical analysis. For assessment of data, chi-square test was used for comparison of hours of deaths besides descriptive statistical methods (mean, standard deviation, frequency) and p <0.05 was accepted statistically significant.

Results

In a 4 year period, a total of 3553 patients (2258- 64% males and 1295- 36% females) had been hospitalized and treated in our clinic and a total of 243 patients of whom 162 (67%) were males and 81 (33%) were females were found to die. Four-year mortality was estimated as 6.8%. Mean age of the dying patients was detected as 68 ± 11 years for males, and 72 ± 12 years for females.

Mean causes of death, additional diseases and hours of death of 202 out of 243 (83%) patients of whose records were reached were analysed. According to this, while mean causes of death were detected as pneumonia (28.2%), COPD (27.2%), malignities of the lung and pleura (18.1%), pulmonary thromboembolism (6.6%), respectively, causes of death could not be determined in 15 (6.2%) (Table 1).

Table 1.	Main	causes	of	^c death	in	dving	patients
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Main causes of death	n	%
Pneumonia	57	28.2
COPD	55	27.2
Lung/pleura malignity	44	21.8
Pulmonary thromboembolism	16	7.9
Pulmonary tuberculosis	2	1.0
Interstitial lung disease	4	2.0
Cardiac diseases	4	2.0
Unclassified diseases	15	7.4
Unknown	5	2.5
Total	202	100

An additional disease was detected in 135 (56%) out of 202 dying patients. Additional diseases were determined as cardiac diseases (25.7%), extra-pulmonary diseases (23.3%), hypertension (20.8%) (Table 2). RF was detected in 99 (49%) of dying patients.

Table 2. Additional diseases of dying patients

Additional diseases	n	%
Cardiac diseases	52	25.7
Extra-pulmonary diseases	47	23.3
Hypertension	42	20.8
Diabetes mellitus	32	15.8
Neurologic diseases	24	11.9
Non-pulmonary malignities	10	5.0
Unclassified diseases	21	10.4

In order to analyse time of death of patients, one day (24 hours) was divided into four equal time periods (06:00-12:00 h, 12:00-18:00 h, 18:00-00:00 h, 00:00-06:00 h). According to this, patients with RF were detected to die more between 00:00 h and 06:00 h (p=0.049) (Image 1). Except this, a statistically significant relationship was not detected between demographic features, causes of death, additional diseases and hours of death.



* $PaO_2 < 60 \text{ mm Hg or } PaCO_2 > 50 \text{ mm Hg in blood gas}$ sample obtained in room air ** P < 0.05

Figure 1. Comparison of death times in dying patients with and without respiratory failure

Discussion

While infectious diseases related deaths are gradually reducing due to widespread use of antibiotics and efficient vaccination policies, both community acquired and nosocomial pneumonias are still causes of high morbidity and mortality (4,5). It is known that community acquired pneumonia develops in four million individuals in USA each year and it is the 6. leading cause of general deaths and the first leading cause of infection related deaths (5).

COPD is a common disease worldwide and deaths related to this disease is gradually increasing during recent 30-40 years. Despite the fact that coronary artery disease related deaths reduced 59%, stroke related deaths reduced 64% and other cardiovascular diseases related deaths reduced 35% between 1965-1998, COPD related deaths increased 163% during the same period. Changes in demographic structures in the world goes faster than the change in smoking epidemiology and works as a more important determinant in elevation of COPD (6,7). However COPD's being insufficiently known and diagnosed affects reliability of mortality data negatively. Additionally, COPD's being reported as the comorbidity in death reports despite its being the main cause of death leads to a reduced number of mortality than the real rates (8). For example, when death reports of 312,624 COPD patients who died between 1993-1999 were analysed, it is reported that COPD has been reported as the first leading cause of death only in 59.8% of the patients or it was reported as the additional disease (9).

While lung cancer is a rare disease at the beginning of 20. century, its incidence gradually increased in parallel with the elevation in smoking incidence and has become the most common cancer type in worldwide (10). Lung cancer accounts for 12.8% of cancer cases and 17.8% of cancer related deaths in the world (11). While 5 year of survival after diagnosis was 12% between 1974-76, it elevated little between 1992-97 and reached to 15% (12). Lung cancer incidence tended to decrease among men after 1980 as the result of anticigarette campaigns in United States and Western Europe communities. Incidence of lung cancer is gradually elevating in Eastern Europe countries and in our country because of increase in smoking habit among women (13).

As disesaes like lung cancer, pneumonia, COPD may frequently co-exist, it may be difficult to distinguish which is the primary disease leading to death or which is the comorbidity. This condition leads to different coding in death reports and causes reporting different ratios about mortality and comorbidity in international literature (14). For example, in analysis of 31 million US death certificates between 1979-1993, while COPD was detected to be reported in death certificates of 8% of dying patients, COPD was seen to have been recorded as the first leading cause of death only in 43% of them (15).

Kaynar et al. reported that 306 out of 9464 patients who were hospitalized and treated in clinics of pumonary diseases between 1988-2001 and mortality rates gradually increased over the yaers and elevated to 6% from 2%. Again in this study, they reported that when death reports and files were analysed, causes of death were recorded accurately only in 54% of dying patients, the most frequently seen main causes of deaths were COPD (36.2%), lung cancer (18.8%) and pneumonia (9.9%), respectively (16). Sezgi et al. reported that 384 (8.6%) out of 4417 patients who were hospitalized and treated in their clinic between 2004-

2009 had been died and the most common main causes of death were pneumonia (33.1%), COPD (31.2%), lung cancer (18.6%) (17).

In our study, similarly to the studies of Sezgi et al. 4-year mortality was estimated as 6.8%, the most common causes of death were detected as pneumonia (28.2%), COPD (27.2%), lung cancer (21.8%), respectively. As acute exacerbations of COPD is frequently presented with tracheobronchial infections and pneumonia, exactly distinguishing main causes of death may not be possible. However according to the results of both Kaynar and Sezgi et al. and our study, we may state that the most common causes of mortality in clinics of pulmonary diseases are pneumonia, COPD and lung cancer. Additionally, we may make a simple inference as that mortality will reduce with the reduction in smoking due to causation between these diseases and smoking.

In our study, when additional diseases of dying patients were analysed, as in the study of Sezgi et al, diseases like cardiac diseases, pulmonary diseases, neurologic diseases that are likely to be seen in advanced ages have been detected more frequent.

Number of studies comparing times of death according to hours of death in pulmonary patients is not enough in literature. Fletcher et al. reported that mortality increased in COPD patients between 01.00-07.00 (18). In a study of Nocturnal Oxygen Therapy Trial (NOTT) group, unexpected deaths were reported to increase in COPD patients during sleeping times at night, in other words sleep was reported to be a risk factor for these patients (19). In our study, one day was divided into four equal time periods and death times of the patients were compared. According to this, a difference was not found between patients when they were compared in terms of demographic features, causes of death, additional diseases, hours of death. Besides, the fact that patients with RF died more between 00:00-06:00 h (sleeping time) regardless of the primary disease was found to be consistent with data in literature.

Oxygen saturation decreases in supine position during sleep, especially in the elderly. This condition is related with reduced lung elasticity due to aging, impairment of respiratory regulation due to autonomic dysfunction and insufficient venti-

lation due to pulmonary or cerebral diseases (20). Nocturnal oxygen desaturation was reported to lead to arrhythmias, elevation in pulmonary artery pressure and mortality in acute phase in COPD patients (21). Dying patients in our study were generally the elderly (male: 68.4±11.3 years, female: 72.5±12.5 years). Additionally, most of them had pulmonary, cardiac and neurologic diseases. Advanced age and comorbidities enables to correlate high death rates during sleeping times with nocturnal desaturation. However it is not completely possible to examine whether this is resulted from patient-related causes or hospital or hospital staffrelated causes with the data of our study. This is the limitation of our study. Thus further miscallenous studies are needed to investigate why pulmonary patients with RF die more during sleeping time.

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Weight and neuro-psycho-motor development in children discharged from neonatal intensive care unit

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Abstract

Background: Low birth weight affects child growth and development, requiring the intensive use of health services. There are conversely proportional associations between prematurity and academic performance around the world. In this study we evaluated factors involved in weight and neuropsychomotor profile in one and two years old discharged from Intensive Care Units (ICU).

Methods/Design: We investigated 203 children from the ICU who were followed for 24 ± 4 months. The research was conducted by collecting data from medical records of patients in a Follow-up program. We investigated the following variables: inadequate weight at one year old; inadequate weight at two years old and a severe neurological disorder at two years old.

Results: We observed increase of almost 20% in the proportion of children which weighted between the 10th and 90th percentiles and decrease of around 40% of children below the 15th percentile, from one to two years old. In almost 60% of the cases neuropsychomotor development was normal at 2 years old, less than 15% of children presented abnormal development. Variables that remained influential for clinical outcome at 1 and 2 years old were related to birth weight and gestational age, except for hypoglycemia. Neurological examination was the most influential variable for severe neurological disturbance.

Conclusion: Hypoglycemia was considered a new fact to explain inadequate weight. The results, new in Brazil and difficult in terms of comparison, could be used to identify risk factors and for a better approach of newborn discharged from ICUs.

Key words: Child; Advance Care Planning; Epidemiology.

Introduction

Improvement in Medicine is a very important issue to be discussed nowdays [1-8]. Medical and technological advances in the last four decades has enabled significant improvement in survival rates of severe low birth weight and preterm newborns, providing reduction of neonatal mortality rates, especially regarding high-risk newborns survival. Progress of care quality reflected decrease in neonatal mortality rate as well as decrease in the severe disability rate from the '60s [9]. In the last 15 to 20 years this improvement was not accompanied by decrease in morbidity rate, which remained virtually constant throughout the world [10], and previous studies are focusing on treatment on this population [11-13].

Considering that birth and disability rates are keeping stable and that survivors rate is increasing, it is observed increase in the number of children at risk, often accompanied by severe neurological damage, which indicates the problem as related to public health area, due deleterious family, community, social, economic and individual effects that it causes [14].

Technology improvement exponentially raised costs, since the survivors need more intensive care and stay longer in the neonatal Intensive Care Unit (ICU) [15]. In addition, many infants present special characteristics after discharge, which makes them more likely to develop clinical problems, neurological disorders and growth and development deviations [10]. In order to monitor these disturbances it was created follow-up services of newborns at risk, which aim to identify and intervene in cases of persistent developmental abnormality, to recognize the natural history of transient abnormalities, to advise the family, to maintain a proper balance between security and diagnostic function, to reduce costs and to evaluate the performance of neonatal ICU [9].

During the first year of life, beyond the high risks of illness and death, the effects of low birth weight extended into the area of child growth and development, requiring the intensive use of health services [16, 17]. Throughout the first childhood preterm newborn present approximately 40 to 50% probability of special education care necessity. Learning is the main factor in this relationship of variables [18]. Moreover, there are conversely proportional associations between prematurity and academic performance [19-21]. Therefore, in this study we endeavored to evaluate factors associated to weight and neuropsychomotor profile in one and two years old children discharged from ICUs.

Methods

Study Population

We studied 203 children from the neonatal ICU, registered in the Follow-up Infant Risk Program of the Hospital Dr. Dorian Silva, Serra, Espírito Santo, Brazil (CNEP, 2000), who were followed for 24+4 months, from November 1994 to October 2004. The research was conducted by collecting data from medical records of patients in the Follow-up program. The hospital is part of the Unified Health System (Sistema Único de Saúde - SUS) and it is managed and maintained by the State Institute of Public Health (Instituto Estadual de Saúde Pública – IESP), linked to the Ministry of Health Secretary (Secretaria de Estado da Saúde - SESA, Epírito Santo). It is a general hospital which presents secondary and tertiary level profile and is located in Serra city, Espírito Santo, Brazil.

All newborns who are discharged from the neonatal ICU and that meet the admission criteria to the program were accompanied by their literacy or until complete seven years old. Due the discharge protocol from the program, an overview of the High Follow-up was given to the patient and included in the medical records.

Inclusion Criteria

We included children who were hospitalized in the neonatal ICU and when were discharged they attended the follow-up until two years old (24 ± 4) months), from November 1994 (program onset) to October 2004. It was included children who attended at least 4 appointments, including the last visit, around two years old. Once screened for inclusion criteria, among the 1000 patients enrolled in the Program during the period we selected 203 who met all these criteria simultaneously.

In order to assess whether the selected sample was representative of all patients admitted to the program we compared the sample of 203 patients with a sample of 37 patients randomly selected among 797 unselected. We evaluated the information relating to birth weight, gestational age [22]; Apgar score at 1 minute and 5 minutes of life, patient's origin (municipality), birth type, gender, the adequacy of birth weight to gestational age, the ICU neurological examination and the presence of hypoglycemia in the neonatal ICU. We concluded that the sample was representative.

Variables Evaluation

We evaluated the following variables regarding physical and neuropsychomotor parameters: inadequate weight at one year old; inadequate weight at two years old and a severe neurological disorder at two years old.

Prematurity was classified as: moderately preterm infants - gestational age from 33 to 36.9 weeks old and; severe preterm infants - gestational age between 28 and 32.9 weeks old. Newborns with extreme prematurity (23 to 27.9 weeks old) or borderline prematurity (gestational age lower than 23 weeks old) were not evaluated [23, 24] because they were not discharged from the ICU (death or transfer) or they parents did not look for the service after discharge or because they did not met the inclusion criteria.

Birth weight was defined as: macrosomic birth weight lower than 4000 g; appropriate birth weight - birth weight between 2500 and 3999 g; moderate low birth weight - birth weight between 1500 and 2499 g; very low birth weight - birth weight between 1000 and 1499 g [25 and; extremely low birth weight - birth weight lower than 1000 g [26, 27]. When we performed statistical analysis we decided to consider macrosomic and appropriate birth weight as only one group.

It was done adequacy of birth weight to gestational age (GA) related to two variables: birth weight with postmenstrual gestational age at birth. The relationship between these two variables gives rise to the following classification [28]: AGA newborns - appropriate birth weight for gestational age; LGA newborns - low birth weight for gestational age and; HGA newborns - high birth weight for gestational age.

In relation to neurological disorders, we considered the presence or absence of any neurological abnormality during the hospitalization in the neonatal ICU, any changes in neurological examinations, presence of seizures, any altered neurological complement test, for instance, transfontanelle ultrasound, presence of meningitis or any neurological diagnosis already established as central nervous system malformations (congenital hydrocephalus, brain and meningomyelocele) and genetic syndromes which damages central nervous system. We considered abnormal neurological examination during hospitalization in the neonatal ICU any child who showed any neurological sign at any of his/her neurological examination. For example: weak suction of neurological origin, persistent hyper or hypotonia; crying disorders; comatose states and lethargy or hyperexcitability of central origin. Epilepsy was not considered a change in neurological examination, but a new explanatory variable, depending on its importance. In other words, patients who presented epilepsy cases were not included among the patients with abnormal neurological examination.

The neurological examination was classified as normal or abnormal depending on the presence or absence of weak sucking of neurological origin, persistent hypertonia or hypotonia, neurological cry, coma and lethargy or hyperexcitability of central origin. Response variables were proposed as related to growth, inadequate weight at 1 year (IW1) and 2 years (IW2) old. Regarding response variables related to neurological performance we evaluated the presence of serious disorder of neuropsychomotor development at 2 years old, transitory neuro-motor dysfunction, cerebral palsy, neuro-motor retardation, behavioral disorders and comitial disturbances. Weight was measured close to 1 year and 2 years old, but not exactly on the birth day. To satisfy the normality assumption of residuals in these models we used the square root transformation of corrected age. Subsequently, the weight at 1 and 2 years old was compared to values presented in the NCHS (National Center for Health Statistics) curve. These measures were considered inadequate when they were below the 5th percentile or above the 95th percentile.

With regard to neuropsychomotor development at 2 years old, children who presented unfavorable neurological outcome at this age were classified into two categories: severe neurological disorder and mild/moderate neurological disorder, based on type of problem we had during the follow-up.

The dependent variable in logistic regression analysis was the occurrence of severe neurological disorder at 2 years old and it was classified as: Severe - Cerebral palsy (neuromotor dysfunction), Genetic or congenital disorders with central nervous system impairment, autism and West Syndrome associated to severe neuromotor retardation and; Mild/moderate - Transitory neuromotor dysfunction; behavior disorders and neuro-motor retardation.

Statistical Analysis

In order to compare quantitative variables we used Student t test, in cases of nonparametric distribution we applied Mann-Whitney test. Differences were considered significant when the probability of a Type I error was lower than 5% (p < 0.05). In qualitative variables we used the chi square test and when the expected frequency in any cell was lower than 5 we used Fisher's exact test.

To assess whether the physical and neuropsychomotor performance were influenced by his/her maternal and pregnancy complications, whether they were influenced by birth conditions as well as the newborns characteristics and their evolution in the neonatal ICU, we used generalized linear models (simple regression models and simple and multiple logistic regression). Given the number of explanatory variables, we used a stepwise method. To assess whether the models were well adjusted we performed residues analysis [29].

Initially, we applied univariate analysis; we calculated the number and percentage of patients who presented the considered outcome of the classes according to each explanatory variables category. Subsequently, for each explanatory variable it was adjusted univariate logistic regression model, from which it was obtained the initial estimative of odds ratios regarding its level of specification and the -2 *value (logarithm likelihood) used to provide us an idea of the model adjustment quality. For each variable we calculated odds ratio through a simple logistic regression model. Odds ratio was interpreted as the chance of a child with some characteristic (for example, who presented asphyxia at birth) provide inadequate weight at one year old, compared to a child without that feature (in this case, who did not present asphyxia birth). When the explanatory variable had more than two categories (i.e., birth weight) the odds ratio was calculated in relation to a reference category (in the case of birth weight, the category of normal weight or macrosomic). Next, we performed multivariate analysis. When there was high number of explanatory variables, we used the stepwise forward method [29].

Results

Figure 1 presents proportion of children in different percentiles at one and two years old. There was increase of almost 20% in the proportion of children which weighted between the 10th and 90th percentiles and decrease of around 40% of children below the 15th percentile, from one to two years old.



Figure 1. Children proportion in different percentiles at one and two years old

We observe in Table 1 and Table 2 the classification of newborns according to gestational age and birth weight, respectively. More than 50% was preterm, including moderate and severe preterm and great part of children presented low birth weight. *Table 1. Newborns classification according to gestational age*

Classification	Number of cases
Term (= or > 37 weeks)	68 (33.5%)
Moderate preterm (33-36.9 weeks)	85 (41.9%)
Severe preterm (28-32.9 weeks)	50 (24.6%)
Total	203 (100%)

Table 2. Newborns classification according to birth weight

Classification	Number of cases
Extreme low weight	8 (3.9%)
Very low weight	35 (17.2%)
Moderate low weight	85 (41.9%)
Adequate or marcosomic	75 (37%)
Total	203 (100%)

Table 3 displays neurological examinations in children at two years old. Almost 60% presented normal neuropsychomotor development. We noted that in relation to the type of neurological outcome severe cases (cerebral palsy, genetic or congenital disorder, autism and West syndrome) represented 14.8% and mild/moderate cases (transitory neuromotor dysfunction, behavior disorders and neuromotor retardation) represented 25.6% (Table 4).

Table 3. Neurological examinations in two years old children

Result (NPMD)	Number of cases
Normal	121 (59.6%)
Abnormal	82 (40.4%)
Total	203 (100%)
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NPMD: Neuro-psychomotor development

Table 4. Type of neurological outcome in two years old children

Туре	Number of cases
Neurological impairment absence	117 (57.6%)
Asymptomatic hydrocephalus	4 (2%)
Cerebral palsy	18 (8.9%)
Genetic or congenital disorder	9 (4.4%)
Autism	2 (1%)
West Syndrome	1 (0.5%)
Transitory neuromotor dysfunction	31 (15.3%)
Behavior disorders	15 (7.4%)
Neuromotor retardation	6 (2.9%)
Total	203 (100%)

We report in Table 5 final model estimative adjusted to inadequate weight at one year old (IW1). It is noted significance for very low and extreme low birth weight, presence of hypoglycemia and severe asphyxia.

In Table 6 we present final model estimative adjusted to inadequate weight at two years old (IW2). It is noted significance for low birth weight

associated to gestational age, presence of infectious problem and presence of perinatal process.

Table 7 displays final model estimative adjusted to neurological disorders at two years old. It is noted significance only for presence of abnormal neurological examination at the ICU.

Table 5.	Final model	estimative	adjusted to	inadequate	weight at	one year o	old	(IW1)
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Birth weight	Coefficient	OR	IC (OR, 95%)	p
Adequate or macrossomic				
Moderate low	0.24	1.28	0.53 : 3.06	0.59
Very low	1.71	5.50	2.03 : 14.93	< 0.01
Extreme low	2.93	18.66	1.79 : 194.43	0.01
Hypoglicemy				
Absent				
Present	1.02	2.78	1.16 : 6.67	0.02
Asphyxia				
No asphyxia				
Mild or moderate	0.81	2.26	0.50 : 10.09	0.29
Severe	1.16	3.18	1.42 : 7.12	< 0.01

Table 6. Final model estimative adjusted to inadequate weight at two years old (IW2)

Variables	Coefficient	OR	IC (OR, 95%)	p
Birth weight adjusted to gestational age				
Adequate				
Low	1.62	5.07	1.92 : 13.39	< 0.01
Infectious problem				
Absent				
Present	1.88	5.56	1.70 : 25.38	< 0.01
Perinatal infeccious process				
No				
Yes	0.89	2.44	1.06 : 5.59	0.04
Hypoglicemy				
Absent				
Present	0.94	2,56	0,98 : 6,68	0.05

Table 7. Final model estimative adjusted to neurological disorders at two years old

Variables	Coefficient	OR	IC (OR, 95%)	p
Abnormal neurological examination at ICU				
No				
Yes	1.09	2.98	1.20 : 7.38	0.02
Infectious problem				
Absent				
Present	1.10	2.99	0.83 : 10.74	0.09
Fetal pathologic process				
No				
Yes	0.71	2.04	0.86 : 4.83	0.10

Discussion

In this study we evaluated factors associated to weight and neuropsychomotor profile in one and two years old children discharged from ICUs. As main results we reported the following: increase of almost 20% in the proportion of children which weighted between the 10th and 90th percentiles; decrease of around 40% of one and two years old children below the 15th percentile; in approximately 60% of the cases neuropsychomotor development was normal at 2 years old; less than 15% of children presented abnormal development; variables that remained influential for clinical outcome at 1 and 2 years old were related to birth weight and gestational age, except for hypoglycemia and; neurological examination was the most influential variable for severe neurological disturbance.

We observed that 21% of the cases presented very low and extreme low birth weight. Among the 128 low birth weight newborns (low, very low and moderate low birth weight), only 8 (3.9%) weighted less than 1000 g and were all small for gestational age. An important issue related to children development is the maturity degree, which directs critical care interventional procedures to the most affected premature newborns [30]. In this study, the sample consisted of approximately 2/3 of premature newborns. Among them, approximately 2/3 was moderately preterm and 1/3 was very preterm newborns.

Due their special category behavior, small newborns for gestational age have deserving specific studies, directed to their particular problems that they have or are likely to present, different condition of appropriate and high birth weight newborns for gestational age. Only 38 children (18.7%) were small newborns for gestational age, among them 10 were term and 28 preterm (20 moderate preterm and 8 very preterm) newborns. However, the vast majority consisted of appropriate newborns for gestational age.

The 82 children who had adverse neurological outcomes were classified into two categories based on type of problem which they presented until up to 2 years old. Severe disorder was noted in 30 children (36.6%) and 52 (63.4%) presented mild to moderate disorder. Cerebral palsy accounted for 8.8% of all cases, 21.9% presented abnormal

neurological outcome and 60% belonged to severe cases. In mild/moderate cases there was predominance of transitory neuro-motor dysfunction, accounting for around 60% of mild/moderate. With respect to behavior disorder, the only change was hyperactivity (15 cases, 15.3%). Delayed neuromotor strains cases were still present at two years old, which corresponds to only 2.9% of children. Our findings are different of Barbosa [31]. who found only 44.4% of healthy children against 55.6% of children with any neurological disorder. Nevertheless, we found similar results to previous findings in the Central Hospital of IASERJ - Brazil [31], regarding the percentage of patients with cerebral palsy (9%). In the Hospital São Lucas -RJ – Brazil, 20% of preterm newborns developed cerebral palsy. However, we should consider that this study followed the children until 7 years old [31]; it may have contributed to this difference.

Some studies have already evaluated clinical profile of children admitted in ICU during the neonatal period. Hack et al [32] found 35 to 80% of patients without any neurological deficits, 8 to 57% with moderate disability and 6 to 20% with severe disability. Our results are in agreement with this report. Regarding the type of disorder, 10 to 20% presented mental retardation, 5 to 8% cerebral palsy, 2 to 11% blindness and 1 to 2% deafness [31]. McCormick [33] found 7.7% of cerebral palsy in newborns weighing less than 1500 g. Vohr et al [34] examined the neurofunctional development and prognosis of extreme low birth weight newborns at the units of the U.S. research network at the National Institute of Health, born between 1993 and 1994. A total of 1158 survivors with average weight of 768g were examined between 18 and 21 months old. The incidence of cerebral palsy was 17%, 2% were blind, 3% needed help for hearing and 37% presented serious development problems (developmental quotient assessed by Bayley < 70). It was previously detailed the incidence of mild moderate and severe sequelae in extreme low birth weight newborns and it was indicated that the incidence of severe sequelae ranged from 6 to 16% and 60% of extreme low birth weight newborns did not present development problems. This finding reflects the improved quality of care that has been occurring in developed countries which are currently directing their studies to extreme premature patients [23].

After inclusion of all explanatory variables, the following variables remained in the model: birth weight, hypoglycemia and asphyxia degree. The description of these variables in our study directs special attention to one and two years old children since the great majority of cases presented hypoglycemia.

By providing estimative of the final adjusted model to inadequate weight at 2 years old outcome, we reported that the variables that contributed the most to explain the late neuro-motor development outcome were appropriate weight for gestational age, infection problem, infectious process in the current pregnancy and perinatal hypoglycemia.

The explanatory variable related to obstetric evolution (perinatal infection process) remained significant in multivariate analysis, almost at the same odds ratio as in the univariate analysis, associated to this, it also remained significant the fact that the newborn presented infectious problem in the neonatal ICU with an odds ratio higher than the univariate analysis. We highlight the importance of infectious diseases on the evolution of newborns discharged from the ICU in the first 2 years of life. Hypoglycemia was also a significant variable with an odds ratio in the multivariate analysis higher than the univariate analysis. Regarding the influence which this fact exerted on weight inadequacy at 1 year old, it is noted that this was the only explanatory variable related to the newborns evolution in the ICU that remained significant for both univariate and multivariate analysis at 1 and 2 years old. This fact further strengthens its importance with respect to birth weight inadequacy in the first 2 years of life. With regard to newborns profile, it remained significant only appropriate weight for gestational age, where appropriate weight for gestational age and birth weight were significant. It reinforces the importance of birth weight on weight development in the first two years of life.

The only significant explanatory variable in the final adjusted model for severe neurological disorder outcome at 2 years old was abnormal neurological examination performed in the neonatal ICU. The others (infection problem and fetal disease process), however, although marginally significant, must be worthy of attention and their presence may mean a warning sign for future neurological problems, because it is not impossible that these variables provide different meanings.

In relation to severe neurological disorder development at two years old the significant variables presented close relationship, based on its definition, with some alteration of neurological nature. The only variable with no neurological connotation problem was the presence of infection in the neonatal ICU. We suggest this issue as a warning sign for future investigations.

In conclusion, among all variables analyzed, hypoglycemia was considered a new fact to explain inadequate weight while abnormal neurological examination at the ICU was related to neurological disorders at two years old. We emphasize the significance of these variables on the development of newborns discharged from the ICU in the first 2 years of life. The results, new in Brazil and difficult in terms of comparison, could be used to identify risk factors and for a better approach of newborn discharged from ICUs.

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Is standard cervical mediastinoscopy still a valuable operation?

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Abstract

Background: Mediastinoscopy is a widely used surgical procedure in the diagnosis of mediastinal disease and the staging of lung cancer.

Objective: To question the feasibility of mediastinoscopy procedure at a newly established thoracic surgery center.

Methods: Fifty patients who underwent mediastinoscopy at the Thoracic Surgery Clinic of Duzce University School of Medicine, between January 2009 and January 2011 were reviewed retrospectively.

Results: In a majority of cases, mediastinoscopy was conducted with diagnostic purposes, and frequently, sarcoidosis and tuberculosis diagnoses were made. Among patients with malignancy who had mediastinoscopy for staging purposes, N2 or N3 were determined in half of them. In mediastinoscopy, which has a 98% success rate, 16% morbidity rate was determined, where hoarseness due to nervus laryngeus recurrens damage and pneumothorax are frequently observed. There was no mortality among patients.

Conclusions: Although mediastinoscopy may cause various complications in newly established thoracic surgery centers, it is an essential surgical procedure that should be routinely applied to patients.

Key words: Lymph Nodes; Mediastinum; Mediastinal Diseases; Carcinoma, Bronchogenic; Mediastinoscopy; Morbidity

Introduction

Generally, in benign and malignant diseases associated with mediastinal lymphadenopathy, to be able to determine the most appropriate treatment approach, initially, tissue diagnosis obtained by histopathological examination is necessary. Through minimally invasive or invasive diagnostic methods applied for this purpose, ability to obtain sufficient tissue sample for histopathological and immunological studies is essential [1].

Today, standard cervical mediastinoscopy is frequently used at many clinics by thoracic surgery specialists due to its advantages such as high diagnostic reliability, and low morbidity and mortality rates. Mediastinoscopy is an invasive diagnostic method used in cases where a diagnosis cannot be established through non-invasive methods used for the staging of lung cancer patients and determining histopathological tissue type in primary mediastinal mass, malignant/benign diseases associated with mediastinal lymph nodes, and in a group with certain general diseases such as lung carcinoma that has mediastinum invasion or metastatic spread in mediastinal lymph nodes. Through mediastinoscopy, mediastinal lymph nodes can be imaged endoscopically and biopsy can be obtained from this region [2]. According to the lymph-node map proposed by Montain and Dresler [3], the lymph nodes that can be accessed via standard cervical mediastinoscopy are the highest mediastinal (Station 1), the upper paratracheal (Stations 2R and 2L), the prevascular and retrotracheal (Station 3), the lower paratracheal (Stations 4R and 4L), the subcarinal (Station 7), and sometimes the tracheobronchial (Station 10), and sufficient amount of biopsy materials can be taken from these lymph nodes [4].

In this study, by discussing indications, anesthesia method, complications formed, their management and results obtained from the mediastinoscopy procedure took place at a newly established thoracic surgery clinic we aimed to question the applicability of mediastinoscopy in this type of centers.

Material and methods

Population

In this study, 50 consecutive patients who underwent mediastinoscopy with diagnostic and staging purposes, at the Thoracic Surgery Clinic of Duzce University School of Medicine, between January 2009 and January 2011 were reviewed retrospectively.

Study design

The present study was carried out in accordance with The Declaration of Helsinki, and approved by the regional ethic committee.

During the pre-operative period, all patients received routine hematological and biochemical blood tests, and they had posteroanterior-lateral chest roentgenogram and thorax tomography. In case of the presence of mediastinal mass determined with radiological methods or mediastinal lymphadenopathy short-axis diameter measuring 1 cm and longer, to establish a tissue diagnosis in patients, non-invasive or invasive procedures such as bronchoalveolar lavage, bronchoscopic biopsy, transbronchial needle biopsy, transthoracic needle biopsy or scalene biopsy, one or more methods were used, however, unsuccessful cases were considered as an indication for diagnostic mediastinoscopy. On the other hand, in lung cancer patients whose tissue diagnosis are obtained and determined to have positron emission tomography with 18F-fluoro-2-deoxy-D-glucose method (PET) positive mediastinal lymph nodes, before surgical resection, histopathological examination of mediastinal lymph nodes is considered as mediastinoscopy indication with staging purposes [5]. In addition to demographic data such as gender and age, the patients were evaluated based on symptoms, mediastinoscopy indications, complications and histopathological results obtained.

Surgical procedure

Following the cervical mediastinoscopy incision and exploration, initially, the highest mediastinal region, including the deep jugular and brachiocephalic areas were examined; determined lymph nodes were excised and recorded as Station 1. Then, the mediastinoscope was inserted and multiple punch biopsies were obtained from the mediastinal mass or lymphadenopathies in diagnostic mediastinoscopies, and from 2R, 2L, 4R, 4L and 7 lymph node stations for staging purposes. All mediastinoscopy procedures were carried out by two thoracic surgeons and, in line with the routine practice, the number of samples was kept around the ideal number, sufficient to yield a result.

Histopathological examination

The specimens were promptly fixed in 10% formalin, processed for paraffin embedding, and 5 mm. sections were prepared. Hematoxylin-Eosin stained sections were used to evaluate histopathological findings by light microscopy. All of the samples were assessed by a single pathologist.

Management of anesthesia

All patients operated with general anesthesia received electrocardiogram, pulse oximetry and arterial monitoring with radial artery catheter in operating room. For anesthesia induction, intravenous 2 mg/kg propofol (1% Propofol flacon, Fresenius Kabi, Istanbul), 1 µg/kg remifentanil (Ultiva flacon, Glaxo SmithKline, Istanbul) and 0.6 mg/kg rocuronium (Esmeron flacon, Organon, Istanbul) were used. In 48 (96%) patients, intubation was carried out with appropriately sized spiral endotracheal tubes. In 2 (4.0%) squamous cell lung cancer patients, selective intubation with Carlens tube was carried out, thinking anatomic lung resection could be conducted at the same session with mediastinoscopy since there was no mediastinum involvement, however, when the mediastinoscope could not be inserted to the mediastinum along the anterior surface of the trachea, these tubes were replaced with spiral single-lumen tubes. Anesthesia was maintained using 10 mg/kg/h propofol and 0.2 µg/kg/min remifentanil, provided with 50% oxygen and 50% air. Propofol infusion was gradually reduced to a dose of 8 mg/kg/h and then down to 6 mg/kg/h. All patients were extubated at the operation room during the postoperative period without any problem, and then transferred to thoracic surgery services.

Statistical analysis

The results were recorded by the principal investigator and analyzed statistically upon completion of the study. The statistical analysis was performed using SPSS software, version 11.5 (SPSS, Inc., Chicago, IL). Clinical data were expressed as the median \pm the standard error of mean (minimum-maximum). The nonparametric Chi-square test was used for the comparison of categorical values, and a *P* value less than 0.05 was considered statistically significant.

Results

Patients comprised of 27 male (54.0%) and 23 female patients (46.0%). The mean age was 52.9 \pm 6.0 (26–77) years.

The most frequent symptoms were coughing (n=30, 60.0%), dyspnea (n=15, 30.0%), chest and/ or back pain (n=12, 24.0%), fever (n=7, 14.0%) and weight loss (n=4, 8.0%). There were statistically significant differences only for coughing and dyspnea (P<0.0001).

Mediastinoscopy was conducted in 40 (80.0%) patients for diagnostic and in 10 (20.0%) patients for staging purposes for a total 50 patients (P<0.0001).

Among the patients, while 3 (6.0%) had nervus laryngeus recurrens damage associated vocal cord dysfunction and resulting hoarseness, 2 (4.0%) had single-sided partial pneumothorax, 1 (2.0%) had vena cava superior damage associated hemorrhage, 1 (2.0%) had subcutaneous hematoma, 1 (2.0%) had wound infection, for a total of 8 patients (16.0%) with complications, there was no mortality. All of the results were statistically analyzed and no statistically significant difference between these complications could be determined (P>0.05).

Among patients who received diagnostic mediastinoscopy, sarcoidosis was determined to be the most frequently observed disease with 14 (28.0%) cases. Based on the histopathological examinations conducted on biopsies obtained from this group separately, tuberculosis lymphadenitis (granulomatous inflammation with caseation necrosis) in 13 (26.0%) patients, squamous cell lung cancer metastasis in 3 (6.0%) patients, Hodgkin lymphoma in 3 (6.0%) patients, lung adenocarcinoma metastasis in 1 (2.0%) patient, reactive lymph node hyperplasia in 1 patient (2.0%), thymoma in 1 patient (2.0%), small cell lung cancer metastasis in 1 patient (2.0%), histiocytosis in 1 patient (2.0%), thyroid tissue in 1 (2.0%) patient and nonHodgkin lymphoma in 1 patient (2.0%) were determined. All of the results were statistically analyzed, and statistically significant differences were determined based on sarcoidosis and tuberculosis lymphadenitis diagnoses (*P*=0.001).

Among patients who received mediastinoscopy for staging purposes, in 5 (10.0%) of them squamous cell lung cancer, in 4 (8.0%) of them lung adenocarcinoma, and in 1 (2.0%) of them malignant mesothelioma diagnoses were reached though non-invasive and invasive techniques used during the preoperative period. In this group, mediastinal involvement could not be determined in 5 (10.0%) patients, among 3 (6.0%) squamous cell lung cancer and 1 (2.0%) adenocarcinoma patients, N2 positivity, and in 1 (2.0%) adenocarcinoma patient N3 positivity were determined. No statistically significant difference could be determined between these results (P>0.05).

Discussion

This study underlines six points: (a) Mediastinoscopy was mainly conducted in patients with mediastinal mass or lymphadenopathies with unknown etiology for diagnostic purposes. (b) Patients who received mediastinoscopy commonly presented with coughing and dyspnea. (c) When the arising complications were examined, nervus laryngeus recurrens damage associated hoarseness and pneumothorax were observed more frequently. (d) In 98.0% of patients, diagnosis was made using the mediastinoscopy procedure. (e) In a majority of patients who had diagnostic mediastinoscopy, sarcoidosis and tuberculosis diagnoses were established. (f) In half of the patients who had mediastinoscopy for staging purposes, N2 or N3 were determined.

Mediastinoscopy is a golden standard surgical method since it fundamentally provides a good exploration area in the examination of mediastinal masses and mediastinal lymph nodes, it is effective, enabling the collection of numerous and sufficiently big tissue biopsy for histopathological examination, it can be easily implemented in a short time, cost-efficient and causes minimal discomfort to patients. Although, in recent years, the indication of mediastinoscopy has been expanded to include resection of mediastinal masses or removal of me-

diastinal foreign objects, throughout the world, the primary indication is the staging of mediastinal lymph nodes before thoracotomy in patients with lung cancer [6-9]. In this study, diagnostic/staging ratio of the mediastinoscopy procedure is 4/1. At our clinic, in patients who are diagnosed with lung cancer, we use PET, in order to investigate the possible presence of metastasis by scanning the whole body, and also to do staging by investigating the involvement of mediastinal and hilar lymph nodes. During the routine practice, despite the high positive predictive value of PET, since it is possible to obtain false positive results with PET in case of some infection and inflammatory disease, in lung cancer patients with positive PET, we use various invasive lymph node sampling methods including mediastinoscopy. However, since its negative predictive value is higher, in cases with negative PET, we do not perform invasive staging [8, 10]. The reason why this application is preferred is the high prevalence of infectious diseases and associated mediastinal lymphadenopathy in our country [9]. We believe that, the total number of mediastinoscopy performed on lung cancer patients have decreased for these reasons [11]. On the other hand, one of the main reasons for the high number of mediastinoscopy with diagnostic purposes is the low 'socio-cultural and economic status of the population' in Western Black Sea region, where the study was conducted, in addition to the failure to eradicate tuberculosis in this region due to insufficient regional healthcare system. Additionally, environmental antigens such as insecticides, talcum, aluminum, zirconium that initiate the inflammatory process causing the lymphoid tissue to become hyperactive are thought to be responsible for the etiology of sarcoidosis in these patients, and they are frequently encountered in this region due to the industrial sector and their frequent use in agricultural pesticides. Sarcoidosis is a multisystemic disease that is characterized by noncaseating granulomatous inflammation of affected structures, mainly mediastinal lymph nodes and the lungs [12]. Thus, this situation has led to an increase in the number of diagnostic mediastinoscopy used for the investigation of causes of mediastinal lymphadenopathies.

In patients with diffuse mediastinal lymph node enlargement, lymphadenopathy causing disease such as lung cancer, tuberculosis, sarcoidosis and lymphoma mainly causing respiratory system related symptoms such as coughing, dyspnea, chest and back pain, weight loss; in addition to formation of symptoms such as coughing and dyspnea due to the mechanical pressure of lymphadenopathies on the trachea and main bronchi are known to occur [13, 14]. In our study, the distribution frequency of similar symptoms we determined in our patients is consistent with the information from the literature.

Although mediastinoscopy in experienced hands carries low morbidity and mortality, serious complications such as hemorrhage, pneumothorax, recurrent nerve paralysis, tracheobronchial laceration, esophageal perforation, phrenic nerve paralysis, thoracic duct injury, mediastinitis and venous air embolism can be encountered, which warrants additional surgical interventions [15, 16]. In general, the prevalence of these types of complications seen in mediastinoscopy varies between 2-3% [16]. In this study, morbidity rate was determined to be 16.0% and there was no mortality. The complication we most frequently encountered was nervus laryngeus recurrens damage associated hoarseness. In all these cases, left vocal cord paralysis was determined through indirect laryngoscopy; 2 patients improved during the early period, in 1 patient, hoarseness was permanent. All cases consisted of lung cancer patients who received mediastinoscopy for staging purposes. In these patients, we believe that left recurrent laryngeal nerve damage occurs especially during the dissection of lymph nodes in lower left paratracheal and tracheobronchial areas. All these cases developed during the initial months of the study. In following patients, wide dissection was avoided in the low left paratracheal region and the development of this complication was prevented by not using cautery in this region.

The second most frequently encountered complication is pneumothorax. This complication which does not lead to any symptom was detected by chance in the routine chest roentgenograms during the postoperative early period. In both patients, an approximately 10-15% pneumothorax region with apical location was found on the right side, and these patients were observed by just giving them 100% oxygen, without tube thoracostomy. In these cases, spontaneous resolution was observed within a few days. We believe that, pneumothorax formation to be associated with mediastinal parietal pleura damage due to dissection especially around the right tracheobronchial angle.

Among all the complications, the most serious is the massive bleeding associated with vena cava superior damage in a female patient as a result of diagnostic mediastinoscopy. The bleeding area was packed with gauze compress for about 40 minutes with the mediastinoscope left in place, however when the bleeding did not stop, median sternotomy was performed and primary repair was done on the lacerated area located on the posterior wall of the middle of the vena cava superior. In cases of subcutaneous hematoma and wound infection each present in a patient, they were treated with hematoma drainage and suitable antibiotics, respectively.

In fact, this high morbidity rate is not an expected situation. Nevertheless, among these complications, only permanent hoarseness and vena cava superior damage created serious problems, other complications were treated easily. However, due to complications, the length of hospital stay increased and the total cost of the mediastinoscopy process, which is already a costly procedure, also increased even more. This situation may not be welcome at a newly established thoracic surgery center. Especially in case of major complications such as massive bleeding associated with large vascular damage consisting of pulmonary artery, vena cava superior or aortic arch or its branches; infrastructures, facilities and the adequacy of surgery-anesthesia team are crucial for amelioration of complications. However, we believe that surgical teams working at such centers should continue mediastinoscopy procedures without despair, since the management of associated complications can be successfully carried out, which was the case in this study.

In our country, although obtaining epidemiological data is still an unsolved problem, when the studies conducted are examined, in cases of diagnostic mediastinoscopy in our country, frequently sarcoidosis, tuberculosis and lymphoma diagnoses were obtained, and results from our study are consistent with this data [5, 9, 17]. During diagnostic mediastinoscopy procedure in this study, most frequently, sarcoidosis diagnosis was made. Among sarcoidosis patients, diagnosis can be made with mediastinoscopy in more than 95% of cases [2]. In all 14 sarcoidosis patients found here, sarcoidosis was is first place among the most likely diagnoses in the preoperative period and in all of them, diagnosis could easily be established through mediastinoscopy. On the other hand, in a study from Turkey, conducted by Demircan et al., tuberculosis lymphadenitis diagnosis using mediastinoscopy was determined to be 16.8% [18]. In our study, we believe the 26.0% rate that was determined to be due to tuberculosis still being a wide spread disease in this region. Diagnosis could not be made in only one patient (2.0%) among this group and histopathological examination of the biopsy material was reported as reactive hyperplasia. In this case, mediastinum was evaluated with video-assisted thoracoscopic surgery and large cell carcinoma diagnosis was established. In a study by Baysungur et al., among 357 patients who had diagnostic mediastinoscopy, final diagnosis was reached in 334 (93.0%) of them [17]. In general, since lymph node biopsies obtained through mediastinoscopy are suitable for microbiology, molecular biology and tissue culturing in addition to histopathological examination, high diagnostic rates can be reached. In our study, 98.0% diagnostic rate is consistent with information from the literature and this is encouraging for us [19, 20]. Additionally, we believe that patients receiving mediastinoscopy in the region they live and starting their treatment would reduce economic and business power loss to a great degree.

Lung cancer is a fatal disease whose incidence has been rapidly increasing in recent years, it is observed more in advanced countries due to cigarettes and environmental factors. In lung cancer patients, the disease is considered to be limited to the lungs, and among those without mediastinal lymph node involvement, anatomic resection and mediastinal lymph node dissection are still considered to be the most effective treatment method [21]. Among patients with lung cancer, mediastinoscopy enables histopathological examination necessary for the prognostic evaluation and establishing the real stage of the disease. Thus, by determining the operability of lung cancer patients, they can be directed to the correct treatment. In addition to this, the greatest contribution of mediastinoscopy to patients and hospital cost is its ability to prevent unnecessary thoracotomies. In

all cases where mediastinoscopy for staging was used, our goal has been reached and mediastinal nodal involvement could be assessed. In 5 out of 10 patients, N2 or N3 was determined, and thoracotomy was not performed on these patients, considering them inoperable, instead, neoadjuvant treatment protocol was used. However, 4 lung cancer patients who were determined to have N0 and 1 mesothelioma patient were operated on. The important role of mediastinoscopy in choosing the right treatment method for lung cancer patients and in extending survival time is supported by these results we obtained.

The present study has clear limitations. Limited number of cases stands at the forefront of these constraints. In addition, this study being a singlecenter one and the cost effectiveness of the procedure not having been established by determining the effect of complications on hospital costs are among some of them. We believe that the results obtained from this study can gain more meaning by further multicenter studies including greater number of patients. Furthermore; comparison of the results obtained by conventional mediastinoscopic lymph node biopsy with those obtained by lesser invasive methods such as needle aspiration under the guidance of endoesophageal/endobronchial ultrasound or extended/video-assisted mediastinoscopy could yield useful information in choosing the most appropriate technique [22-25].

Conclusion

Mediastinoscopy is an indispensable surgical method with high diagnostic rates; it is crucial in lung cancer staging and diagnosis of mediastinal lymphadenopathies or masses that cannot be diagnosed with any other methods. Besides advanced centers, although mediastinoscopy can also lead to complications at newly established thoracic surgery center, with devoted and courageous work of the surgical and anesthesia teams, it can be easily performed on all patients with an indication. Thus, frequent use of mediastinoscopy will provide the opportunity for this technique to be standardized, facilitating a careful and effective biopsy and dissection to be performed.

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Prevalence of Hepatitis B virus genotypes with HBsAg positive patients in the Northern of Iran (Mazandaran) during 2010-2011

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Abstract

Background: HBV infection is a major global health problem and eight genotypes (A to H) and multiples subtypes of HBV have been identified, and they show some distinct geographic distributions. The available data on HBV genotype in Iran are very heterogeneous and limited. Therefore in this study, we tried to identify the HBV genotypes by using polymerase chain reaction.

Methods: In this cross-sectional study, HBVpositive serum samples of 100 patients with chronic hepatitis from 2010 to 2011 were studied. HBV-DNA was extracted from plasma samples using QIAamp[®] MiniElute[®] Virus Spin Kit (Qiagen). Plasma samples from HBsAg positive were confirmed the presence of HBV nucleic acid and determined the genotypes of HBV genome by PCR using the DNA PCR kit (Cinagene) with Taq-DNA polymerase enzyme and type of specific primers. All samples were examined in the virology laboratory of Sari Medical School.

Results: The mean age of patients were 45 ± 25 (range, 20 to 70) year that 58 (58%) patients were male and 42 (42%) were female. The majority of HBV positive patients had a major surgery (44% patients) and then 32% patients had a family of hepatitis B virus infected. In this study, 69% had genotype D, 7% genotype B and 24% genotype D&B.

Conclusion: This study indicates that the genotype D is the most frequent followed by the mixed genotypes D&B and genotype B in our region. Prevalence and incidence of HBV genotypes are with distributed among of areas and different

genotypes may show different responses with antiviral therapy.

Key words: Hepatitis B virus, Genotype of HBV, PCR

Background

Hepatitis B virus (HBV) infection can cause liver diseases including chronic hepatitis, cirrhosis and hepatocellular carcinoma (1, 2). Current estimates that there are nearly two billion people worldwide have been infected with this virus and more than 350 million of people live with chronic infection, of these; 0.5-1.2 million people die annually from complications of chronic hepatitis B (3-5) which is the 10th leading cause of death worldwide. Throughout the world, carrier variability rate for hepatitis B infection is estimated to be 0.1% to 20% (6), with regions classified as having low (<2%), intermediate (2-7%) and high (>8%) endemimicity. In Iran, it is estimated that near 35% of population have been exposed to HBV and the endemicity is intermediate, with a carrier rate 3% (7). It was reported that the HBV infection indicates an intermediate rate in this country and the distribution of carrier rate of HBV infection in the different provinces of Iran shows different (1.3% to 6.3%) (8). After HBV vaccination program, Iran can be considered one of the countries with low HBV infection endemicity (9).

The HBV belongs to hepadenaviridae family and is an enveloped, double-stranded DNA genome of approximately 3200 bass pairs. So far, eight HBV genotypes (A-H) and multiple subtypes have been identified (10-13) and HBV genotypes have distinct

geographical distribution of the world (14-16). The study was shown that Turkish patients with chronic hepatitis B infection indicated very little genotypic heterogeneity. Genotype D of HBV represented almost the whole Turkish patient population infected with HBV (17, 18). In Pakistan, genotype D was the predominant type found in 128 (64%) patients followed by A in 47 (23%) and mixed A/D in 26 (13%) (19). A study was reported that 65.34% were classified into genotype D, 26.73% were of genotype B while 4.95% had genotype A. So in 2.98% samples, multiple genotypes were detected (genotype A+B; 1.98% and genotypes B+D; 1%) (20). In India, HBV genotype D was the most predominant (56.0%) genotype followed by HBV genotype C (23.4%) and HBV genotype A (20.6%) (21). The study demonstrated that genotype D (35.67%) is the predominant genotype circulating in Afghani's population and followed by genotype C (32.16%), genotype A (19.30%), and genotype B (7.02%) (22). In Iran, Several studies were shown that the only genotype circulating in the some provinces of Iran found genotype D. in different clinical forms of HBV infections (23-28).

The distribution of HBV genotypes may guide us in determining disease burden. HBV genotypes have been shown to differ with regard to prognosis, clinical outcomes and antiviral responses (29, 30). So, it is important to know the epidemiologically of HBV genotyping as well. The available data on HBV genotype in Iran are very heterogeneous. Therefore, this study was designed to determine and analyze the distribution of HBV genotypes among patients with HBsAg positive in Mazandaran province in the North of Iran by using polymerase chain reaction (PCR).

Materials and Methods

Samples

During 2010-2011, serum samples from 100 HBsAg positive patients with chronic hepatitis referred to Interior and Infections Disease Center in Sari Hospitals (Mazandaran province, north of Iran) were collected. Chronic hepatitis B was defined as infectious if the virus was persistent for more than six months. The blood samples were centrifuged and plasmas were separated and immediately stored at -70°C. All patients had elevated serum aminotransferases a positive test for HBsAg using enzyme linked immunosorbent assay (ELISA), and HBV genotypes were determined by DNA extraction kit using standard protocol. Factors such as, age, gender, suspected sources of infection (high-risk sexual relation, injective addiction and blood injection), last laboratory tests results (AST and ALT) were chosen through questionnaire for all patients. The data analyzed with SPSS 17 and Chi-square test.

DNA extraction

DNA extraction from plasma samples was extracted by QIAamp® MiniElute® Virus Spin Kit (Qiagen) using standard protocol. HBV was isolated from serum on following procedures; 25µl protease, 200µl plasma of patients with 200 µl AL Buffer (Lyses Buffer) mixed for 15 seconds by vortex and incubates at 65°C for 15 minutes, and centrifuges quickly. To add 250 µl Ethanol (96%-100%) and mixed for 15 seconds by vortex and incubates at room temperatures, after that all of them add to QIAamp Mini Elute columns. Samples were centrifuged for one minute at 8000 revolutions per minute (rpm) after finishing centrifuge, overlaid fluid separated and added in to the same volume. Next, tube content remained solution washed with 500µl of AW1 Buffer and centrifuged for one minute at 8000 rpm and discharged overlaid fluid, and washed with 500µl of AW2 Buffer and then washed with 500µl of Ethanol 96%-100%. Sample tubes centrifuge again for one minute at 8000 rpm and incubate for 3 minutes at 65°C for drying. Finally, 50 µl sterile distilled water or AVE Buffer added in the central above columns and incubated 1-2 minutes at room temperature, centrifuged at 14000 rpm for 1 minute. DNA quantification was determined using a spectrophotometer and resulted residue solved for next stages. All samples were examined in the virology laboratory of Sari Medical School.

PCR Test

Total DNA was isolated from serum samples and was done PCR-Test using DNA PCR kit (Cinagene) with Taq-DNA polymerase enzyme and according to special protocol with individual primers (31). Examination method summarized as follow: To make Master Mix of 1120 µl distil water, 30 µl dNTP, 150 µl 10x PCR Buffer and 90 µl $MgCl_2$. 11.5 µl of above reaction mix with 0.2 µl of Taq DNA polymerase, 40 pmol of each forward and reverse primers, 2 ng of DNA sample and up to 20 µl dH₂O. The above reaction placed into the Eppendorf Master Cycler PCR Machine and amplified. PCR program for amplification consisted of 95°C for 5 minutes, followed by 35 cycles of 94°C for 1 minute, 58.5°C for 1 minute and 72°C for 1 minute and finally, 72°C for 10 minute.

Gel Electrophoresis

Agarose gel electrophoresis is an easy way to separate DNA fragments by their sizes and visualize them. We use 1.5% agarose gel to run PCR product (DNA fragment) from samples. This is a graphic representation of an agarose gel made by "running" DNA molecular weight markers. These gels are visualized on a UV analyzer by staining the DNA with a fluorescent dye (Ethidium bromide which is *very* carcinogenic). The DNA molecular weight marker is a set of DNA fragments of known molecular sizes that are used as a standard to determine the sizes of fragments.

Results

During study period, 100 patients who had been infected to be HBsAg positive were enrolled in this study. It has been demonstrated that 91% of patients had chronic hepatitis and 9% of patients had acute hepatitis. The mean age of patients were 45 \pm 25 (range, 20 to 70) year that 58 (58%) patients were male and 42 (42%) were female. Eighty nine patients (89%) were married and eleven patients (11%) were single. The mean serum level of AST and ALT was 89.5 and 103.7 IU/lit respectively. In this study, majority (44% patients) of HBV positive patients had a history of surgery, and 32% patients followed by intra familial of hepatitis B virus infected and 11% of HBV positive patients had a history of blood transfusions. Our result also showed that some patients had cirrhosis.

Genotyping was using polymerase chain reaction of HBV DNA positive serum samples. Of these, 69 (69%) of cases were infected with genotype HBV-D, 7 (7%) were infected with genotype HBV-B, 24 (24%) were infected with genotypes HBV-D and HBV-B.

The most prevalent genotype in patients was genotype HBV-D (Table 1). There was no significant relation between HBV genotypes and according to gender, disease and age group (Table 2). *Table 1*. *Distribution of Hepatitis B virus genotypes*

in patients who referred t	o Sari Hospitals
table 1. Distribution of E	tepainis в virus genoiypes

Genotype	Frequency (%)
HBV-D	69 (69%)
HBV-B	7 (7%)
HBV-D+B	24 (24%)
Total	100 (100%)

PCR for identification of HBV genotypes by gel electrophoresis:

The method for detection subgenotypes of HBV was done agarose gel electrophoresis, which is an easy way to separate DNA fragments by their sizes and visualize them, and it could distinguish the genotypes of HBV. The size of HBV subgenotypes B and D were identified.

		Туре			Total (0/)	n valua	
		B (%)	D (%)	B+D (%)	10tal (70)	p-value	
Condor	Female	5 (11.90)	29 (69.05)	8 (19.05)	42 (100)	0.28	
Gender	Male	2 (3.45)	40 (68.97)	16 (27.59)	58 (100)	0.38	
Type of	Acute	1 (11.1)	4 (44.4)	4 (44.4)	9 (100)	0.252	
infection	Chronic	6 (6.59)	65 (71.43)	20 (21.99)	91 (100)	0.555	
	<25	2 (18.18)	7 (63.64)	2 (18.18)	11 (100)		
Age	25-45	3 (5.45)	44(80)	8 (14.55)	55 (100)	0.106	
	>45	2 (5.88)	18 (52.94)	14 (41.18)	34 (100)]	

Table 2. Genotypes distribution according to gender, disease and age group



Figure 1. The electrophoresis pattern of HBV genotypes by genotype specific primers amplification (31). 1-4 are HBV-D positive Samples (189 bp), 5 is a control positive, 6 is a control negative and 7 is 100 bp DNA marker



Figure 2. The electrophoresis pattern of HBV genotypes by PCR using genotype specific primers (31). 1 is 100 bp DNA marker, 2 is a positive sample (331 bp), 3 is a control positive and 4 is a control negative.

Discussion

The carrier variability rate for hepatitis B infection is estimated from 0.1% to 20% throughout the world (6). In the Middle East, it has been reported that HBV infection is an intermediate rate, varying between 2% and 7% in different countries (32). In blood donors, this rate was 0.8 % in Iran (33), 4 % in Pakistan (34), 1.1-3.5 % in Kuwait (35), 4.19 % in Turkey (36) and 1.9 % in Saudi Arabia (37). It can be concluded that HBsAg rate among blood donors in Iran is still less in comparison with other neighbouring countries of Iran. At present, HBV has been classified into eight different genotypes (A-H) by genome sequencing of HBV strains (10-13). Genotypes of HBV have different geographic distribution in the world (38, 39). The aim of this survey was to determine HBV genotype among of HBsAg positive patients who referred to Sari hospitals in the Northern of Iran. In this study, the majority of HBV positive patients had a surgery (44% patients), and 32% patients had a family of HBV infected, and 11% of patients had a history of blood transfusions. The results showed that among the 100 samples, the proportions of genotype D, B and mixed genotype (D+B) were 69%, 7% and 24% respectively. Same to our study, it has been shown the HBV genotype D is distributed worldwide, and reported frequently (20-23, 40). It has been reported that the distribution of HBV genotypes was not just one genotype but some samples were mixed. It has been reported that 62.2% were found genotype D, 13% were found genotype A and 12%. Mixed genotype D+A was found in 12% of acute patients, 5.6% of chronic patients and 5.6% of carriers (40), 85.1% were genotyped as type D/E, 4.4% were genotyped as type A, 1.4% were genotyped as type C, and 0.7% were genotyped as type F (41) and other study was indicated the HBV genotype frequencies were: B, 57.9%; C, 16.0%; and BC, 26.1% (42). A study conducted among injecting drug users showed that the presence of genotype D in 62%, genotype A in 9% while 29% individuals were found to be infected with both of genotype A and D (43). But some studies from different part of Iran have reported that the genotype D is the only detectable genotype in the different clinical forms of HBV infection, including carriers HBV, chronic liver disease and cirrhosis (23-28) that is not the same as our results because we found HBV genotype D, B and mixed D+B. Genotypes A and D were most prevalent in co-infected patients with HIV and so, HBV subtype A was present among three-fourth of patients infected through sexual contact, whereas the same percentage of subtype D was isolated among injection drug users (44).

HBV genotyping may guide us in selection of the duration and type of antiviral therapy and to predict the likelihood of sustained HBV clearance after therapy. It seems that there are different types of HBV genotypes in different parts of countries, due to wide range of geographical distribution and influence of the neighbors in the abundance of different types of HBV genotypes. Furthermore, factors such as repeated blood transfusion and treatment of the patients also can be some of the most important criterias which can cause this wide range of different genotypes. In conclusion, the present study describes HBV genotyping in Mazandaranian (in the north of Iran) patients infected with HBV. This preliminary report describes that the genotype D is not the only genotype in the patients with HBsAg, which is different as other studies. Thus, further studies are needed to achieve the confirmation and so to determine the distribution of genotype of HBV subtype in patients with HBV positive.

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Oxidative Stress And Altered Levels of Oxidants And Antioxidants in Acute Ischemic Stroke Patients in A Region of East Turkey

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Abstract

Background and purpose: Ischemic stroke is one of the most important diseases causing severe disability and death. Hypertension is the most important risk factor in strokes, representing roughly 70% of all cases. Oxidative stress plays an important role in acute ischemic stroke (AIS) pathogenesis. It is believed to be one of the mechanisms taking part in neuronal damage in stroke. Free radical formation and subsequent oxidative damage may be a factor in stroke severity. In 28 patients with AIS and 28 healthy individuals were investigated with regard to relationship between ischemic-stroke and glutathione peroxidase (GSH-Px), catalase (CAT) activities, malondialdehyde (MDA), glutathione, β -carotene, vitamin A levels.

Methods: GSH-Px, CAT activities and MDA, GSH, vitamin A, β -carotene levels were measured by spectrophotometry in 28 subject (15 females and 13 males aged 67.1±13.3years) with AIS and 28 age-matched healthy subjects (13 females and 15 males aged 65.9 ± 10.1).

Results: In the patients with acute ischemic stroke, GSH-Px activity and MDA, GSH, vitamin A levels were found increased (p<0.001). Whereas there was no significant difference in level of β -carotene and CAT activity between AIS patients and control group (p>0.005).

Conclusions: Our results suggest deleterious effects of oxidative stress on clinical outcome in AIS. There was a significant increase in levels of MDA, GSH-Px and GSH. GSH elevation seemed to be a part of adaptive mechanisms

Key words: Stroke ischemic; Oxidative Stress; Antioxidants; Oxidants; Risk factors.

Introduction

Interrupted blood flow to an area of the brain caused by a clot or ruptured blood vessel can result in the death of brain cells, or stroke. According to the National Stroke Association, up to 80 percent of strokes are preventable, yet stroke is the third-leading cause of death or adult disability in America. Antioxidants may play a significant role in reducing the abnormalities underlying or causing damaging functional changes associated with stroke(1, 2, 3). Stroke is the third most common cause of death in most western populations after coronary heart disease and cancer (4, 5). Ischemic stroke accounts for about 75% of all cases while hemorrhagic stroke is responsible for almost 15% of all strokes. Acute ischemic stroke (AIS) is a sudden loss of brain function resulting from interference with the blood supply to the central nervous system (1, 2, 3, 6).

Brain injury after AIS develops from a complex series of pathophysiologic events including oxidative stress and inflammation (7). In acute cerebral infarct, fractional uptake of oxygen in brain tissue is not sufficient to maintain cellular oxidative metabolism. This causes metabolic changes and possibly cellular death. The brain is especially prone to free radical damage for several reasons. It is very rich in polyunsaturated fatty acids, which are particularly vulnerable to free radical induced peroxidation, but also has a low content of antioxidant enzymes such as catalase (CAT) and glutathione peroxidase (8) Restoration of blood flow could have negative consequences such as generation of free oxygen radicals. Superoxide (O_2^-) and hydroxyl (OH^-) react with unsaturated lipids of biomembranes, resulting in the generation of lipid peroxide radicals, lipid hydroperoxides and fragmentation products such as malondialdehyde (MDA). MDA is known as marker of the oxidative damage (9,10).

Reactive oxygen species (ROS) play key roles in the cascade of brain injury after stroke, and strategies to increase the antioxidant defenses of neurons after stroke hold great promise. Glutathione (GSH) is a sulfhydryl (SH) containing tripeptide (Glu-Cys-Gly). It has several major physiological functions: it maintains SH groups of proteins in a reduced state, participates in amino acid transport, detoxifies foreign compounds, enzymatically degenerates endogenous peroxides, forms bioactive molecules and acts as a coenzyme in several enzymatic reactions. It possibly acts as a major defense against the toxicity ROS and reactive nitrogen species (RNS) in the brain (11). GSH reacts readily and favorably with RNS, thus affording cellular protection against oxidative damage (12, 13). Plasma glutathione peroxidase (GSH-Px) is a major antioxidant enzyme in plasma and as a member of the selenocysteine-containing GSH-Px family, scavenges hydrogen peroxide and organic (lipid) hydroperoxides produced during normal metabolism or after oxidative insult (14). Catalase (CAT) is present in the peroxisomes of nearly all aerobic cells and serves to protect cells from the toxic effects of hydrogen peroxide by catalyzing its decomposition into molecular oxygen and water without ROS production (15). CAT is one of antioxidative factors involved in elimination of ROS (10). In some recent clinical studies, one or several of these antioxidant enzymes were measured in blood as possible biological indicators. This study was designed to examine the serum levels of GSH-Px, GSH, CAT, MDA, vitamin A, b-carotene in acut ischemic stroke and the correlations between them and with stroke severity. Free radical formation and subsequent oxidative damage may affect stroke severity.

Materials and Methods

Subjects

This study consisted of 28 patients with AIS (15 females and 13 males) from Department of Neurology, School of Medicine, Firat University, in Elazig region of Eastern Turkiye. 28 normal healthy volunteers (13 females and 15 males) composed the control group. All the subjects were Turkish. All patients were classified according to Trial of ORG 10172 in Acute Stroke Treatment criteria (TOAST).

A CT scan of the brain was performed in all patients. Subjects with hemorrhagic stroke, with other neurological diseases, or taking iron or antioxidant vitamins during the months preceding the enrollment were excluded. Control subjects were age- and sex- matched healthy relatives of hospital employees. None of the controls was undergoing pharmacological treatment. All the members of patient and control groups were informed about the study and all subjects gave informed consent to participate in the study. On admission, all patients underwent full physical and neurological examinations. Vascular risk factors, including hypertension, diabetes, and smoking habits, were recorded.

Methods

We measured levels and activities of several antioxidants in plasma during the first week after acute ischemic stroke to verify whether they were associated with stroke severity and early outcome. In the patient groups, an initial sample of blood was collected in a sodium heparin tube on admission (T1) and then after 7 days (T6). In the control group, blood was obtained in the morning after an overnight fast. The levels of GSH-Px, MDA, CAT, GSH and β -carotene, vitamin A were measured. All samples were centrifuged at 3000 rpm for 15 minutes at +4°C, and after sera were separated, then the sera were stored at - 20°C until analysis.

Antioxidant Measurements

Glutathione Peroxidase Assay: Erythrocyte GSH-Px activity was measured by the method of Beutler in which cumene hydroperoxide was used as substrate (16). Oxide glutathione (GSSG) produced by the action of erythrocyte GSH-Px and cumene hydroperoxide was reduced by glutathione reductase and NADPH. The decrease of the NADPH concentration was measured at 340 nm. The enzyme activity in erythrocytes was expressed as units per gr of Hb (U/g Hb).

Glutathione Assay: Total GSH measurements were performed by the method of Tietze (17). The absorbance was measured at 412 nm using a spectrophotometer. The GSH concentration was determined using Standard aqueous solutions of GSH. Results were expressed as mmol/g Hb. *Malondialdehyde Assay:* The end-product of polyunsatured fatty acid peroxidation, MDA, which reacts with thiobarbituric acid in serum samples, was determined by the methods of Satoh and Yagi (18, 19). Reaction of MDA with thiobarbituric acid (TBA) has been applied widely to assess lipid peroxidation in biological material. The reaction yields a red MDA-TBA adduct, the product of 2 mol of TBA plus 1 mol of MDA. The colored complex can be quantified spectrophotometrically from its visible absorbance (max 532 nm) and is readily extractable into organic solvents such as butanol. The values of MDA reactive material was expressed as MDA quantities for plasma volume (nmol/ml plasma).

Catalase Assay: Erythrocyte CAT activity were determined according to the method of Aebi and expressed as K/gHb (20). The decomposition of H_2O_2 can be directly followed by the decrease of absorbance at 240 nm. The difference in absorbance at 240 nm per time unit allows to determine the CAT activity.

Vitamin A and \beta-carotone assay: Serological tests were used to measure the levels of Vitamin A and β -carotone. Vitamin A and β -carotone in serum samples were determined according to the method of Suzuki and Katoh (21).

Statistical Analysis

The Statistical Package for the Social Sciences (SPSS) 15.0 (SPSS Inc, Chicago, IL, USA) was used for statistical analysis and statistical significance was defined as P<0.05 and P<0.001. Results were given as mean \pm standard deviation. Comparisons of numeric values of all variables were performed using the Mann-Whitney U-test or Student's t-test for continuous variables. Multivariate odds ratios (ORs) and 95% confidence intervals (CIs) for family history variables and risk factors in cases versus controls were calculated using Student's *t*-test. The multivariate model included age, sex, smoking status, hypertension, diabetes, hyperlipidemia and family history variables. The graphics s were additionally drawn in the scattle plot graphic mode in SSPS.

Results

This study included 28 acute ischemic stroke patients, of whom 15 were female (53.5%) and 13

were male (46.4%). Their ages were between 30 and 83 years (mean, 67.1 ± 13.3). The control group consisted of 28 volunteers with ages between 38 and 88 years (mean, 65.9 ± 10.1). There were 13 females (46.4%) and 15 males (53.5%) in this group. In the patient groups, an initial sample of blood was collected in a sodium heparin tube on admission (T1) and then after 7 days (T6). In the control group, blood was obtained in the morning after an overnight fast. There was no significant difference between the patient and control groups with regard to age or gender (p>0.05). Stroke risk factors, mainly hypertension (HT), diabetes mellitus (DM), arrhythmia and heart failure were evaluated in the patient and control group using the t- test. We found statistically significant difference between the patients and the control group (p < 0.05) (Table 1). Demographic characteristics and prevalence of selected risk factors of the participants are presented in Table 1. Stroke cases more often had hypertension were more often smokers and had higher levels of cholesterol compared with controls. According to a classification based on the TOAST were divided in 4 major etiologic categories: (1) Atherosclerotic vasculopathy: cerebral infarction caused by large-vessel atherosclerotic vasculopathy or small vessel disease; (2) Small vessel occlusion (lacunar infarct); (3) cardiac/transcardiac embolism and (4) other: cerebral infarction that did not meet the criteria for one of the categories outlined (22, 23). Atherosclerotic vasculopathy was the presumed cause of infarct in 14 cases (50%), small vessel occlusion (lacunar infarct) in 17 cases (60.7%), cardiac/transcardiac embolism in 18 (64.3%) cases and other causes in the remaining 2(7.13%) cases.

The antioxidant levels (on admission and then after 7 days) of stroke subjects and controls are reported in Table 2. On admission, mean antioxidant levels were compared with the controls by parametric tests (t-test). Mean antioxidant levels were lower in patients than controls. Significance was reached for vitamin A, (P<0.001). During the days after the acute event, all antioxidants tended to increase. GSH-Px, GSH, MDA and Vitamin A levels were found to be higher in patients than controls. Among the groups there were significant difference in the serum GSH-Px, GSH, Vitamin A (P<0.001) and MDA levels (P<0.05). There was no observed significantly difference in serum CAT

Characteristic	Stroke Patients (N:28)	Control Subjects (N:28)	Totaly (N:56)	P values
Age (years)	67.1 ± 13.3	65.9 ± 10.1	60.0 ± 13.3	>0.05
Sex				
Male	13 (46.7)	15 (53.5)	27 (100.0)	>0.05
Female	15 (53.5)	13 (46.4)	29 (100.0)	>0.05
Family history of stroke	6 (21.4)	-	6 (10.7)	0.010*
Conventional vascular risk factor				
Hypertension	23 (82.1)	-	23 (41.1)	0.001**
Diabetes mellitus	4 (14.3)	-	4 (7.1)	0.040*
Hypercholesterolemia	19 (67.4)	-	19 (33.9)	0.001**
Hyperlipidemia	3 (10.7)	-	3 (5.4)	0.078
Smoking	9 (32.1)	-	9 (16.1)	0.001**
Alchol	1 (3.6)	-	1 (1.8)	0.317
Obesite	11 (39.3)	-	11 (19.6)	0.001**
Cerebrovascular	10 (35.7)	-	10 (17.9)	0.001**
Cardiac arrhythmia	17 (60.7)	-	17 (30.4)	0.001**
Onset age	4 (14.3)	-	4 (7.1)	0.040*
Migren	1 (3.6)	-	1 (1.8)	0.317
Large atherosclerotic vasculopathy	14 (50.0)	-	14 (25.0)	0.001**
Cardioembolism	18 (64.3)	-	18 (32.1)	0.001**
Small vessel occlusion (lacunar infarct)	17 (60.7)	-	17 (30.4)	0.001**
Other causes	2 (7.1)	-	2 (3.6)	0.154

Table 1. Demographic and Clinical Characteristics of Stroke Patients and Controls

Differences between cases and controls were examined with Student t test for continuous variables. p < 0.05, *p < 0.001 as significant level.

Table 2.	Comparisons of MDA,	CAT, GPX,	GSH, β -carotene and	vitamin A levels	(on Admission [[T1]
and After	· 1 Week From Stroke C) nset [T6]) i	n patient and control	groups		

Variables	Patients (N:28)	Control (N:28)	Total (N:56)	Р	95 % CI
MDA (mmol/L)	9.9 ± 2.2 (T1) 12.1 ± 3.3 (T6)	6.9 ± 1.7	8.4 ± 2.4	0.05*	1.95 - 4.03
CAT (k/g Hb)	$59.9 \pm 17.4(T1)$ $58.9 \pm 16.9(T6)$	55.1 ± 14.1	53.5 ± 15.7	0.456	-11.6 - 5.3
GSH-Px(U/g Hb)	64.1 ±14.1(T1) 74.1 ±24.1(T6)	28.6 ±18	46.3 ±24	0.001**	26.9 - 44.1
GSH (mmol/g Hb)	5 ±1.2(T1) 7.5 ±3.2(T6)	2.5 ±1.1	3.5 ±1.5	0.001**	1.4 - 2.6
b-carotene (mgr/dl)	$40.2 \pm 16(T1)$ $41.2 \pm 16.1(T6)$	40.1 ±15.3	40.2 ±15.3	0.959	-8.1 - 8.5
Vitamin A (mmol/L)	6.2 ±3.4(T1) 9.2 ±6.4(T6)	1.6 ±1.04	3.8 ±3.4	0.001**	3.4 - 6.0

p*<0.05, *p*<0.001 as significant level.

Values are mean \pm *standard deviation. MDA*=*malondialdehyde. GSH*= *glutathione. CAT*= *catalase. GSH*-*Px* = *glutathione peroxidase.*

and β -carotene levels in patients and control groups (*P* =0.456). After 1 week, antioxidant levels were found higher in patients than controls, with the exception of serum CAT and β -carotene levels, which remained similar (Table 2).

The serum CAT levels of each groups were given in Figure 1. There was no observed significantly difference in serum CAT level between patients and control groups (P = 0.456).



Figure 1. The distribution of serum CAT level in the study groups

Group 1: Patients with acute ischemia stroke (n=28), Group 2: Healty control (n=28).

When the b-carotene levels were examined by the same method, the level of β -carotene levels were not found significantly differences in ischemic patients and control group (*P*=0.959), (Fig. 2).



Figure 2. The distribution of serum b-carotene level in the study groups

Group 1: Patients with acute ischemia stroke (n=28), Group 2: Healty control (n=28).

Discussion

Oxidative stress is one of the mechanisms involved in neuronal damage induced by ischemia (24, 25). Oxidative stress causes damage in both acute and chronic neurodegenerative diseases like Parkinson disease (PD), amyotrophic lateral sclerosis (ALS) and stroke (26). Acute ischemia leads to increased production of free radicals and ROS in tissue and plasma. The increased production of free radicals in acute cerebral ischemia can arise from several mechanisms (8, 24).

Classically, stroke risk factors include hypertension, diabetes, hyperlipidemia, smoking and genetics. The first four of these factors are modifiable and treatments are available to lower these risks for stroke. In contrast, genetic factors have long been considered unmodifiable, significantly limiting treatment options for individuals with maximally treated or nonexistent modifiable risk factors (27, 28, 29).

MDA levels are widely accepted as markers of lipid peroxidation in oxidative stress. In some studies MDA levels were found to be increased in acute stroke. In the literature, MDA and 4-hydroxynonenal (HNE), which are both breakdown products of lipid peroxidation, were found to be increased in cardioembolic stroke patients. Lipid peroxides were also found to be higher in ischemic stroke (30). In another study serum MDA levels of 45 acute ischemic stroke patients were found to be elevated at the end of 48 h (31). In our study, plasma level of MDA is different as between the two groups. MDA levels were found to be elevated in thrombotic strokes and subarachnoid hemorrhages and to be less elevated in embolism and intracerebral hematoma, leading to the conclusion that increased levels of MDA could indicate a tendency to intravascular thrombosis (32). This may also play a role in clinical outcomes. Patients with less neurologic deficit had lower MDA levels.

Oxidative stress plays an important role in acute ischemic stroke. It may cause deleterious effects and indicate a worse clinical outcome. Keeping this in mind, we found elevated levels of MDA and GSH in our accute stroke patients. GSH is a part of the intracellular nonenzymatic small molecule antioxidant defense system. It is a free radical scavenger and a proton donor for GSH-Px. It is also neuroprotective (33).

Even though GSH levels were found to be lower in patients with previous stroke history, this significant increase may be due to a defense mechanism against oxidative stress in the acute phase of stroke. Decreased GSH levels have been found in several neurodegenerative diseases (33). It has also been shown that patients with stroke history have lower GSH levels associated with increased oxidative stress. This result is probably associated with the neuroprotective effects of GSH. In the literature there is only one study where elevated GSH levels were found in the first hours after stroke (34). However, their study group consisted of only 11 patients. In this study, we found higher GSH levels in acute stroke patient group. Our study group consisted of only 28 patients. Elevated GSH levels could be a part of first-line defense mechanisms against oxidative stress, providing neuroprotection against amino acid excitotoxicity in stroke.

In normal brain tissue, the production of ROS is balanced by endogenous enzymatic (GSH-Px, CAT) and nonenzymatic (for example, glutathione) antioxidative defense. GSH-Px and CAT protect the cells from the toxic effects of hydrogen peroxide by catalyzing its decomposition into water without free radical production. However, after acut ischemia and particularly reperfusion, this free radical production is dramatically increased and overwhelms endogenous antioxidant systems, leading to a disruption of the equilibrium. This massive free radical production may be generated by various pathways (35).

This study also found that high GSH-Px levels correlated with low neurological deficit on admission as well as good outcome after 1 week. In the literature it has been shown that GSH-Px has protective effects in brain damage and reduced GSH-Px levels are associated with an increased stroke risk (36). In spite of this no correlation between GSH and clinical outcome was found in the mentioned study (34). Thus, we conclude that overexpression of GSH-Px is neuroprotective.

In future studies MDA, GSH and GSH-Px levels can be compared with ischemic core and penumbra volume to find a possible association between them. Stroke location, reperfusion and thrombotic state may also have effects on these parameters. Unfortunately we did not study these relationships which may affect stroke severity and clinical outcome. It is clear that there is a need for larger studies on this subject. Such studies may be helpful in increasing the physician's awareness of oxidative stress in acute stroke and the planning of future research projects.

Because ROS play a major role in brain damage in cerebrovascular diseases, antioxidant enzymes are good candidates for testing as therapeutic agents. The present study is the first to demonstrate that catalase over-expression using viral transfection before ischemia is neuroprotective in a rat transient focal ischemia model. Delivery of catalase-expressing vector 2 or 5 h after ischemia onset was not protective. Thus, the delayed CAT over-expression may come too late to protect against ROS-mediated damage. CAT over-expression improved neuron survival when delivered before ischemia onset (*P<0.01), but not after ischemia onset (15).

In our case-control study, revealed a decrease in plasma CAT activity in patients with ischemic stroke as compared to control group. However, this deviation did not reach a statistical significance (P=0.456). Pre-ischemic over-expression of catalase resulted in a 2-fold increase in surviving neurons, but post-ischemic delivery of the catalase vector was not protective. While this study confirms the role of catalase as an important antioxidant enzyme system in stroke defense. We can conclude that in ischemia stoke patients the decrease in plasma CAT activity is the consequence of oxidative modifications. These results suggest that ischemi stroke patients have significantly increased oxidative damage. These oxidative stress markers also seem to be useful as prognostic predictors of stroke outcome.

Vitamins A, represent an important part of the antioxidant defense system acting against free-radical damage. Imbalance between oxidative stress and antioxidant capacity which leads to free radical damage is considered to be an aetiological factor of ischaemic heart disease (37). Cherubini et al. also found evidence of reduced antioxidants concentrations in ischaemic stroke patients and that higher vitamin A levels were associated with poor early clinical outcome (38, 39). We found that stroke patients had higher levels of vitamin A than controls on admission, reaching plasma concen-
trations similar to those of controls 1 week after stroke. Our results suggest that may be a beneficial effect of a high serum vitamin A concentration on early outcome in ischaemic stroke. Enhanced antioxidant capacity after stroke therefore may protect against the adverse effects of free radical production during ischaemia and reperfusion.

Previous studies showed that plasma levels of β -carotenes are significantly lower in patients with acute ischemic stroke than in normal controls (40). In this study we showed that plasma levels of β -carotenes was identical in patients with acute ischemic stroke and normal controls. The levels of β-carotenes in acut ischemia stroke patients were not significantly different than those in healthy controls (P>0.05). These findings are not generally in accord with those of previous reports (40, 41). The discrepancy between our own studies is unexplained but may suggest that increased oxidative stress may be affected by other factors such as ascorbate and carotene levels and the majority of plasma carotenoids are lowered immediately after an ischemic stroke, perhaps as a result of increased oxidative stres (41).

In human studies, most plasma levels have been shown to be decreased immediately after an ischemic stroke, possibly a consequence of increased oxidative stres (40). In a previous study, we also found that patients with acute ischemic stroke had lower levels of plasma (40). All these findings suggest that measurements of antioxidant concentrations in patients with ischemic stroke may have some clinical implications because the status of antioxidants is related to our defense capacity against oxidative stress and may be related to clinical outcome.

Cerebral ischemia results in the activation of a cascade of molecular events as a result of which several substances with the potential characteristics of biomarkers are released into the peripheral blood. Biomarkers of excitotoxicity, inflammation and oxidative stress have been demonstrated as being useful in the prediction of ischemic lesion enlargement and secondary neurological deterioration. However, for these biomarkers to become applicable to routine clinical practice, faster tests to perform the analyses are required and further studies must be undertaken to validate and generalize the results. These results provide further evidence that oxidative stress and impairment of the antioxidant system may play a role in stroke. Antioxidant activity of plasma may be an important factor providing protection from neurological damage caused by stroke-associated oxidative stress. However oxidative stress in patients with acute ischaemic stroke may be the result of an imbalance in oxidant/antioxidant homeostasis.

Conclusion

Free radical generation and consequent oxidative stress have a role in the pathogenesis of acute ischemic stroke. This may also cause defense mechanisms to be activated. Our data support the hypothesis of the deleterious effects of oxidative stress on clinical outcome in acute ischemic stroke. There was a significant increase in levels of MDA, GSH-Px and GSH. GSH elevation seemed to be a part of adaptive mechanisms. However, the exact mechanism is not clear yet. Further studies may help us to obtain a broader view of oxidative stress in cerebral infarct pathophysiology and to suggest novel treatment strategies.

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Collaboration in the provision of mental health care services: a cross-sectional survey of Lithuanian general practitioners

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Summary

The aim of this cross-sectional study was to assess the collaboration between GPs and mental health team members. Our study demonstrated a low level of contact. When collaboration did take place, it was to compensate for GPs' lack of expertise in the area.

Abstract

Background. General practitioners (GPs) often become the first point of care for mental health issues. Improved collaboration between GPs and mental health teams can make a GP's mental health services more efficient.

Objective. The aim of this study was to assess the collaboration between GPs and mental health team members and determine predictors for better collaboration.

Methods. In this cross-sectional study, a 41item questionnaire was distributed to a random sample of 797 Lithuanian GPs. The purpose of this questionnaire was to obtain knowledge about current practices of GPs in providing mental health care for patients as well as GPs' collaboration with metal health teams.

Results. The response rate was 52.2%. GPs collaborated closest with psychiatrists: 30.7% of them reported that they discuss the mental health care of their patients with psychiatrists. Predictors of greater collaboration with mental health teams were a lack of GPs⁴ confidence in their communication skills and ability to diagnose the most frequent mental disorders, prompt referral to mental health team specialists, low estimation of the prevalence of non-managed mental disorders, and location of mental health team in another health facility.

Conclusions. Our study demonstrated a low level of networking between GPs and mental health teams. When collaboration did take place it was to compensate for GPs' lack of expertise in the area. This study underscores the need to begin a wider assessment of the potential barriers and opportunities for a collaborative approach in mental health care between GPs and mental health teams in Lithuania.

Key words: GPs, mental health, collaboration, Lithuania

Introduction

The global shortage of human resources for mental health care, particularly in low and middleincome countries [1], necessitates the wider implementation of integrated and collaborative care models that improve management possibilities for mental health problems [2,3], continuity of care [4] and client satisfaction [5]. Studies have shown that this can be via improved interdisciplinary communication and co-ordination [6], decreased fragmentation of care [5] and urban specialists linked with rural practitioners [7].

Primary health care institutions often become the first point of care for mental health issues within the formal health systems [8], creating a set of new responsibilities for primary health care providers. Some studies indicate struggles in integrating mental health services in primary care. Surveys performed in Australia in 1997 and 2007, for example, demonstrated non-changing trends in accessing general practitioners (GPs) for mental health problems despite a significant increase of population access to dedicated mental health services [9]. Although GPs feel responsibility for their mentally ill patients and consider themselves as a part of the care system for these patients [10], research underlines the need to improve GPs' collaboration with mental health teams in general and psychiatrists' in particular to make GPs' mental health services more efficient [11,12].

In Lithuania primary mental health services are provided by primary health care teams (GPs and community nurses) as well as by mental health teams (psychiatrists, psychologists and social workers). Mental health teams work in mental health centres, which are independent health care facilities that patients can address directly without being referred by a GPs. Mental health centres receive capitation fees from the Patient Fund for mental health care, the same way as GPs receive capitation fees for primary health care. All primary health care institutions have to have their own mental health centres or a contract with other mental health centres.

In spite of the existing primary mental health care system, the Lithuanian Mental Health Strategy underlined the pivotal role of GPs in mental health care provision and the imperative of GPs' collaboration with psychiatrists and other specialists of mental health teams [13]. Existing research demonstrates the urgent necessity to improve mental health services provided by Lithuanian GPs [14] and that a lack of a collaborative approach in is one of the major issues [15]. However, there have been no earlier studies examining actual collaboration between GPs or mental health teams during the provision of mental health services.

The aim of this study was to assess the collaboration between GPs and mental health team members and to determine the predictors for better collaboration.

Methods

The sample included all GPs working in Lithuania under the contract with national Patient Funds. Since all Lithuanian GPs who provide primary health care services have contracts with the Patient Fund, we used the complete roster of Patient Fund listings in November 2009 to identify a sample of 880 GPs and the primary health care settings for each of the GP included in the sample.

A 41-item questionnaire was used in this crosssectional study. The questionnaire addressed the following issues: - sociodemographic data;

- perception of the prevalence of mental disorders among their patients, the main mental health problems addressed, the reasons for referral;
- assessment of the collaboration with mental health teams and community nurses;
- perceived GP's competence in mental health care, possibilities to provide mental health services and willingness to become more active in providing mental health care;
- perceived competence in management of suicidal patients;
- the need for continuing medical education in mental health care;
- potential measures to increase GP's involvement in mental health care.

Only minor revisions were made after pilot testing of the questionnaire with 18 GPs. After finalizing the questionnaire, the Bioethics Committee of the Lithuanian University of Health Sciences determined that it was not necessary for this kind of study to obtain the consent of the committee.

Questionnaires were distributed to all of the GPs from the identified sample who would be at work during the 12 week survey period, starting at the end of January 2010. In total, 797 questionnaires were distributed. Respondents were informed in writing about the selection procedure, the purpose of the questionnaire and the planned publications. We also guaranteed them full confidentiality of their responses.

We used the Statistical Package for the Social Sciences for Windows (SPSS), version 19.0, to code and analyse the resulting data. Aiming to assess GPs involvement in collaboration with mental teams, the study participants' responses to four statements: I' discuss with a psychiatrist the diagnostic, treatment and care issues of my patients with mental disorders," I discuss with psychologists the diagnostic, treatment and care issues of my patients with mental disorders," A social health care worker is taking part in managing the psychosocial assistance of my patients with mental disorders," I have the possibility to discuss all uncertainties with mental health team while providing mental health services"were given points. The answer "never" was given 0 points, "rarely"

- 1 point, "sometime"- 2 points, "often" - 3 points and "always" - 4 points. Next, the points were totalled, the maximum possible score was 16 points. The GPs who collected 9 points or more were labelled "high collaborators".

Chi-square tests were used to investigate the statistical correlation between the higher GPs' involvement in collaboration with other categorical variables. Finally, we carried out binary logistic regression and calculated odds ratios to check for any differences between the reference group ("the high collaborators") and each of the other variables, setting the statistical significance level at P<0.05.

Results

Respondents

The response rate was 52.2% (416 completed questionnaires). The majority (87.3%) of the respondents were female (see Table 1). Almost one-third of the GPs (30.8%) practised in private health care centres that had contracts with Lithuanian Patient Funds, while the remainder (67.3%) practised in public health care centres. Solo practitioners accounted for 7.5% of the respondents. Slightly less than half of the participants (46.4%) had fewer than 1550 patients on their list. Half of the GPs (49.3%) indicated that a mental health provider or team is situated in the same institution as they are working; others indicated that their primary health care institution has an agreement with a mental health centre located in another institution. Additional characteristics of the respondent sample are presented in Table 1.

GPs collaboration with other mental health providers

GPs were asked to indicate how often they collaborate with other mental health providers in delivering mental health services for their patients (Table 2). The closest collaboration was observed with psychiatrists: slightly less than one third (30.7%) of the study participants discussed different aspects of the mental health care of their patients with psychiatrists. GPs' collaboration with psychologists, social worker and community nurse, in providing mental health services was very limited.

GPs' collaboration with mental health teams was assessed considering their answers to the last

four statements provided in Table 2. Although the maximum score was 16 points, more than half of the participants (52.6%) had 6 points or less, and 15.4% of the GPs had more than half of the possible total. The mean of this computed indicator was 5.44 ± 0.154 , 95% CI [5.13 - 5.74].

Predictors for higher GPs involvement in collaboration with mental healthteams

The multivariate analysis (Table 3) revealed that low confidence in one's communication skills with patients having mental disorders, low confidence in one's ability to diagnose the most frequent mental disorders, prompt referral to mental health team specialists while suspecting mental health problems, low estimation of the prevalence of non-diagnosed and non-treated mental health disorders among his/her patients and location of mental health team (centre) in another health facility as significant predictors for greater collaboration of GPs with metal health teams.

Discussion

GPs are the professionals at the core of the health care system in Lithuania and their collaboration with other health care providers can greatly impact on the efficiency of the system as a whole. This study was the first one to assess the collaboration between GPs and mental health teams in the country.

Our data demonstrated a rather low level of networking between GPs and mental health teams. The mean score of 5.44 points out of a maximum of 16 suggests that collaboration with mental health team members is not among the routine activities of Lithuanian GPs. Even in countries where considerable numbers of mental health professionals are working in primary health care [16], it would be a worrying indicator. In the Lithuanian context, where primary health care teams consist only of GPs and community nurses, this finding become even more concerning. Taking into account the extremely low level of involvement of community nurses in mental health care -72.8% of GPs were rarely or never helped by community nurse to assess the mental status of the patients and 62.2% of the respondents were rarely or never assisted by community nurse in the delivery of home care services for mentally ill patients - the level of collaboration of GPs in primary

Variable*	Number (n=416)	%
Gender		
Male	47	11.3
Female	363	87.3
Not given	6	1.4
Age group		
\leq 50 years old	177	42.6
\geq 51 years old	234	56.2
Not given	5	1.2
Type of practice		
Public	280	67.3
Private	128	30.8
Not given	8	1.9
Location of practice		
Urban	294	70.7
Rural	87	20.9
Not given	35	8.4
Size of practice		
Solo practice	31	7.5
Group practice)	358	86,1
Not given	27	6.4
Location of mental health care centre		
Mental health care centre or mental health care provider located in the same institution	205	49.3
Mental health care centre located in another institution	169	40.6
Not given	42	10.1
Number of the patients on the patient list	100	
≤ 1550	193	46.4
\geq 1551	210	50.5
Not given	13	3.1
Average number of consultations per week	104	
≤ 110	184	44.2
\geq III	210	50.5
Not given	22	5.3
Average number of patients with mental health problems consulted during one week	010	50 T
≤ 10	219	52.7
\geq 11	174	41.8
Not given	23	5.5

Table 1. Description of General Practitioners in the study sample

Collaboration activities	Responses "always" and "often" (n=416)	Responses "rarely" and "never" (n=416)
Community nurse helps me in assessing the mental status of the patients	46 (11.1%)	303 (72.8%)
Community nurse helps me in delivering home care services of mentally ill patients	61 (14.7%)	259 (62.2%)
I am discussing with psychiatrist diagnostic, treatment and care issues of my mentally ill patients	128 (30.7%)	167 (40.2%)
I am discussing with psychologists diagnostic, treatment and care issues of my mentally ill patients	45 (10.8%)	295 (70.9%)
Social health care worker is taking part in managing psychosocial assistance of my mentally ill patients	48 (11.5%)	299 (71.8%)
I have possibility to discuss all uncertainties with mental health care team while providing mental health care services	149 (37.3%)	153 (36.8)

Table 2. Collaboration with other providers in delivering mental health care services

Table 3.	Multivariate log	gistic regression	model to predi	ct GPs invol	lvement in c	ollaboration [.]	with mental
care teal	ms						

Variables (reference value given in parenthesis)	B	P-value	OR	95% CI for OR
Gender (male)	0.018	0.978	1.01	(0.29–3.54)
Age (51 or older)	0.778	0.059	2.17	(0.97–4.88)
Felt responsibility for the management of patients' mental health problems (responsibility perceived)	0.227	0.807	1.25	(0.20–7.76)
Involvement in the management of patients' mental health problems (not-involved)	0.560	0.523	1.75	(0.31–9.75)
Self confidence in own knowledge in mental health care (no self confident)	1.230	0.120	3.42	(0.72–16.10)
Self confidence in own communication skills with mentally ill patients (self confident)	1.323	0.029	3.75	(1.14–12.29)
Self confidence in own ability to diagnose the most frequent mental disorders (self confident)	1.362	0.021	3.9	(1.23–12.34)
Willingness to improve knowledge and skills in mental health care (willing to improve)	0.736	0.525	2.08	(0.21–20.16)
Willingness to collaborate more with mental health team (willing to collaborate)	1.007	0.500	2.73	(0.14–51.00)
Prompt referral to mental health team specialists while suspecting mental health problems (no prompt referral)	1.935	0.026	6.92	(1.26–37.94)
Perception of the prevalence of mental health disorders among his/her patients (estimation less than 30%)	0.214	0.674	1.23	(0.45–3.35)
Perception of the prevalence of non-diagnosed and non-treated mental health disorders among his/her patients (estimation more than 30%)	1.619	0.001	5.04	(1.85–13.69)
Number of the patients on the patient list (≤ 1550)	0.912	0.058	2.49	(0.96-6.40)
Average number of consultations per week (≥111)	0.941	0.062	2.56	(0.95-6.88)
Average number of patients with mental health problems consulted during one week (≤ 10)	0.543	0.218	1.72	(0.72–4.08)
Sufficient possession of diagnostic scales and other diagnostic instruments for the assessment of mental status of the patients (yes)	0.683	0.457	1.98	(0.32–11.97)
Possibility to have longer consultations for mentally ill patients (no possibility)	0.754	0.232	2.12	(0.61–7.32)
Practice ownership (private practice)	0.478	0.337	1.61	(0.60-4.27)
Location of practice (urban)	0.603	0.323	1.82	(0.55-6.03)
Type of practice (solo practice)	0.653	0.527	1.92	(0.25–14.50)
Location of mental health centre (mental health centre in the same institution)	2.038	<0.001	7.67	(2.70-21.74)

B: logistic regression coefficient, CI: confidence interval, OR: odds ratio.

care teams is also brought into question. Conflicting GP and community nurse views of their roles in the identification and management of mental health problems and unclear expectations among GPs of mental health services provided by specialists could explain why collaboration is so poor [17]. On the other hand, our insight about limited collaboration in providing mental health services in primary care is based on the GPs' self-reported data. Low interest among GPs in collaboration, reported in other studies [18], could possibly affect GPs' perceptions about existing collaboration. Future assessments of community nurses and mental health team members' perspective on this issue would be instrumental in aiming to better understand collaboration in primary care.

Another ambiguity concerns predictors for greater collaboration of GPs with mental health teams. Among the statistically significant predictors for higher collaboration several negative factors were apparent: low self confidence in communication skills and in the ability to diagnose the most frequent mental disorders, prompt referral to mental health team specialists while suspecting mental health problems. Insufficient mental health training of GPs and the frequent transfer of patients with mental disorders from primary care were found in other countries to be negative indicators of the management of patients with mental disorders in primary care [11]. In our study, the same indicators become predictors for greater collaboration of GPs with mental health teams. This rather unexpected finding raises the question of what is the nature of collaboration between GPs and mental health teams in Lithuania and complements ongoing discussions about ambiguity in understanding collaboration and partnership in health care [19]. One explanation is that GPs tend to collaborate with mental health teams in order to compensate for their lack of expertise in the area, although studies suggest that collaboration alone is not sufficient to improve skills and knowledge transfer in the management of mental health conditions [20]. This insight is in line with the suggestion of Hojat et al [21] that health professionals with more powerful positions have the least interest in collaboration. Higher self-confidence in professional skills could increase the sense of power of GPs and, eventually, decrease their willingness for collaboration.

The strongest predictor for greater collaboration from GPs - location of mental health team in another institution - contradicts previous research findings [20]. Mental health teams working in the same institution as GPs could increase GPs' reliance in the management of mental health problems of their patients without their involvement. Presuming that collaboration is perceived by GPs mainly as a tool to cover their deficiencies, then the absence of a mental health team in the health facility could become a strong motivator for them to contact mental health team professionals. This merits future research. Better understanding of GPs' as well as community nurses, mental health team specialists perceptions of the nature of collaboration, their experiences and expectations could be instrumental in enhancing a collaborative approach in Lithuanian primary health care [22].

Our study has certain limitations. First, the response rate was only around half. However, similar studies which have addressed GPs, show even lower response rate [10,11,16]. Second, it has a cross-sectional design, which does not permit causal inference. Third, the data collected were self-reported; the results must be considered as an approximation of actual GP practice. Fourth, the GPs' involvement in collaboration with mental health teams was estimated ranking the frequency of GPs' communication with mental health team specialists (psychiatrist, psychologist, social worker) in the management of patients with mental disorders. As in Lithuania there was no formalized description of collaboration activities between GPs and mental health teams to design the questionnaire, we associated the frequency of communication between GP and mental health teams with the degree of collaboration. However, in applying this approach to assess collaboration we reduced the potential richness of the phenomenon by equating collaboration with communication between health care providers.

In spite of the aforementioned limitations of the study and the ambiguity in the understanding of collaboration between GPs and mental health teams the inconsistent predictors for greater collaboration revealed by our study underscores the need for Lithuania to begin a wider assessment of the potential barriers and opportunities for a collaborative approach in mental health care between GPs and mental health teams.

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Assessing the Efficiency of Exercises Intervention after Ischemic Stroke on Activities of Daily Living

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Abstract

This pretest-posttest study was conducted in order to assess the effect of ROM (Range of Motion) exercises, performed on patients with stroke, on the level of activities of daily living.

Population of the study comprised of maximum 20-day cases, were diagnosed with ischemic stroke for the first time, taken under treatment at the hospital within the first 72 hours following the development of the stroke, and who completed their medical treatment at the hospital. The study was conducted on 70 patients with ischemic stroke, who were selected from the population using the randomized sampling method.

The questionnaire and Barthel Index (BI) of Acitivities of Daily Living were used to collect data. Chi square tests, multivariate variance,Mauchly's test in repeated measurements, correlation-regression analysis, and independent groups t-test were used to conduct the statistical analysis of the data.

After practice of the exercise, the difference between the Barthell Index scores of patients in the experimental group was found to be statistically significant (p<0.001). Mean BI scores of patients in the experimental group increased after Week 8 and 12 of the practice and there was a significant increase in their activities of daily living (p<0.001).

Key words: Stroke, Activities of Daily Living (ADL), Exercises, Nursing Intervention

Introduction

Stroke constitutes an issue in the healthcare system of many countries, at a significant level, in terms of mortality and morbidity rates (1). Numerous complications develop in patients with stroke during acute and chronic period. Various studies reported that the complication development that occurred after the stroke ranged between 40-96%. Being aware of complications that could develop after the stroke and starting the treatment in an early phase yield a decrease in stroke mortality and disability rates (2,3).

Rehabilitation is commonly used in decreasing the disability rate in stroke patients. The recommendation is that rehabilitation practices are started as soon as the medical condition of the patient becomes stabile. Starting these practices late causes to develop complications such as pressure sores, obliteration and inflammation in deep veins, joint stiffness, osteolysis, and bladder and bowel dysfunction (3,4).

The statistical data related to the stroke shows geographical, racial and ethnic differences including the incidence and the studies conducted in the last twenty years concluded, that while stroke incidence is between 1-3/1000, its prevalence is 6/1000 (5-7). In a study conducted in our country, the stroke etiology was ischemic in 70% of the patients and hemorrhagic in 23% (8).

While 20 - 30% of the post-stroke patients could be brought to the normal level with a good rehabilitation program, 75% of them could be able to walk independently (9-12).

The studies conducted on home-exercise programs point out that the exercise is an effective method for the improvement of mobility in stroke patients (13,14). Home-based exercises that are applied to stroke patients enable them to maintain the rehabilitation for a long time. Besides, it will be an effective method in providing the rehabilitation treatment, for which financial resources are be used more efficiently (13,15-18).

In stroke that proceeds with loss of the function, the fact that an individual maintains daily life activities should be an important target of the nursing functions. Nurses, who organize a new life for patients in line with their changing bodies and some lost functions, shall be supported to be recovered from feelings, such as fear and uncertainty (11,12). The purpose of the study was to assess the efficiency of range of motion exercises, which were applied on patients with ischemic stroke by the researcher at home, on the level of the activities of daily living.

Material and method

Type of the Study

This study was a single-blind and quasi-experimental with the control group.

Inclusion Criteria for the Study Individuals, who;

1. Were diagnosed with ischemic stroke,

2. Were taken under medical treatment at the hospital within the first 72 hours after the stroke,

3. Received BI scores between 60-80 during the first assessment,

4. Were told by the physician or physiotherapist that there was no drawback to do exercise,

5. Could understand and respond to verbal conversations,

6. Had no lack of memory and communication,

7. Had no serious cardiac symptoms or other health problems that could limit exercises and who accepted to participate in our study were included in the sample group of the study.

Procedure

Aim of the exercises that were given to the experimental group is to improve the level of the activities of daily living. Before performing the practice on the experimental group, the physiotherapist was collaborated, and a guideline was created by the researcher to be followed in the light of the current studies in the literature. The exercises were ordered within a flexible hierarchy in accordance with the balance difficulty.

The researcher enabled them to do the ROM exercises twice a week.

BI was conducted at the end of each four weeks, in an attempt to identify the developments.

In order for the stroke individual to receive support from his/her healthy part, the initial step was to perform warm-up exercises for five minutes with abduction, adduction, extension, flexion, compression and rotation movements of the healthy extremity. The second step was to perform exercise on the affected arm. Active-assisted ROM exercises were performed in a way to enable a slight range of motion for the purpose of forming the voluntary movement. The exercise was repeated for at least three times on each joint in order to activate the resistance point. The arm exercises were followed by hip-leg exercises.

Range of motion (ROM) exercises are performed as active, active-assisted and passive. The active ROM is performed by the person, active-assisted ROM is performed by the person with the help of another person or an object, and finally, the passive ROM is that movements the individual is not able to make are performed by the help of another person. The performance and continuity of ROM exercises makes great contribution to the wheelchairor bed-bound individual. ROM exercises help the person to maintain and improve the existing health level of their joints and muscles. Unless the exercises as activity and stretching are performed, the blood flow and flexibility of joints gradually decrease. Joints such as knee and elbow stiffen and get locked without the ROM exercises. Passive ROM exercises help to stretch joint areas; however, these movements do not strengthen the muscles.

Only the scales were applied to the control group. No other intervention was made on the control group by the researcher except for clinical practices.

Data Collection Tools

Questionnaire

The questionnaire consists of questions assessing the personal number, address information, age, gender, marital status, educational level, economic condition, paralytic side, hospital stay period and presence of chronic disease.

Barthel Index

The Barthel index (BI) is the scale of activities of daily living. The BI is one of the most commonly used disability scales for rehabilitation patients. It evaluates the mobility and self- care activities. The Barthel index was used for the functional evaluation. The index evaluates the physical independence in activities of daily living. The Barthel index is an index that is detailed, objective, easily applicable, and understandable and exactly assesses all specific stages of activities of daily living. 0-20 scores indicate totally dependence, 21-61 scores indicate advanced dependence, 62-90 scores indicate moderate dependence, 91-99 scores indicate slight dependence and 100 scores indicate totally independence. The sensitivity of the index was increased using a five-stage scoring system in the Modified Barthel Index modified by Shah. The Modified Barthel Index was adapted into the Turkish society and the index was proved to be valid and reliable for patient groups with stroke and spinal cord injury. Its modified form is also used for stroke patients. The scale adaptation alpha coefficient of the index is 0.93 for stroke patients in the Turkish society (19,20).

The Barthel Index was developed in order to assess the independence of patients, regarding their self care duties. The 10-item BI evaluates the feeding, transfer from chair to bed, grooming, sitting on the toilet, bathing, ambulation, stair climbing, dressing, bladder and bowel control. The Barthel Index takes some criteria, such as bladder and bowel control, grooming, toilet use, feeding, transfer, mobility, dressing and bathing into consideration.

Population and Sample Group

The population is consisted of maximum 20day cases, who reside in the city center of Yozgat, and were diagnosed with ischemic stroke for the first time. The sample group of the study was consisted of 70 people in experimental (35) and control (35) groups, who were hospitalized in Internal Medicine-Neurology clinics of Yozgat State Hospital between January-September 2008, met the study criteria and were chosen from the population using the randomized sampling method.

Collecting Data

Pretest data was collected by applying the questionnaire and the BI on the experimental and control groups in the sick room on the discharge day.

Posttest data was collected by applying the BI on the experimental and control groups in their houses at the end of the week 12.

Completing the questionnaire and the BI took 10 minutes for each patient. The researcher asked questions and recorded their answers.

Experimental-control groups were formed from 1 February 2008 to 1 September 2008. The researcher continued the exercises in the houses of the patients by getting appointments from them. The follow-up was performed twice a week for the ROM exercise practice in such a way not to exceed the exercise range of three days.

Evaluation of Data

Windows SPSS 11.0 version was used to evaluate pre-test and post-test of the experimental and control groups by coding them in computer package programs. Chi square tests, multivariate variance, Mauchly's variance analysis in repeated measurements, correlation-regression analysis, and independent groups t-test were used to conduct the statistical analysis of the data.

Ethical Principles

Permission was obtained from the Ethics Committee of Institute of Health Sciences of Atatürk University in order to conduct the study. The purpose of this study was explained to the patients to be included in the study and the required institutional permissions were obtained from Yozgat Provincial Directorate of Health and Yozgat State Hospital for this study.

Individuals who accepted to participate in the study were informed about the purpose, expected results and estimated time of the study and that they may withdraw from the study at any stage; the volunteer people were included in the study. The individuals were informed about risks of exercises and medical benefits expected from the study.

Those who voluntarily accepted to participate in the study were included in the study.

Limitations and Generalizability of the Study

The results obtained from the study could be generalized to the stroke patients included in the study. The limitation of the study is that BI, of which validity and reliability studies were conducted for our society, could not reflect other effects of the exercise intervention.

Results

Table 1 illustrates descriptive features of the patients included in the study. Considering patients who were included in the study in terms of gender distribution, female patients were 54.3% of the experimental group and 51.4% of the control group. There is no statistically significant difference between both groups, in terms of gender (Table 1).

	Groups					
Demographical Features	Experim	ental	Conti	ol	Total	
Gender	Number	%	Number	%	Number	%
Female	19	54.3	18	51.4	37	52.9
Male	16	45.7	17	48.6	33	47.1
			X ² =0.05	p>0.05		
Age groups						
35 - 44	8	22.9	5	14.3	13	18.6
45 - 54	16	45.7	21	60.0	37	52.8
55 - 64	11	31.4	9	25.7	20	28.6
			X ² =1.56	p>0.05		
Educational Status						
Literate	15	42.8	9	25.7	24	34.3
Primary School Graduate	11	31.4	18	51.4	29	41.4
Secondary School Graduate	9	25.7	8	22.9	17	24.3
	X ² =3.24 p>0.05					
Occupational Status						
Housewife	19	54.3	19	54.2	38	54.3
Worker	4	11.4	5	14.3	9	12.9
Civil servant	3	8.6	3	8.6	6	8.6
Other	9	25.7	8	47.1	17	24.2
	K	olmogo	rov-Smirno	ov Z=0	.12 p>0.05	
Economic Condition						
Low	20	57.1	17	48.6	37	52.9
Moderate	14	40.0	17	48.6	31	44.3
High	1	2.9	1	2.9	2	2.8
	K	olmogo	rov-Smirno	ov Z=0	.35 p>0.05	
The Area Exposed to Stroke						
Right side	20	57.1	22	62.9	42	60.0
Left side	15	42.9	13	37.1	28	40.0
	X ² =0.24 p>0.05					
Chronic Disease That Accompanies the Stroke		1			1	
Yes	29	82.9	20	77.1	56	80.0
No	6	17.1	8	22.9	14	20.0
	X ² =0.57 p>0.05					

Table 1. Distribution of Descriptive Features of Patients

Table 2. Distribution of BI mean scores of experimental and control groups at the beginning and in Week 4, Week 8, and Week 12

	Groups					
Duration of Exercise	Experimental		Con	trol	T test	
	\overline{X}	S.D	\overline{X}	S.D	t	р
Beginning BI	67.2	5.6	67.8	5.1	0.00	1.00
Week 4 BI	69.2	5.3	68.5	4.6	0.60	.55
Week 8 BI	74.4	5.7	69.4	4.1	4.15	.00
Week 12 BI	82.0	5.1	69.5	4.4	10.79	.00

It was determined that 45.7% of the patients in the experimental group were in the age range of 45-54 and 60% of the patients in the control group were in the age range of 45-54. The difference between the groups was statistically insignificant (p>0.05).

As illustrated in Table 2, while there was no difference between the initial mean BI scores of patients in experimental and control groups and their mean BI scores of the Week 4, there was statistically significant difference between their initial mean BI scores and their mean BI scores of the Week 8 and 12 (p<0.01).

When comparing the mean BI scores of patients in the group, mean BI score of the control group was 67.4 ± 5.1 before the practice of exercise, 68.5 ± 4.6 four weeks later, 69.4 ± 4.1 eight weeks later and 69.5 ± 4.4 twelve weeks later during the last measurement. There was statistically insignificant difference in terms of the mean BI scores of patients in the group according to duration (p>0.05).

Mean BI score of patients of the experimental group was 67.4 ± 5.6 before the practice of exercise, 69.2 ± 5.3 four weeks later, 74.4 ± 5.7 eight weeks later and 82.0 ± 5.1 twelve weeks later during the last measurement. There was statistically significant difference in terms of the mean BI scores of patients in the group according to duration (p<0.001).

When examining the mean BI scores in the experimental and control groups according to gender, education, occupational status, economic condition, presence of other chronic diseases and the area affected by the stroke, there was no statistically significant difference (p>0.05).

While the variable of age had no effect in the experimental group (r = -0,18 p > 0,05), difference in the BI scores increased as the age decreased in the control group; the difference is statistically significant (r = -0,35 p < 0.05).

Results of the multivariate analysis of variance –MANOVA showing effects of all variables at the same time in assessing the effect of the exercise practice on the patients who were included in the study concluded that there was no statistically significant difference between the mean BI score of the experimental group during the first assessment and mean BI score of the experimental group obtained at the end of the Week 12 in terms of age groups (f=3.13 p>0.05), gender (f=0.78 p>0.05), educational status (f=0.13 p>0.05), occupational

status (f=2.22 p>0.05), presence of other chronic diseases (f=2.24 p>0.05) and the area affected by the stroke (f=0.99 p>0.05).

On the other hand, there was no statistically significant difference between the mean BI score of the control group during the first assessment and the mean BI score of the control group obtained at the end of the Week 12 in terms of age groups (f=4.83 p>0.05), gender (f=0.72 p>0.05), educational status (f=0.35 p>0.05), occupational status (f=0.12 p>0.05), presence of other chronic diseases (f=1.23 p>0.05) and the area affected by the stroke (f= 3.17 p>0.05).

When assessing the difference between mean BI scores of patients, who were included in the study, at the end of the exercise intervention (Week 12) in comparison to those obtained before the exercise practice (first assessment) according to gender, while it was 15.3 ± 3.5 for women in the experimental group, it was 13.7 ± 3.5 for men in the experimental group. The score difference in women was higher.

In terms of age groups, the difference of mean BI scores was 14.4 ± 3.2 for the age range of 35-44, 15.3 ± 2.8 for the age range of 45-54, and 13.6 ± 4.5 for the age group of 55-64 in the experimental group; the difference of mean BI score was 5.0 ± 0.0 for the age range of 35-44, 1.9 ± 2.5 for the age range of 45-54, and 1.1 ± 2.2 for the age range of 55-64 in the control group. In the experimental group, the highest mean score difference was statistically insignificant (p>0.05). However, difference of mean BI scores was slightly higher only in the age range of 35-44 in the control group. The difference was statistically significant (p<0.05).

Discussion

Being the top of the neurological problems in the world, the stroke also has a very important place for the individual to become dependent and for repeated hospital stays (21). It is estimated that there are 50 million stroke individuals in the world, who have sensorial and cognitive deprivation, certain physical losses and are also dependent on another person at a rate of 25%-74% while performing the activities of daily living (22-24).

Such individuals are in need of follow-up and rehabilitation in order to enable their adaptation to life and increase their functionality. Although the recovery and its level change in post- stroke patients, the majority of neurological recovery occurs within the first 1 - 3 months; while this recovery process slowly continues up to 6 months, it is possible to see some publications stating that it continues up to the 12th month and even for a few years in 5% of the patients (10). When the patient becomes stabile neurologically and medically, s/he shall be taught the in-bed, sitting and transfer activities in order to prevent the complications that could occur due to immobilization. Following the discharge, on the other hand, house exercise programs and occupational therapy could be provided. Conventional methods include the maintenance of normal joint motion range, exercises for strengthening the muscles, balance and activity exercises and exercises for improving the activities of daily living (25). There are evidences related to the application types for stroke individuals in different programs in literature (26-29). Post-stroke complications are commonly encountered. Complications not only make the care difficult, but also decrease time and quality of life (30-32).

The primary objective of rehabilitation programs is to increase the functionality of paretic extremity, especially that of the hand, in the daily life of the patient. Alon investigated whether or not the home-based (home exercise program) stimulation program, which was applied to develop the hand functions, improved the hand functions and disorders of 77 stroke patients with chronic upper extremity paresis in his study, and he completed the home-based stimulation program combined with the training of clasping, holding and unclasping by using the wrist and finger extensors and flexors, as a result of a 5-week multidirectional training program with pretest and posttest. The participants were trained 2-3 times a day and for 7 days of the week. And then an improvement of 58,7% and an average decrease were observed on the spasticity of the elbow and wrist, and it was reported that the 5-week specific stimulation program and the practice of daily home training improved the selected hand functions and upper extremity disorders in patients with chronic stroke (32).

The purpose of the study was to investigate the effect of the exercise on the level of activities of daily living towards the ordinary treatment by performing the passive ROM exercises and if possible, active-assisted or active ROM exercises on individuals with ischemic stroke during the postacute period. In order to achieve this purpose, the study was completed by dividing 70 patients with ischemic stroke, who were determined during their hospital stay, into 2 groups as well as offering the training of ROM exercises on the external group and making only assessment on the control group. Barthel Index scores were assessed in order to evaluate the change on the activities of daily living in the Beginning, Week 4, Week 8 and Week 12.

When the study was completed, the ROM exercises, which were applied and taught as a therapeutic intervention during the post-stroke acute period, were found to have a positive effect on the results. Active and passive ROM exercises were performed on stroke individuals for nearly 1 hour in our study, and the intensity and duration of exercises were improved in a way for them to tolerate. However, measuring the physical response given by individuals to the intervention and the change in a sensible way was made complicatedly. BI is actually known to have a ceiling effect. Since the inclusion criteria was the initial BI score interval of 60-80 in our study, there was a very little interval left for the progress of individuals in experimental and control groups, regarding their initial and last mean scores. After the follow-up, the similar development continued in both groups; however, this increase was significant in the experimental group (p<0.001).

In the study carried out by Eskiyurt et al, 193 stroke patients were assessed with policlinic follow-ups within the first 3 months after the stroke, during the 4th-6th months, 7th-12th months and 13th month. As a consequence, BI scores were higher at statistical significant level as from the 7th month after the stroke, in comparison to the scores of the first 3 months (30).

In their study, Kumar et al divided the patients into groups during the acute period of the stroke; they performed passive ROM exercises on the first group, play board exercises on the second group and overhead pulley exercises on the third group. At the end of third month, while the highest pain experience was gained by the group that performed exercise with overhead pulley, the lowest pain experience was determined in the group that performed passive ROM exercises (33).

In this study, the increase in the mean BI scores of the experimental group was found to be statistically significant (p<0.001). The results obtained from the previous studies concluded that a better functional development was obtained in patients, who performed the exercise during the post-stroke acute period (34-43). In this study, after the ROM exercise practice, as a result of the increase in the mean BI score, the level of the activities of daily living increased and ROM exercises contributed to the patients. As a matter of fact, the results obtained at the end of the study were compatible with the literature information (44,45). However, the reason behind the expected difference, which occurred in the experimental group, may be the comparison made with a group that had received no practice in the study. In addition, calling the control group "untreatable" is not an acceptable choice, taking the health service under the conditions of our country into consideration.

When the mean BI scores of patients were compared within the group according to duration in the study, the difference was statistically significant (p<0.001). The previous studies reported that the functional development occurred and the level of the activities of daily living increased, as long as the post-stroke exercise and rehabilitation practices were continued (34,46). Similar studies concluded that performing exercise within the first 90 days after the stroke increased the functional capabilities of patients. In another study (47), the highest mean BI score was obtained as a result of the rehabilitation that was performed in 0-3 months after the stroke and these rehabilitation practices were more efficient. Study results show parallelism with these results.

There was statistically insignificant difference between the mean BI scores in experimental and control groups in terms of the gender, education, occupational status, economic condition, and presence of another chronic disease.

Some of the studies that investigated the relation between the functional result obtained in stroke as a result of rehabilitation and the gender proved that gender did not have any effect on the rehabilitation results (8,48-49). Results of this study concluded that gender was not effective on the functional results obtained after the stroke, which was compatible with the results of above-mentioned studies.

As stated in literature, the rehabilitation results of patients in the advanced age group were more negative compared to young patients (50-52). Bates and Stineman (51) indicated that young patients with stroke responded to rehabilitation much better. Another study demonstrated that patients younger than 65 had higher BI scores during discharge (8) (Table 3).

When assessing the difference of mean BI scores of patients in the experimental group according to their educational status, the difference was statistically insignificant (p>0.05).

In their studies, Dambovy et al (52) indicated that educational level affected the rehabilitation results positively. According to the conclusion of this study, such effect was thought since the educational level of patients who constituted the sample group was low in general.

In terms of the area affected by the stroke and difference of mean BI scores, the mean BI scores of patients, whose right side was affected, were lower than those, whose left side was affected, in experimental and control groups.

In the study carried out by Pantano et al (53), no relation was found between the affected side (right, left) and motor and functional recovery. Likewise, Wade et al (54), found no relation between the af-

Table 3. Comparison of BI mean scores of experimental and control groups at the beginning and in Week 4, Week 8, and Week 12

	BI Mean Score					
Chona	NI	Beginning	Week 4	Week 8	Week 12	Manahly?a
Groups		$X \pm SD$	$X \pm SD$	$X \pm SD$	$X \pm SD$	Mauciny s
Control Group	35	67.4 ± 5.1	68.5 ± 4.6	69.4 ± 4.1	69.5 ± 4.4	W=.284 sd=1 p>0.05
Experimental Group	35	67.4 ± 5.6	69.2 ± 5.3	74.4 ± 5.7	82.0 ± 5.1	W=.853 sd=1 p<0.001

fected area and recovery. Titus et al (55) examined the relation between the exposure condition of right and left side and activities of daily living and determined that activities of daily living were affected in both situations. When comparing the mean BI scores of patients whose right and left sides were affected, no significant difference was found in the study (p>0.05). BI score decreased in both groups. Thus, there was a decrease in BI scores of stroke patients, whose right and left sides were affected. The result of this study was compatible with the results of the previously conducted studies.

When examining the difference of mean BI scores according to the presence of other chronic disease that accompanies the stroke, difference in mean BI scores of patients in experimental and control groups was statistically insignificant (p>0.05).

As a result of their study, Bardak et al (45) reported no significant relation. The result of this study was compatible with the results of the study performed by Bardak et al.

The studies determined that home exercise programs applied to stroke patients were almost as useful as the institutional rehabilitation and they decreased the hospital stay period (15,45). Patients cannot benefit from adequate treatment facilities, due to the expert, equipments and some socio-cultural reasons (8). The study, which was conducted for the first time in the region and had the characteristics of a pilot study, indicated that individuals with ischemic stroke could increase their functions with the help of an ordinary care. Even though the exact effects of exercises could not be assessed sensitively, the increase in the activities of daily living was considered remarkable. Besides, there was an increase in the upper extremity functions of patients in the experimental group. Since the obtained functional results were not measured exactly, it could be suggested to study with more sensitive measurement methods in a broader sample group. The fact that mean BI score was higher in the experimental group compared to control group supports the hypothesis of the study. This study is important in terms of the accessibility of therapeutic exercise practice for stroke patients at home.

Conclusion

Individuals with stroke could be discharged with limited functions and some certain permanent disabilities. There is no common opinion about what the treatment and method yielding best results in the past were and how it was succeeded. Providing objective evidences for the benefits of home-based therapeutic interventions is necessary in terms of service providers. In this study, the efficiency of home-based post acute therapeutic intervention was found to be highly important. Rehabilitation practices shall be started as soon as the conditions are suitable. The future studies could be conducted with broad sample groups, where the physical development of patients such as the exercise practice period, start time and intensity of exercise and cardiovascular resistance is revealed more clearly.

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The effect of fermented yogurt on rotavirus diarrhea in children

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Abstract

Rotavirus represents the most common etiologic agent associated with diarrhea in the children both in developing and developed countries. Although the role of probiotic bacteria in the treatment of pediatric diarrhea is fairly well established, Probiotic dairy products are increasingly gaining popularity. We studied the effect of fermented yogurt containing lactobacillus on pediatric rotavirus diarrhea in north of IRIRAN tertiary referral hospital. This study was prospective randomized double blind controlled clinical trial in Booalisina children hospital for using probiotic yogurt in the treatment of acute rotavirus diarrhea between October 2009 - October 2010. Children between 6 months to 6 years presenting with acute watery diarrhea of less than 72 hours duration were screened for rotavirus infection by stool using Enzyme - Linked ImmunoSorbent Assay. All patients with acute diarrheal disease were randomized to receive probiotics (107lactobacillus) fermented yogurt or non probiotic yogurt using in control group does not contain live bacteria. All patients received 100^{cc} yogurts 3 times per day and ORS with a composition as recommended by WHO. We were interview or call parents every day until 72 hours.Data were analyzed by commercial software SPSS16. The difference between the 2 groups analyzed using t- test. The p value ≤ 0.05 was taken as statistically significant. 140 patients were randomized into 2 groups as case and control. A total of 20 cases were excluded for various reasons during the study and finally a total of 120 (60 in cases and 60 in control). Rotavirus identified in 48 patients (33.3% in control group, 46.7% in case group). Mean duration of diarrhea, duration of treatment and stay in hospital was compare in case and control group. No significance was observed in the frequency and duration of diarrhea between case and control group. In our study commercially fermented yogurt with 10⁷ lactobacillus probiotics had no significant impact on minimizing any of symptoms in acute watery diarrhea or proven rotavirus diarrhea .We conclude, importantly, our study emphasized the need for a cautious approach towards commercially probiotic fermented yogurt in the acute management of diarrheal disease in children.

Key word: Fermented yogurt, Rotavirus, Diarrhea, Probiotics

Introduction

Diarrhea is the number one cause mortality in children less than 5 years age. Mortality is highest in developing countries where sanitation is poor. ^(1, 2,3) Oral rehydration therapies (ORT) are the mainstay of management of acute watery diarrhea (AWD). Adjuvant therapy to ORT with probiotics has been investigated since 1998. ^(4, 5)

Rotavirus represents the most common etiologic agent associated with diarrhea in the children both in developing and developed countries. ^(6, 7, 8, 9) This agent is responsible for approximately 600,000 deaths per years. ⁽⁶⁾ Approximately 85% of rotavirus-induced deaths occur in poorest regions of Asia and Africa. ^(10, 11)

Although the role of probiotic bacteria in the treatment of pediatric diarrhea is fairly well established, Probiotic dairy products are increasingly gaining popularity. Yogurt is produced by two starter cultures. Lactobacillus and streptococcus to milk during the fermentation, hydrolysis of the milk proteins occurs, the PH drops, the viscosity increases and bacterial metabolites are produced that contribute to the taste and possibly to the he-alth promoting properties of yogurt.^(3, 12)

We studied the effect of fermented yogurt containing lactobacillus on pediatric rotavirus diarrhea in north of IRIRAN tertiary referral hospital.

Patients and Methods

This study was prospective randomized double blind controlled clinical trial in Booalisina children hospital for using probiotic vogurt in the treatment of acute rotavirus diarrhea between October2009 october2010. The study protocol was approved by Mazandaran Medical University Ethics Committee. Consents were obtained from parents of all the children who met the inclusion criteria for the study. Expecting a 20 % reducing in frequency and duration of diarrhea, using 2 tailed α of 0.05 and power $(1-\beta)$ of 80% we calculated total sample size of 120 patients. Rotavirus unvaccinated Children between 6 months to 6 years presenting with acute watery diarrhea of less than 72 hours duration were screened for colitis by stool examination. If the patients haven't colitis(WBC ≥ 8) they were screened for rotavirus infection by stool using Enzyme-Linked ImmunoSorbent Assay. Then answer sheet were filled for patient by pediatric resident. Exclusion criteria was colitis(WBC 28, dyentery), previous antibiotics usage, pathogenic agents in stool exam such as Giardia, Ecoli, Campylobacter..., Immunodeficiency, chronic disease such as failure to thrive. All patients with acute diarrheal disease were randomized to receive probiotics (10⁷ lactobacillus L-Acidophylus and Bifidobacter) fermented yogurt or non probiotic yogurt using in placebo group does not contain live bacteria. These bacteria produced by Christen Hansen SBY1 and SBY2 starters. Both yogurts were analyzed, quality assured and approved by IRAN Ministry of health. Both products were supplied directly by Kalle manufacture twice a week and were kept well refrigerated until consumption. Both enveloped and coded boxes were prepared offsite and randomization was concealed until recruitment, data collection and analyses were completed. All patients received 100 ^{cc} yogurts 3 times per day and ORS with a composition as recommended by WHO. If necessary, because of excessive vomiting and clinical sign of dehydration, parenteral rehydration was established. The study preparation was given as soon as possible after randomization and did not await rehydration. We were interview or call parents every day until 72 hours. Data were analyzed by commercial software SPSS16. The difference between the 2 groups analyzed using t- test. The *p* value ≤ 0.05 was taken as statistically significant.

Results

During the study period, 400 patients were diagnosed acute watery diarrhea (AWD). 280 patients were excluded from the study at the beginning (inclusion criteria were not fulfilled in 260 patients and parents of 20 patients did not give consent) and finally a lot of 140 patients were randomized into 2 groups as case and control. A total of 20 cases were excluded for various reasons during the study and finally a total of 120 (60 in placebo and 60 in treatment). (fig1)



Figure 1. Flow of participations in the study

All the two groups were comparable with respect of age, sex, weight, stay in day care center, breast feeding, clinical dehydration on the start of study, duration of diarrhea before the study and ORT. (Table 1)

Rotavirus identified in 48 patients (33.3% in placebo group, 46.7% in treatment group). Mean duration of diarrhea, duration of treatment and stay in hospital was compare in case and control group. No significance was observed in the frequency and duration of diarrhea between case and control group (Table 2). No significance was observed in the frequency and duration of diarrhea between case and control in outpatient and admitted group (Table 3, 4).

Table 1. Demographic and baseline characteristics

Characteristics	Controls No =60	Cases No =60	P Value	Confidence Interval
Age, month(mean±SD)	22.81±15.5	26.48±19.5	0.25 *	(-10.06, 2.72)
Weights, kg(mean±SD)	11.16±2.9	11.58±3.94	0.51*	(-1.68, 0.85)
Mean Duration of diarrhea after study,Day(mean±SD)	2.96±0.82	2.88±0.92	0.6 *	(-0.23, 0.4)
No(%) of Rotavirus	20(33.3%)	28(46.7%)	0.13 **	
No(%) of Daycare center attendee	2(3.3%)	3(5%)	1.0**	
No(%) of Breast feeding	44(73.3%)	34(56.7%)	0.056 **	
No(%) of ORT	41(68.3%)	29(48.3%)	0.03 **	
No(%) of Pts requiring IV therapy on admission	12(20%)	37(61.7%)	0.0 **	
No(%) of Clinical dehydration on Admission Mild	27(54%)	27(45%)	0.60**	
Moderate	33(55%)	33(55%)	0.00	
No(%) of Admited	11(18.3%)	6(60%)	0.0**	
No(%) of Vomiting No	16(26.7%)	20(23.3%)		
1-2 times	35(58.3%)	28(46.7%)	0.44 **	
>3 times	9(15%)	2(20%)		

Table 2. Principal Outcome

	placebo	treatment	P Value
	Mean±SD	Mean±SD	
Frequency of diarrhea with Rota ⁺	3.95±1.73	4.71±1.92	0.16*
Frequency of diarrhea with Rota-	4.82±2.64	5.19±3.01	0.59*
Duration of diarrhea with Rota ⁺	3.25±0.96	3.03±1.03	0.47 *
Duration of diarrhea with Rota-	2.82±0.71	2.75±0.8	0.67 *

Table 3. Principal Outcome of frequency and duration of diarrhea between Rotavirus+ and Rotavirus- diarrhea in outpatient and admitted group

	Outpatient	Admited	P Value
	Mean±SD	Mean±SD	
Frequency of diarrhea in control group with Rota ⁺	3.62±1.5	5.25±2.22	0.09*
Frequency of diarrhea in control group with Rota-	4.33±1.86	7.14±4.37	0.14 *
Frequency of diarrhea in case group with Rota+	4.10±1.59	5.06±2.04	0.21*
Frequency of diarrhea in case group with Rota-	5.43±2.5	5.0±3.41	0.69*
Duration of diarrhea in control group with Rota ⁺	3.38±0.96	2.75±0.96	0.26 *
Duration of diarrhea in control group with Rota-	2.79±0.69	3.0±0.82	0.48*
Duration of diarrhea in case group with Rota ⁺	2.70±0.95	3.22±1.06	0.21*
Duration of diarrhea in case group with Rota-	2.57±0.65	2.89±0.90	0.27*

Discussion

Prevention and treatment of acute diarrhea is an important public-health challenge. Booalisina hospital is a tertiary referral center in north of IR-IRAN for a large adjoining area. Acute watery diarrhea is a major cause of referral and hospital admission needing a lot of resources. Even in developed countries at least 30% of hospital admissions for acute gastroenteritis in young children are the results of rotavirus infection. The effect of different probiotic species and strains on diarrhea is currently well accepted; however, the dose required to obtain the best results is less clear. A metaanalysis of 18 eligible studies indicated that coadminstration of probiotics and standard rehydration therapy reduced duration of acute diarrhea by approximately 1 day. There is no recommendation for the dose selection of probiotics. In some study probiotics likely to be limited benefit in treating diarrheal illnesses of short duration such as viral enteritis. Not all commercially probiotic preparations are effective in children with AWD. The bebeficial effects of probiotics may be limited to prophylactic usage in high-risk populations.^{(13,} ^{14, 15)} In our study commercially fermented yogurt with 107 lactobacillus probiotics had no significant impact on minimizing any of symptoms in acute watery diarrhea or proven rotavirus diarrhea. Furthermore, we were unable to demonstrate any improvement in small intestinal recovery during the trial period using the methods we described. Our findings are consistent with other published trials that don't demonstrate a beneficial effect from use of commercially probiotic fermented yogurt therapy in diarrheal disease.

Conclusion

In our study commercially fermented yogurt with 107 lactobacillus probiotics had no significant impact on minimizing any of symptoms in acute watery diarrhea or proven rotavirus diarrhea We conclude, importantly, our study emphasized the need for a cautious approach towards commercially probiotic fermented yogurt in the acute management of diarrheal disease in children.

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The effect of magnesium on emergence agitation in children undergoing adenotonsillectomy under sevoflurane general anesthesia: a prospective randomised clinical trial

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Abstract

Background: The aim of this study was to assess the effect of magnesium on the incidence of emergence agitation in preschool-aged children undergoing adenotonsillectomy with sevoflurane anaesthesia.

Patients & Methods: 42 children, aged between 3 to 7 years, were randomised into either group M (magnesium, n=26) or group C (saline for controls, n=26). Anesthesia was induced by mask with 8 % sevoflurane in nitrous oxide and oxygen. Magnesium 15 mg.kg⁻¹ or saline was administered in about 20 minutes after the endotracheal intubation intraoperatively. All patients were ventilated with 60% nitrous oxide and sevoflurane was given at 1-1.5 MAC in oxygen. Mean blood pressure, heart rate, pulse oximetry, eye-opening time, extubation time were recorded in the operating room. In recovery, patients were evaluated using modified Aldrete score, the Pediatric Anesthesia Emergence Delirium (PAED) scale and the Oucher visual analog Pain Scale. Postoperative nause, vomiting, and airway complication and first analgesic application were recorded.

Results: Time to eye opening, tracheal extubation, and first analgesic administration were not different between the groups. There were no statistically significant differences in mean arterial pressure and heart rate, pain score and PAED peak scale between the groups (p > 0.05). The modified Aldrete score was significantly lower in the magnesium group (p=0.004). There was no statistically significant difference between the groups regarding side effects.

Conclusions: We conclude that the administration of magnesium 15 mg.kg⁻¹ did not have any significant effect in reducing the incidence of emergence agitation in children undergoing adenotonsillectomy under sevoflurane anaesthesia.

Key words: Emergence agitation; sevoflurane; magnesium

Introduction

Sevoflurane is currently the most popular inhaled anesthetic in pediatric anesthesia but emergence from sevoflurane anesthesia is often associated with agitation in preschool aged children (1,2). The prevelance of EA in children ranges from 25 to 80% of those undergoing general anesthesia with sevoflurane (3). Non-purposeful discomfort and agitation, crying or groaning, loss of orientation and incoherence are common findings in this phenomenon (4). EA may be dangerous and may sometimes result in physical harm to children. Also additional treatment may prolong the postanesthesia care unit (PACU) length of stay and families are worried about seeing their child agitated (5).

Various pharmacological interventions were used to prevent occurrence of EA such as fentanyl, midazolam, clonidine and dexmedetomidine, ketamine, propofol, acetaminophen (2,4,6,7). Magnesium has been used for various anaesthetic practice especially in obstetrics and perioperative analgesia. Magnesium has antinociceptive efficiency and have decreased pain by acting as an antagonist of NMDA receptor (8,9). The presence of pain during the perioperative period is one of the possible mechanism of agitation mechanism of possible occurrence (5). Recently, it has been reported that magnesium was not successful in the prevention of EA following general anesthesia in patients aged between 3 and 16 years in doses 30 mg.kg⁻¹ as an infusion (10). Because only one research about pediatric magnesium use has been done, the indications for the use of magnesium in children are uncertain.

Therefore the purpose of this study was to determine the effects of intraoperative magnesium infusion on the incidence and severity of emergence agitation in pediatric patients.

Material and Methods

After Institutional Ethics Committee approval (Inonu University Medical School, Malatya, Turkey), written informed parental consent of each patient were obtained. The patients (n = 52, American Society of Anesthesiologists physical status I and II; age range, 3–7 years) were scheduled for adenotonsillectomy with or without myringotomy and pressure equalization tube placement procedures under sevoflurane anesthesia.

Exclusion criteria were known allergy to the study drugs, sensitivity, or contra-indication to opioids or local anesthetic, renal or liver impairment, acute pharyngeal infection, history of asthma, or clotting disorder and patients with ASA classification III or more.

The children were premedicated with midazolam 0.5 mg.kg⁻¹ orally one hour before the induction of anaesthesia. Paracetamol 30-40 mg.kg⁻¹ was applied rectally to all children one hour before the induction of anesthesia. Parents were allowed to accompany their children into the operating room and stay during the anesthesia induction if children were agitated despite premedication. With standard hemodynamic monitors in place (electrocardiograph, heart rate (HR), pulse oxymeter oxygen saturation, noninvasive blood pressure), anaesthesia was induced by mask with 8 % sevoflurane in nitrous oxide and oxygen (50% /50%) mixture with a 5 L.min⁻¹ fresh gas flow. Following 22 gauge IV cannula insertion, blood samples from the children were collected to assess preoperative plasma magnesium level. Then cisatracurium 0.2 mg.kg⁻¹ and alfentanil 20 mg.kg⁻¹ IV was applied to facilitate tracheal intubation. Anesthesia was maintained using nitrous oxide 60% and sevoflurane 1.5 % to 2.5 % in oxygen. The patients were ventilated through controlled mechanical ventilation to sustain the end-tidal carbon dioxide (ETCO₂) concentration between 30 and 35 mmHg. Age and nitrous oxide affect the MAC of sevoflurane to different degrees; therefore an age/ nitrous-adjusted MAC anestetetic level was provided for each child before surgical incision and throughout the procedure. Children were assigned one of two groups according to a computer-generated randomization program. Two minutes after intubation, in group M (n = 26), patients received an infusion of magnesium sulphate 15 mg.kg¹ in 20 mL 0.9% NaCl for 20 minutes. In group C (n = 26), patients received only the same amount of 0.9% NaCl. Each syringe was labelled with the patients' number, and neither the treatment assignment nor the contents of the syringe were known to anaesthesia staff. Randomisation and allocation of the subjects into the groups were carried out using computerised numbers by an anaesthesiologist not participating in the study.

The HR, mean arterial blood pressure (MAP), oxygen saturation (SpO₂), were recorded before and after induction of anesthesia, and every 5 minutes during the operation. Five minutes before the extubation, blood samples from the children were taken to determine postoperative plasma magnesium level. At the end of the operation, following the discontinuation of sevoflurane and nitrous oxide, neostigmine 50 mg.kg⁻¹ and atropine 20 mg.kg⁻¹ were administered to reverse the effect of the residual neuromuscular blockade according to the response to a nerve stimulator (TOF-Watch SX[®], Organon, Ireland). Oropharyngeal secretions were aspirated and then extubation was performed when normoventilation was achieved and the patients regained gag or cough reflex. Thereafter, patients were transported from the operating room to the Post Anesthesia Care Unit (PACU). At the end of the procedure, time from opening mouth to the finishing the operation (the duration of surgery), time to start of induction until discontinuation of sevoflurane (the duration of volatile administration) and time to tracheal extubation were recorded. Pre-operative and post-operative level of blood magnesium were also recorded. A research observer who was blinded to the treatment allocation,

pain score and severity of EA and sedation score were evaluted. For assessment of agitation, Sikich and Lerman's Pediatric Anesthesia Emergence Delirium (PAED) scale was used, a recently published 5-point scale with 5 gradations for each item (11). [Table 1]. Patients were considered agitated if they had a score of 16/20 or higher. Pain was assessed with the Oucher visual analog Pain Scale (12). PAED and Oucher visual analog Pain Scale were evaluated every 10 min intervals for 1 h in the PACU. In a recovery room a modified Aldrete score was used to assess recovery from anaesthesia (13). If a Oucher Pain Scale was scored 5 or more, the patients were judged to have pain sufficient to necessitate opioid analgesia meperidin 0.5 mg.kg⁻¹. The time to administration of first analgesic drug was recorded. The incidence of adverse events such as postoperative nausea and vomiting (PONV), laryngospasm, desaturation and breath-holding, after endotracheal extubation and during PACU presentation were also recorded. In addition, with signs of hypermagnesemia facial flushing, sweating, decreased reflexes, CNS depression were noted. If these symptoms occured, the patient required treatment held in the PACU until determination of the blood postoperative blood Mg levels. When the modified Aldrete score was higher than 9, patients were considered ready for discharge from the PACU.

Table 1. Pediatric Anesthesia Emergence Deliri-um (PAED) Scale

1.The child makes eye contact with the caregiver	4 = not at all
2. The child's actions are purposeful 3. The child is aware of his/her	3 = Just a little 2 = quite a bit 1 = very much
surroundings	0 = extremely
4. The child is restless	0 = not at all
5.The child is inconsolable	1 = just a little 2 = quite a bit 3 = very much 4 = extremely

Statistical Analysis

Data are given as the mean $(\pm SD)$ and median as appropriate. The number of patients required in each group was determined before the study by a power calculation. Forty % decrease in the primary end-point PAED score after adding magnesium infusion sevoflurane anaesthesia was found to be the minumum clinically important difference. We estimated that the standart deviation of PAED score values would be up to 4.9. As a result 21 patients per group were required with power of 80 %. Patients characteristics were analysed using Sample t test for the comparison of the two groups. Categorical data were compared using the Yates corrected chi-square test. A p value of <0.05 was considered statistically significant in all tests. Statistical analysis was performed using SPSS 15.0 (SPSS 15.0, SPSS Inc.; Chicago, IL, USA) by an expert statistician.

Results

A total of 52 patients were enrolled in the study and 26 patients analyzed in each group. The groups were similar with respect to age, weight, ASA status, and duration of surgery and anesthesia and the duration of volatile administration (p > 0.05). The 21 patients were male gender in group M, whereas 12 patients in group C (p=0.02) [Table 2].

Table 2. Patients demographics, duration of surgery and anesthesia

Variable	Group M (n= 26)	Group C (n = 26)
Age (mo)	66.0 ± 17.6	66.0 ± 16.2
Male sex (n/%)	21 (80%)*	12 (46%)
Weight (kg)	22.0 ± 5.0	21.0 ± 4.8
ASA (I /II)	24/2	25/1
Duration of anesthesia (min)	52.4 ± 13.5	52.4 ± 11.0
Duration of surgery (min)	37.3 ± 12.9	38.4 ± 11.7
Duration of volatile administration	53.0 ± 13.6	48.6 ± 12.3

Data are presented as mean \pm SD and number of patients (%) * p = 0.02 yates' corrected chi-square test

Time to tracheal extubation, and, eye opening and time to first analgesic administration were not different between the groups (p > 0.05). The plasma magnesium concentrations in group M were significantly higher than group C (p < 0.05). In group M, plasma magnesium concentrations were below 2.5 mmol. L⁻¹. There was no significant difference between pain score and PAED peak scale between the study groups during the study period (p >0.05). The number of patients with PAED scores \geq

Group	T1	T2	Т3	T4	T5	T6	T7
Group M (n= 26)							
Median (range)	12,5(0-19)	6(0-12)	4(0-12)	3(0-7)	3(0-5)	3(0-5)	3(0-5)
Score $\ge 16/20$ (n)	5	1	0	0	0	0	0
Group C $(n=26)$							
Median (range)	12,5(2-18)	8,5(0-18)	4(0-11)	2(0-8)	1(0-5)	0,5(0-5)	0,5(0-5)
Score $\geq 16/20$ (n)	7	0	0	0	0	0	0

Table 3. PAED score at 0, 10, 20, 30, 40, 50 and 60 min. in PACU

Data are presented as median (range).

16 at least once during the evaluation period were 7/26 (27%) in group C and 6/26 (23%) in group M. The distribution of PAED scores \geq 16 at each of the six time points assessed was presented in Table 3. The modified Aldrete score on arrival in PACU was significantly lower in the magnesium group (p= 0.004) [Table 4]. The patients with Oucher Pain Scale scores \geq 5 at 0 min were 17 in the group M and 15 in the group C, respectively. Oucher Pain Scale scores remain higher than 5 in 2 patients in the group M at 10 min in PACU. In the recovery room meperidine was given to 15 children in Group C, 17 in Group M at 0. min. Meperidin 0.5 mg.kg⁻¹ was again injected to these two patients according to pain scale who remained higher.

	Group M (n= 26)	Group C (n = 26)
Time to tracheal extubation (min)	4.0±2.3	4.5 ± 2.5
Time to open eyes (min)	7.4 ± 4.2	8.4 ± 2.6
Aldrete score in PACU	9.0 (7.0-9.0) ^a	9.0 (7.0-10.0)
Pain score in PACU	5.3 ± 1.6	5.3 ± 2.1
PAED peak scale	12.5 ± 4.3	12.5 ± 4.5
PAED scale $\geq 16/20$ (n),(%)	6 (23)	7 (27)
Time to first analgesic (min)	9.0±2.3	9.0±2.3
Mg level preoperative (mmol/L)	2.0 ± 0.1	2.0 ± 0.1
Mg level postoperative (mmol/L)	$2.3 \pm 0.2^{*}$	2.0 ± 0.1

Table 4. Recovery characteristics of the patients

PACU = postanesthesia care units; *PAED* = pediatric anesthesia emergence delirium.

Data are presented as mean \pm SD or median(range) or number of patients, (%) *p < 0.05, *p = 0.004

There was no statistically significant difference between the groups in the incidence of adverse events such as nausea, vomiting, the incidence of laryngospasm or desaturation [Table 5]. Respiratory depression was not observed, and SpO_2 values during and after operation did not differ between groups. There was no signs of hypermagnesemia in both groups.

Table 5. Adverse Effects (number of patients, %)

	Group M (n= 26)	Group C (n = 26)
Nausea and Vomiting	8 (30)	12 (46)
Breath-holding	1 (4)	2 (4)
Laryngospasm	0	0
Desaturation	0	0

There were no statistically significant changes of MAP and HR, during the intra-operative period in both groups [Figure 1].



Figure 1. MAP changes during study period.

Discussion

The results of this study demonstrate that 15 mg.kg⁻¹ of magnesium sulphate administered i.v. following anaesthesia induction did not reduce the incidence of EA without altering haemodynamics in children undergoing adenotonsillectomy. However, the modified Aldrete score on arrival in PACU decreased in the magnesium group.

EA is a well-known side-effect of recovery from inhalation anaesthesia which is characterized with unpurposed and uncoordinated movements, with hypertonia of the upper extremity and bending of the limbs. These symptoms may be dangerous to the child during the perioperative period and also it may be frightening for parents in PACU (14).

The mechanism of the EA after general anaesthesia has not been defined and also the pathogenesis and treatment of the EA remains still unclear. There are a lot of factors such as rapid recovery from inhalation agent expecially sevoflurane, type of surgery like otorhinolaryngologic surgery, preschool age, pain, genetic predisposition, duration of anaesthesia (2,15). Our study included young children, sevoflorane and otorhinolaryngological procuderes. Therefore, these patients were considered to be at high risk for this complication.

Rapid emergence from inhalation anaesthetics and pain sensation are main causes of EA. So recent studies on this topic focuses on the prevention of pain and use of analgesics should be early and preferably intraoperatively (2,5). Based on these findings pain is not only one factor contributing to the occurence of EA (16).

A number of analgesic and sedative agents have been used to prevent the incidence of EA such as ketamine(2), propofol(4), clonidine(5), dexmedetomidine(15), acetaminophen(7), fentanyl(16), etc.

Opioids are effective agents to reduce the incidence of EA. However opiods increase the airway problems and nausea and vomiting (17).

Bock et al.(18) reported that applying caudal or i.v. 3 μ g.kg⁻¹ of clonidine were effective to prevent EA in children after the sevoflurane anaesthesia. Guler et al.(15) suggested that they observed a reducing of EA with administration of dexmedetomidine i.v. 0.5 μ g.kg⁻¹ after the sevoflurane anaesthesia in children undergoing adenotonsillectomy. But the alpha-2- agonists produce dose-dependently negative effects on blood pressure and heart rate (19).

Ketamine, a NMDA receptor antagonist, has sedative, amnesic and analgesic properties (20). Lee et al. reported that the i.v. administration of ketamine 0.25 mg.kg⁻¹ or 0.5 mg.kg⁻¹ in general anaesthesia with sevoflurane reduced the incidence of EA without any particular side-effects or delays in recovery according to control groups. They also stated that 0.5 mg.kg⁻¹ of ketamine recomended as an appropriate dose to prevent EA (2).

It has known that magnesium as an adjuvant to general anesthesia may modulate nociception. This

is probably via its intereaction with the NMDA receptor related calcium channels (8). Several studies have been reported that the usage of magnesium infusion after anesthesia induction reduced perioperative opioid consumption (21,22). On the other hand, Ko et al. showed that perioperative intravenous administration of magnesium sulfate had no effects on postoperative pain (23). O'Flaherty et al. studied that, administration of small dose of ketamine and/or magnesium to reduce pain or analgesic consumption in children undergonig tonsillectomy. This study did not demonstrate a decrease in pain or analgesic consumption (24).Our results are similar to theese studies, we did not find any difference for postoperative pain scores and analgesics consumptions.

Apan et al.(10) who studied between 3-16 years of age children, who evaluated magnesium influence following sevoflurane anaesthesia for adenoidectomy/tonsillectomy. Different from the mentioned study, age range of our group comprises the ages 3-7 years that EA is most commonly seen. Pain after adenoidectomy is typically described as moderate (17). They may have not found more EA in their study, because some of their patients had adenoidectomy. All of our patients had tonsillectomy operation. They used 30 mg.kg⁻¹ of magnesium just prior to the end of surgery. We used 15 mg.kg⁻¹ of magnesium suggested by Gulhas et al. (25) to decrease side effects of magnesium. And also they used pain/discomfort scale and agitation score to assess EA. They found no significant difference in these scales between the two groups like our study. But we used PAED scale to assess EA. PAED scale is the most exhaustive and valuable scale, which was identified Sikich and Lerhman to measure the severity of EA (11). The Oucher visual analog Pain Scale is a poster developed for children to help them communicate how much pain or hurt they feel. This scale has three ethnic versions to making clinical decision about pain and pain management in 3 to 12 years old Caucasian, Hispanic and African-American children (26). We used Hispanic version of the Oucher pain scale in our study. We did not find any difference in the incidence of EA with current scales like Apan et al.

In conclusion, although magnesium as a common used adjuvant to anesthesia we found no significant decrease in the incidence of EA in preschool age patients receivng magnesium 15 mg.kg⁻¹ and increased recovery times.

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The Predictive Value Of CRP, CEA, IL-6, IL-8, And TNFa In The Diagnosis Of Malignant Pleural Effusions

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Abstract

Aim: In this study, we investigated the potential utility of some simple, rapid, biochemical tests that detect the tumor markers interleukin 6 (IL-6), interleukin 8 (IL-8), tumor necrosis factor alpha (TNF α), C reactive protein (CRP), and carcinoembryonic antigen (CEA) in diagnosing malignant pleural effusions (MPEs) in exudative pleural fluids.

Material and Methods: The study included 70 patients who had exudative PEs. The presence of CRP, CEA, IL-6, IL-8, and TNF α were investigated in the patients' pleural fluids. The cases were grouped into a malignant pleural effusion (PE) group (n = 27) and a benign PE group (n = 43) according to their etiological diagnosis, and the median levels of CRP, CEA, IL-6, IL-8, and TNF α in the two groups were compared.

Results: The levels of pleural fluid CEA and IL-6 were significantly higher in the malignant PE group compared with the benign PE group (p <0.01 and p = 0.002, respectively). A meaningful difference was not found between the median value of the pleural fluid CRP IL-8 and TNF α levels in the two groups (p >0.05). We used Roc curve analysis to determine the sensitivity and specificity of CEA as a marker of malignant pleural effusion. When the CEA cut-off point was 1 ng/ml, the sensitivity was found to be 85%, and the specificity was 17 ng/ml, the sensitivity was 29%, and the specificity was 97%.

Conclusion: Although the number of cases in the study is low, our findings suggested that CEA and IL-6 may be useful in distinguishing whether exudative PEs are malignant or benign.

Key words: Malignant pleural effusion, CEA, IL-6

Introduction

The diagnosis of malignant pleural effusions (MPEs) is based on a cytological evaluation of the pleural fluid or by biopsies of pleural specimens containing malignant cells. A number of tumor markers have been used to optimize the diagnostic sensitivity of malignant pleural fluid in recent years. Tests proposed for the diagnosis of MPEs include electron microscopic investigation of the pleural fluid, pleural fluid cell chromosome analysis, measurement of the carcinoembryonic antigen (CEA) in the pleural fluid, and analysis of lactate dehydrogenase (LDH) isoenzymes levels (1). In addition, the potential diagnostic utility of a large number of tumor markers in the pleural fluid have been studied (2, 3). The most widely studied tumor marker in the pleural fluid is CEA (4). Alatas at al. reported that pleural fluid CEA levels were higher in malignant than in benign fluids (5). Some past studies have reported increases in the CEA level of 34-88% in malignant pleural fluids (6). The CEA value was also reported to have more diagnostic utility, especially in cases with negative cytology (7). CRP is an acute phase protein, which is frequently used for demonstrating inflammation and tissue damage (8). Studies of CRP in PEs have found that this marker was higher in malignant fluids than in benign fluids (9). The pleura is a dynamic and metabolically active membrane due to its cellular elements and cell mediators. Many studies have been conducted to shed light on the immunological mechanisms underlying pleural diseases. Pleural inflammation causes an increase in vascular permeability. Pleural fluid accumulation is the result of increased liquid production and/or decreased lymphatic drainage. The pleural fluid is rich in proteins, inflammatory cells, and mediators (10). The presence of cytokine-producing cells and cytokines has been reported in malignant and benign PEs (10, 11). IL-6 is a lymphoid and non lymphoid multifunctional cytokine, which regulates T and B cell functions. It is also a powerful initiator of the acute phase protein response (12). Studies have reported disparate findings about the ability of IL-6 to distinguish malignant and benign effusions (13). IL-6 has been reported to be associated with acute and chronic pleural infections (14). In another study, IL-6 was found not to be associated specifically with a tumoral formation (15). Pleural fluid IL-6 levels were found to be higher a malignant PE group than in a benign PE group in another study (13). IL-8 plays a role as a mediator and a regulator in leukocyte chemotaxis during the inflammatory processes. In a study comparing the level of pleural fluid IL-8 levels in cancer and noncancer patients, IL-8 levels were higher in patients with cancer (13). In other studies, the IL-8 level was reported to be higher in infectious pleural effusions (PEs) compared with noninfectious PEs (11, 16, 17). TNFa is a proinflammatory cytokine produced by various cell types. TNF α levels have also been reported to be high in malignant PEs in common with infectious PEs (18, 19). We aimed to investigate whether relatively simple, fast biochemical markers such as CRP, CEA, IL-6, IL-8, and TNF α may be useful for differentiating malignant and benign effusions in exudative PEs using well-known diagnostic modalities such as pleural fluid cytology and pleural biopsy.

Materials and Methods

Number of one hundred thirty-eight patients with PEs who were admitted to the Dicle University Medical Faculty of Education and Research Hospital between June 2008 and July 2009 were evaluated for the study. Number of seventy patients with exudative PEs were included in this study. Pleural fluid (50 cc) was obtained by thoracentesis. LDH, total protein, albumin, glucose, and pH levels were detected by arterial blood gas analysis an blood biochemistry analysis in the pleural fluid. The pleural fluid cell count was measured in all of the patients. Ziehl-Nielsen staining and plating to Lowenstein-Jehnsen medium were performed for patients with tuberculosis (TB). suspect Nonspecific culture plating was performed in patients with prospect parapneumonic PEs. A pleural biopsy or video-assisted thoracoscopic surgery (VATS) were performed in cases that could not be diagnosed with noninvasive methods. Pleural fluid (3 cc) was placed in routine biochemistry gel tubes during the first diagnostic thoracentesis, and three tubes were created for each patient. The prepared materials were evaluated in the Dicle University Faculty of Medicine, Department of Biochemistry, Central Laboratory. The pleural fluid samples were centrifuged at 5,000 rpm for 5 min. A large number of CRP, CEA, IL-6, IL-8, and TNF α measurements were performed on the same day, using the upper part of the centrifuged sample.

When cytokine measurement was not possible, we were took 400 microliters from the upper part of the centrifuged pleural fluid samples and stored them at -20 °C for one months. On the day of measurement, the samples were kept at room temperature until dissolution was achieved. Two hundred milliliters of fluid was acquired from the upper part of the pleural fluid, which had been centrifuged for 5 min at 5,000 rpm. This was transferred to a separate tube for CRP measurement. CRP was analysed by the Beckmann Coulter, branded, IM-MAGE/immunochemistry system device and with nephelometric method. The device code was S / N 2528. The CRP was measured in mg/l. IL-6, IL-8, and TNFa measurements were performed with the IMMULITE 1000, Diagnostic Products Corp., Los Angeles, CA, USA device, with specific kits used for each parameter

A 400 ml sample from the upper part of the centrifuged pleural fluid was placed in the sample tube of the device for the measurement of the IL-6, IL-8, and TNF α . The results were measured in pg/ml, and the reference range was (0.0–12.0) for IL-6. For IL-8, the results were measured in pg/ml, and the reference range was (0.0–70.0). Finally, for TNF α , the results were measured in pg/ml, and the reference range was (4.0–10.0).

CEA measurement was performed using the Modular Analytics E170 (Roche Diagnostics, Mannheim, Germany) device. One milliliter of pleural fluid was placed in the sample container of the device. The measurements were made with the electro-chemiluminescent immunoassay method. The results were measured in ng/ml and reference range was - <4.3 for CEA. A posteroanterior chest

X-ray, a complete blood count, analysis of the sedimentation rate, routine blood chemistry, urinalysis, electrocardiography, and sputum smears for bacillus TB were performed in all patients.

The etiological diagnostic criteria for each disease group were determined as follows:

- Tuberculosis pleurisy

TB pleurisy was diagnosed by the presence of bacillus TB in a pleural fluid smear, the growth of bacilli in the PE, and/or the detection of granulomatous inflammation with caseation necrosis in pleural biopsy specimens. In addition, clinical and radiological methods were used to diagnose TB, if the patient's clinical appearance and ages were compatible with TB, based on the presence of lymphocyte dominance in the fluid with >47 ADA levels.

- Malignant PE

The presence of malignancy detected histologically or cytologically in the pleural fluid or in the pleural biopsy specimens (taken with a closed pleural biopsy or VATS).

- Parapneumonic PE

A parapneumonic PE was diagnosed on the basis of clinical symptoms and signs (fever, chills, chills, and purulent sputum), ipsilateral PE with pneumonic infiltration in the chest X-ray, and a clinical response to antimicrobial therapy.

- Dressler's syndrome

In undiagnosed cases, patients with a history of myocardial infarction, coronary artery surgery and/or a response to nonsteroidal anti-inflammatory drugs were considered as having Dressler's syndrome.

- Rheumatoid pleurisy

In patients diagnosed with rheumatoid arthritis, rheumatoid pleurisy was diagnosed on the basis of a pleural fluid glucose value <30 mg/dl, LDH >700 IU/dl, and rheumatoid factor RF titer >1/640, and a low complement level.

- Benign asbestos pleurisy

A history of asbestos exposure and having undergone a 3-year follow-up to rule out other causes of PE were diagnostic for benign asbestos pleurisy.

- Other

Patients with exudative PEs were diagnosed with pleural fluid analysis and a pleural biopsy

Statistical analysis

Mean (\pm) and standard deviation (SD) values are given for descriptive statistics of continuous variables. Median values are given for the descriptive statistics of variables with a discrete or an abnormal distribution. The student's t-test, which examines the average of two independent groups, was used to test age due to variations associated with age were continuous. Gender variables were cross-tabulated and then analyzed with the chi-square test. The CRP, CEA, IL-6, IL-8, and TNF α variables not showing a normal distribution were tested with the Mann-Whitney U-test. Hypothesis were bi-dire c tional and p <0.05 was considered significant. ROC curve analysis was used to identify the cut-off points of the CEA value. SPSS 11.0 (SPSS, Inc., IL, USA) was used for the statistical analysis.

Results

Of the 70 patients, 23 (32.8%) were female and 47 (77.2%) were male. The mean age was 56.5 \pm 15.7 years in the malignant group and 43.6 \pm 20.4 years in the benign group. Forty-three PEs were benign and 27 were malignant. Comparisons were made between the benign and the malignant groups due to the number of cases being fewer in the benign subgroup than in the benign and malignant PE groups. The subgroups of each group are given in Table 1.

Comparison of median CRP, CEA, IL-6, IL-8 and TNF α values in the patients with benign and malignant PEs revealed a significant difference between the CEA and IL-6 values in these two groups (p <0.001 and p = 0.002, respectively) (Table 2).

ROC curve analysis was performed to detect the sensitivity and the specificity of the pleural fluid CEA level. The ROC curve of the pleural fluid CEA levels is given in Figure 1. The cut-off values for the pleural fluid CEA levels based on this curve are presented in Table 3. ROC analysis was not performed for IL-6 values in the malignant PE group (100%) due to these being more than the upper laboratory limit (> 1,000). The pleural fluid IL-6 level was greater than the upper laboratory limit in 19 (44.1%) of 43 patients with benign PEs.

Benign Pleural Effusion	Number of patients	Malignant Pleural Effusion	Number of patients
TB Pleurisy	17	Non-small cell lung CA	9
Parapneumonic Effusion	19	(cell type not classified)	1
Dressler's Syndrome	1	Epidermoid lung CA	1
Rheumatoid Pleurisy	1	Small cell lung CA	2
Chronic Pleurit	4	Lung Adenocarcinoma	7
BenignAsbestos Pleurisy	1	MPM	1
		Breast CA	1
		Ovarian CA	1
		Adenocarcinoma with unknown primary	1
		Thymoma	1
		Malignant melanoma	1
		Skin squamous cell carcinoma	1
		Malignancy with unknown primary	
Total	43	Total	27

Table 1. Subgroups of benign and malignant pleural effusion groups

TB= Tuberculosis CA= Carsinoma MPM= Malignant pleural mesothelioma

Table 2. Pleural fluid median values of CRP, CEA, IL-6, IL-8 TNFa

Marker	Benign effusion Median value	Malignant effusion Median value	р
CRP (mg / l)	22.70	20.0	0.962
CEA (ng / ml)	0,96	4.50	< 0.001
İL-6 (pg/ml)	850	1000	0.002
İL-8 (pg/ml)	605	654	0.511
TNFα (pg/ml)	88.45	48.50	0.072



Table 3. Cut off values for pleural fluid CEA level of sensitivity and specificity

Level of CEA	Sensitivity	Specificity
1,00	0,85	0,51
1,52	0,77	0,65
2,07	0,63	0,76
3,12	0,55	0,86
4,43	0,51	0,95
7,30	0,48	0,95
13,10	0,33	0,97
17,00	0,29	0,97
26,20	0,18	0,97

CEA= Carcinoma embryonic antigen

Discussion

PEs may be related to a variety of different etiologies and may occur during intrathoracic or systemic diseases. It is easy to demonstrate the presence of PEs in clinical and radiological test. However, it is not so easy to determine the etiology of the fluid even with all the diagnostic procedures available, such as radiological methods, biochemical and cellular analysis of the fluid, cytological examination, microbiological analysis, and closed or open biopsy procedures. In a series of pleurisy cases investigated by fluid analysis, biopsies, and other diagnostic tests, Erk et al. previously reported a definitive diagnostic rate of 36%, a possible diagnosis rate of 60%, and the rate of patients that could not be diagnosed as 4% (20). It is important to distinguish the etiology of PEs, particularly benign effusions versus malignant effusions (21). Cytological analysis of the pleural fluid has been reported to be diagnostic in 9–80% of patients with malignancy.

However, a success rate of approximately 60% has been found in many case case series (22). The simultaneous use of a pleural needle biopsy increases the diagnostic accuracy by 7% (22).

Although invasive methods have an important place in the differential diagnosis of PEs, the potential utility of many biochemical and immunological markers has recently been the subject of research due to the high costs and the morbidity and mortality risks associated with the invasive procedures. We aimed to investigate the use of CRP, CEA, IL-6, IL-8 and TNF α for this purpose in this study. CRP is an acute-phase protein, which is synthesized in the liver in response to various stimuli. Pleural fluid CRP levels of benign effusions have been reported to be higher than in malignant effusions (23). In a previous study, the CRP level was found to be >45 mg/l in 44% of benign effusions, and the specificity was 0.95 (24). Vidriales et al. found higher CRP levels in fluid in inflammatory PEs compared with other types of PEs (23). In another study, the parapneumonic effusion group had higher CRP levels in fluid compared with TB and malignant effusions (25). Castano et al measured pleural fluid CRP levels and found that these were significantly higher in a parapneumonic and TB pleurisy group than in a malignant pleurisy group (23). In our study, pleural fluid CRP values were higher in the benign group compared with the malignant PE group. However, the difference between the pleural fluid CRP levels in the two groups was not statistically significant (p > 0.05). The presence of high CRP levels in the fluid in both the malignant and the benign PE groups suggests that this acute phase reactant may increase in malignant processes, as well as in inflammatory events. Many researchers have recently investigated the utility of pleural fluid tumor markers in the diagnosis of malignancy, with the most widely studied marker being the pleural fluid CEA level (4). CEA increases, the most common in colorectal cancers and then in lung cancers (50-77%). A relationship has been identified between the CEA level and the lung cancer stage (26). In pleural fluid studies, CEA levels have been reported to increase between 34-88 % in malignant pleural fluids (6). The CEA level has also been reported to have more diagnostic value, especially in cases with negative cytology (7). Many researchers have found high levels of CEA in malignant effusions compared with benign effusions (27, 28). In our study, pleural fluid CEA levels were also significantly higher in the malignant PE group compared with the benign group (p < 0.001). The results of all of these studies and our study suggest that CEA can be used as a marker to aid the differential diagnosis of malignant PEs. Cytokineproducing cells and cytokines have been reported in PEs of malignant and benign diseases (10, 11, 13). Abnormal levels of IL-6 production by tumor cells have been reported in neoplastic diseases, as well as in autoimmune and inflammatory diseases (29). IL-6 is a multifunctional cytokine, which is involved in the B and T lymphocyte stimulation, megakaryocyte platelet production, and the synthesis of acute phase proteins such as CRP. IL-6 were investigated by researchers in PEs which developed with varying etiologies. However, studies have yielded contradictory findings, with some studies reporting higher IL-6 levels in malignant PEs compared with other exudative PEs (13, 30). Duysinx et al was not associated IL-6 with a tumoral process specifically (31). Pleural fluid IL-6 levels in infectious PEs have also been reported to be higher than in malignant pleural fluids in some studies (11, 32). In our study, the pleural fluid IL-6 levels in the malignant PE group were significantly higher compared with the benign effusion group. The results of all of these studies suggest that there is a need for larger case series and more comprehensive studies to clarify the potential role of IL-6 in the differential diagnosis of PEs. The main effect of IL-8 is activation and chemotaxis of neutrophils, which are dominant cells in PEs that result from acute inflammation. IL-8 is a primary chemotactic cytokine, which facilitates neutrophil migration into the pleural space (33). Alexandrakis et al. compared IL-8 levels in cancer and noncan-
cer patients and found no difference in serum levels, although pleural fluid levels were higher in the patients with cancer (13). Pleural fluid, IL-8, TNF α , and IFN- γ levels were examined in another study and found to be higher in a TB pleurisy group compared with parapneumonic pleurisy and malignant pleurisy groups (34). In our study, the comparison of the pleural fluid IL-8 levels in the malignant and the benign PE groups showed that these were higher in the malignant group. However, the difference was not statistically significant (p=0.511).

TNF α is a proinflammatory cytokine produced by various cell types. It is released from activated macrophages, monocytes, fibroblasts, and other cells such as T and B cells. TNF α is produced by various benign and malignant cells in the microenvironment of solid tumors. Studies of solid tumors have shown that $TNF\alpha$ produced by both tumor cells and host cells that promote tumor growth and metastasis (monocytes, macrophages) (35). Some studies have reported that $TNF\alpha$ levels are high in infectious PEs and in malignant PEs (18, 19). Other studies have reported high levels of $TNF\alpha$ in TB pleurisy cases compared with patients with malignant PEs (36, 37). Odeh at al. found significantly higher pleural fluid TNFa levels in malignant effusions compared with a benign group (38). Increased local production of TNF α in the pleura of malignant PE patients may partially explain this finding. Indeed, macrophages, which are the main source of TNF α production, are dominant cells in malignant PEs (19). Soderblom et al. did not report a significant difference in the levels of $TNF\alpha$ in exudative PEs with different etiologies (37). In our study, although TNF α levels were high in the benign group, there was not a significant difference between the two groups. This result is similar to that of Soderblom et al. who suggested that $TNF\alpha$ is not useful in the differentiation of benign effusions in MPE.

Conclusion

A range of markers (CRP and tumor markers such as various cytokines) have been measured in past studies, and the different etiologies of PEs have been compared, all of which have yielded valuable data about the pathogenesis, differential diagnosis, and progress of PEs. Some measurement kits have not been standardized, and this may lead to differences when reviewing and comparing the results. The approach that we used was heterogeneous in terms of working methods and grouping of cases. The results of this study suggest that CEA and IL-6 could be beneficial in the differential diagnosis of malignant and benign exudative PE. It is clear that multicenter studies of larger case series, which utilize standardized kits and methods, are needed, rather than invasive tests, to aid the differential diagnosis of different etiological groups of PEs and shed light on the potential utility of CRP, CEA, and some cytokines as diagnostic markers of malignant PEs.

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Potential drug-drug interactions in cardiology ward of a teaching hospital

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Abstract

Objective: To identify frequency and nature of potential drug-drug interactions (pDDIs) in cardiology ward and their association with some risk factors.

Methods: Micromedex Drug-Reax software was used to identify pDDIs in clinical records of 400 randomly-selected patients admitted to cardiology ward. Logistic regression was applied to determine the odds ratio for specific risk factors of pDDIs i.e., age, gender, hospital stay and number of drugs.

Results: In this study, 100 interacting drugcombinations were identified that encountered in total number of 1120 pDDIs with median of 03 pDDIs per patient. Overall 310 (77.5%) patients were exposed to at least one pDDI regardless of severity-types, 147 (36.75%) to at least one major pDDI, 279 (69.75%) to at least one moderate pDDI, and 200 (50%) to at least one minor pDDI. Among 1120 pDDIs, most were of moderate (631, 56.3%) or major severity (284, 25.4%); fair (507, 45.3%) or good (470, 42.0%) type of scientific evidence; and delayed onset (565, 50.4%). Top 23 frequently occurring pDDIs included 09 major and 13 moderate and 01 minor pDDIs. Most frequent major pDDIs included heparin + aspirin (39 cases), digoxin + spironolactone (35), spironolactone + ramipril (23), warfarin + aspirin (17), heparin + nitroglycerin (14), warfarin + amiodarone (14), digoxin + amiodarone (13), clopidogrel + omeprazole (11), and spironolactone + captopril (10). There was significant association of the occurrence of one or more pDDIs with patient's age of 65 years or more (p=0.007), male gender (p=0.03), hospital stay of 04 days or longer (p=0.002), and taking 07 or more drugs (p<0.001).

Conclusion: Moderate and major pDDIs were common in cardiology ward. Patients with old age, longer hospital stay, male gender and taking more drugs were at higher risk to pDDIs.

Key words: Drug-drug interaction, potential drug-drug interaction, prescriptions screening, drug related problem, clinical pharmacy.

Introduction

Mortality and morbidity are increased in patients experiencing drug-drug interactions (DDIs). It has been estimated that about 16.6% adverse drug reactions and up to 4.8% of hospital admissions are caused by DDIs [1, 2]. Potential drug-drug interactions (pDDIs) are common with cardiovascular (CV) drugs and patients with CV disorders are more likely to be affected by these DDIs because of complex regimens, polypharmacy and comorbid conditions [1, 3]. In hospital settings, the issue of DDIs deserves more attention because hospitalized patients are often elderly people, suffering from more than one disease, renal or hepatic dysfunction, electrolytes imbalance and to whom drugs are usually administered through intravenous route [4, 5]. PDDIs are often predictable and therefore they can be prevented by proper monitoring [6]. Studies that explore occurrence and nature of pDDIs will help healthcare professionals to identify and prevent these interactions. The aim of this work was to identify frequency & nature of pDDIs in cardiology ward and their association with some risk factors. A second aim was to determine the drug-combinations that were commonly implicated in pDDIs.

Methods

Setting, design and ethical approval

This study was carried out in cardiology ward of a 1000-bed tertiary care teaching hospital, Ayub Teaching Hospital (ATH), Abbottabad, KPK, Pakistan. ATH provides health care and referral services to a population of about 400,000 inhabitants of Abbottabad and Northern Areas of Pakistan. This was a cross-sectional study that involved review of clinical records of 400 randomly-selected patients admitted to cardiology ward of the hospital during a 1-year period from 1st September 2008 to 31st August 2009. This study was approved by the Ethical Committee of the Department of Pharmacy, University of Peshawar.

Data collection and identification of pDDIs

Permission was obtained from hospital administration to conduct this study in cardiology ward of the hospital. Medical charts of 400 patients were selected randomly from a 1-year (1st September 2008 to 31st August 2009) patients' medical records of cardiology ward. A one-year period was selected in order to exclude seasonal variations. Patients' charts were analyzed for identification and categorization of pDDIs using drug interaction screening software, Micromedex Drug-Reax® System [7]. Both routine and PRN (pro re nata: as required) medications were included in analysis. In order to identify nature of the identified pDDIs, they were categorized on the basis of onset, severity and scientific evidence as follows:

Onset

- Rapid: The effect of interaction will occur within 24 hours of administration.
- Delayed: The effect will occur if the interacting combination is administered for more than 24 hours i.e., days to week(s).

Severity

- Contraindicated: The drug-combination is contraindicated for concurrent use.
- Major: If there is risk of death, and/or medical intervention is required to prevent or minimize serious negative outcome.
- Moderate: The effect of interaction can deteriorate patient's condition and may require alteration of therapy.

 Minor: Little effects are produced that don't impair therapeutic outcome and there is no need of any major change in therapy

Scientific evidence (Documentation)

- Excellent: The interaction has been clearly demonstrated in well-controlled studies.
- Good: Studies strongly suggest that the interaction exists except proof of well-controlled studies.
- Fair: Available evidences are poor, but clinicians suspect the interaction on the basis of pharmacologic considerations; or, evidences are good for an interaction of pharmacologically similar drug.
- Poor: Theoretically the interaction may occur but reports are very limited, such as few case reports.
- Unlikely: Data are very poor and lack a proper pharmacologic basis.

Statistical analyses

Results are presented as median, ranges and proportions, where appropriate. Logistic regression was used to calculate the odds ratio for specific risk factors including age, gender, hospital stay and number of drugs. Exposure to pDDI(s) was the dependent variable in the model (0 = absent, 1)= present). The following variables were included in the model as predictors of pDDIs: patient's age (1 = below 65 years, 2 = 65 years or older), gender (1 = female, 2 = male), hospital stay (1 = less than)4 days, 2 = 4 days or above), and number of drugs (1 = less than 7, 2 = 7 or above). "Enter" method was used for analysis. The Hosmer-Lemeshow test was used to check goodness-of-fit of the model. P-value of 0.05 or less was considered statistically significant. SPSS for Windows version 16 (SPSS, Inc., Chicago, IL, USA) was used for all statistical analyses.

Results

General characteristics of study population

Of the total 400 patients, 231 (58%) were males and 169 (42%) were females; median age was 60 years; median hospital stay was 03 days and median number of prescribed medications per patient were 07 (Table 1).

Characteristic	Frequency
Gender	Patients: n (%)
Male	231 (58)
Female	169 (42)
Age (years)	Patients: n (%)
\leq 30	25 (6.25)
31-45	64 (16)
46-64	115 (28.75)
<u>>65</u>	196 (49)
	Years
Median	60
Range	16-90
Hospital stay (days)	Patients: n (%)
<u>≤</u> 3	248 (62)
4-6	137 (34.25)
<u>≥</u> 7	15 (3.75)
	Days
Median	3
Range	1-9
Prescribed medications per	Dationts: n (0/)
patient	1 attents. $n(70)$
<u><</u> 4	88 (22)
5-6	87 (21.75)
<u>≥</u> 7	225 (56.25)
	Drugs
Median	7
Range	1-14

Table 1. General characteristics of study population

Frequency and nature of pDDIs

In our study, we identified 100 interacting drugcombinations that were encountered in total number of 1120 pDDIs. Table 2 shows that overall 310 (77.5%) patients had at least one pDDI regardless of severity-types. As far as nature of severity was concerned, 147 (36.75%) of our study subjects were exposed to at least one major pDDI, 279 (69.75%) to at least one moderate pDDI, and 200 (50%) to at least one minor pDDI. In most of the cases 03 to 05 pDDIs per patient were identified with median number of 03 pDDIs per patient (Table 2).

In Table 3, pDDIs have been quantified on the basis of their nature of onset, severity and scientific evidence. Among 1120 pDDIs, most were of moderate (631, 56.3%) or major severity (284, 25.4%); fair (507, 45.3%) or good (470, 42.0%) type of scientific evidence; and delayed onset (565, 50.4%). Similar pattern was recorded for 100 types of interacting drug-combinations.

Table 2. Prevalence of potential drug-drug interactions (pDDIs)

<u> </u>			
Type of prevalence	Frequency		
Severity of pDDIs	Patients: n (%)		
Overall*	310 (77.5)		
Major	147 (36.75)		
Moderate	279 (69.75)		
Minor	200 (50)		
Number of pDDIs per patient	Patients: n (%)		
1-2	100 (25)		
3-5	168 (42)		
≥6	42 (10.5)		
	PDDIs (n = 1120)		
Median	03		
Range	1-11		
* Overall prevalence means presence of at least one			
pDDIs regardless of severity-type.			

Table 3. Nature of the identified potential drugdrug interactions (pDDIs)

Levels	Frequency in 1120 pDDIs	Frequency in 100 types of pDDIs
	n (%)	n (%)
Severity		
Major	284 (25.4)	40 (40)
Moderate	631 (56.3)	52 (52)
Minor	205 (18.3)	08 (08)
Documentation		
Excellent	143 (12.8)	16 (16)
Good	470 (42.0)	58 (58)
Fair	507 (45.3)	26 (26)
Onset		
Rapid	555 (49.6)	38 (38)
Delayed	565 (50.4)	62 (62)

Drugs commonly implicated in the identified pDDIs

We identified total 100 types of interacting drug-combinations. Commonly occurring pDDIs are shown in Table 4. Top 23 frequently occurring pDDIs included 09 major and 13 moderate and 01 minor pDDIs. Most frequent major pDDIs included heparin + aspirin (39 cases), digoxin + spironolactone (35), spironolactone + ramipril (23), warfarin + aspirin (17), heparin + nitroglycerin (14), warfarin + amiodarone (14), digoxin + amiodarone (13), clopidogrel + omeprazole (11), and spironolactone + captopril (10). While most common moderate pDDIs included ramipril + aspirin (129 cases), nitroglycerin + aspirin (100), furosemide + aspirin (59), digoxin + furosemide (41), spironolactone + aspirin (34), warfarin + spironolactone (34), furosemide + ramipril (29), lisinopril + aspirin (22), insulin + aspirin (19), perindopril + aspirin (12), captopril + aspirin (12), spironolactone + losartan (12), and furosemide + captopril (10) (Table 4).

Association of pDDIs with specific risk factors

Table 5 shows logistic regression analysis and the calculated odds ratio (OR) with 95% confidence interval (95% CI) for some risk factors of pDDIs. In univariate analysis, there was significant association of the occurrence of pDDIs with patient's age of 65 years or more (OR=2.79; 95% CI=1.69-4.63; p<0.001), male gender (OR=2.39; 95% CI=1.48-3.87; p<0.001), hospital stay of 4 days or longer (OR=6.76; 95% CI=3.38-13.54; p<0.001), and taking 7 or more drugs (OR=33.69; 95% CI=14.21-79.90; p<0.001). Multivariate logistic regression analysis was performed for variables with univariate p-values of less than 0.1. In multivariate analysis, there was significant association of the occurrence of pDDIs with patient's age of 65 years or more (OR=2.32; 95% CI=1.26-4.28; p=0.007), male gender (OR=1.94; 95% CI=1.07-3.53; p=0.03), hospital stay of 4 days or longer (OR=3.51; 95% CI=1.60-7.70; p=0.002), and taking 7 or more drugs (OR=26.84; 95% CI =11.11-64.83; p<0.001).

Table 5	Logistic	rearession	analysis
Tuble J.	LOgistic	regression	unuiysis

Table 4.	Frequently of	occurring i	major (and mode	ra-
te potent	ial drug-drug	g interacti	ions		

Interactions	Frequency
Major interactions	
Heparin + aspirin	39
Digoxin + spironolactone	35
Spironolactone + ramipril	23
Warfarin + aspirin	17
Heparin + nitroglycerin; warfarin + amiodarone	14 each
Digoxin + amiodarone	13
Clopidogrel + omeprazole	11
Spironolactone + captopril; potassium chloride + ramipril; potassium chloride + spironolactone	≤ 10 each
Moderate interactions	
Ramipril + aspirin	129
Nitroglycerin + aspirin	100
Furosemide + aspirin	59
Digoxin + furosemide	41
Spironolactone + aspirin, warfarin + spironolactone	34
Furosemide + ramipril	29
Lisinopril + aspirin	22
Insulin + aspirin	19
Perindopril + aspirin	15
Captopril + aspirin, spironolactone + losartan	12
Furosemide + captopril, furosemide + lisinopril	≤ 10 each

	Patie	Patients: <i>n</i> Univariate Mul		Univariate		e
Variable	Interaction present (n = 310)	Interaction absent (n = 90)	OR (95% CI)	P-value	OR (95% CI)	P-value
Patient age (years)						
< 65	141	63				
≥65	169	27	2.79 (1.69-4.63)	< 0.001	2.32 (1.26-4.28)	0.007
Gender						
Female	116	53				
Male	194	37	2.39 (1.48-3.87)	< 0.001	1.94 (1.07-3.53)	0.03
Hospital stay (days)						
< 4	168	80				
\geq 4	142	10	6.76 (3.38-13.54)	< 0.001	3.51 (1.60-7.70)	0.002
Number of drugs						
<7	91	84				
≥ 7	219	06	33.69 (14.21-79.90)	< 0.001	26.84 (11.11-64.83)	< 0.001
-OR = odds ration; CI = confidence interval.						
-Hosmer–Lemeshow	goodness-of-fit	test: $P = 0.65$				

Discussion

In this study, overall prevalence of pDDIs in cardiology ward (77.5%) was higher in comparison to other studies conducted in interanal medicine wards (51% to 60%), pulmonology ward (45%) and oncology ward (63%) [8-11]. Prevalence of pDDIs of major severity (36.75%) was also higher than 13% reported by Fokter et al. and 12.2% identified by Egger et al. [8, 9]. We recorded median number of 03 pDDIs per patient. Average 1.44 pDDIs per patient and median pDDIs of 02 per patient have been reported by other studies. [8, 9]. Straubhaar et al. investigated pDDIs in patients with heart failure and they found pDDIs in 88.8% patients with median number of 03 pDDIs per patient [3]. Although study of Straubhaar et al. included only patients with heart failure, it supports our findings that pDDIs are more prevalent in patients with CV disorders as compared to other patients.

PDDIs are evaluated on the basis of their nature of severity, onset, and scientific evidence. On the basis of theses information, it can be assessed that how much pDDIs are likely to cause negative outcomes. Our findings (Table 3) regarding nature of pDDIs are consistent with many other studies [8-10]. In our study, major and moderate pDDIs were common for which the scientific evidences were excellent, good or fair. These findings are considerable from practice point of view and suggest that negative outcomes are more likely with the identified pDDIs. We recommend proper monitoring of CV therapy to prevent and manage these pDDIs.

List of common interacting drug-combinations (Table 4) will be helpful for health care provider to manage and prevent pDDIs in cardiology ward. Major pDDIs are more dangerous therefore the practitioner should be quite vigilant about their effects and management. In the following section we will discuss the potential outcomes and management of some major pDDIs that commonly implicated in our study-subjects.

Concurrent use of aspirin and heparin increases the risk of bleeding. Although use of this combination may be justified in situations like prophylaxis of ischemic complications of unstable angina, it may be prudent to avoid the combination. It they are used concurrently, it is recommended to monitor coagulation parameters and signs of bleeding [12, 13]. Spironolactone may cause digoxin toxicity that is manifested by nausea, vomiting, and abnormalities in cardiac rhythm. While using this combination, clinical response & digoxin serum concentration should be monitored and the dosage should be adjusted accordingly [7]. Combination of spironolactone with captopril or ramipril may result in increased serum potassium level. Although this effect is usually transient, it is considerable in patients with renal impairment or diabetes, those with a risk for dehydration, and in the elderly. The patient may suffer with severe arrhythmias that may lead to death. It is recommended to monitor the therapy and to keep the dose of spironolactone to not more than 25 mg daily or on alternate day [14]. Concurrent use of aspirin and warfarin is associated with increased risk of bleeding. Although this combination is not absolutely contraindicated, it should be avoided whenever possible. If these drugs are used concurrently, it is recommended to carefully monitor the prothrombin time (PT) or international normalized ratio (INR) and watch the patient for signs of bleeding [15]. The pharmacologic effects of heparin may be decreased by nitroglycerin. Therefore, careful monitoring of the coagulation status of the patient and dosage adjustment of heparin is recommended when heparin and nitroglycerin are coadministered [16]. Concurrent use of amiodarone and warfarin may result in an increased risk of bleeding that in some cases may be very serious or fatal. If concurrent use is necessary, prothrombin time should be monitored and warfarin dose should be adjusted. In patients on chronic warfarin-therapy, dosage reduction of 35% to 65% is recommended at the initiation of therapy with amiodarone. INR greater than 5 occurred most commonly during the first 12 weeks of concomitant warfarin and amiodarone therapy. Intensive monitoring during this period is recommended. The INR should also be closely monitored with the withdrawal of amiodarone, and periodically reassessed during concurrent therapy [7, 17]. Combination of amiodarone with digoxin may lead to digoxin toxicity (nausea, vomiting, cardiac arrhythmias). It is recommended to consider discontinuing digoxin; otherwise close monitoring of serum digoxin levels & evidence of toxicity and reduction of digoxin dose by approximately 50% will be required [18]. Omeprazole may result in reduced clinical efficacy of clopidogrel and increased risk

for thrombosis. It is recommended to use an alternative acid-lowering drug with less CYP2C19 inhibitory effect such as pantoprazole, a histaminergic (H2) blocker (except cimetidine), or an antacid [19, 20]. Concurrent use of potassium chloride with ramipril can lead to severe hyperkalemia that may cause death especially in renally impaired and elderly patients. Patients should be monitored and excessive potassium use should be avoided [7, 21]. Concurrent use of potassium chloride with spironolactone can lead to severe and even life-threatening hyperkalemia. Common manifestations of hyperkalemia include muscular weakness, paraesthesia, flaccid paralysis of the extremities, fatigue, bradycardia, ECG abnormalities and shock. Potassium chloride and other potassium supplements are better to avoid during spironolactone-use, otherwise close monitoring of serum-potassium level is required [22, 23].

In our study the significant association of pD-DIs with old age, long hospital stay, male gender and taking increased number of drugs are consistent with other studies [10, 24-26]. These findings suggest that patients with one or more of these risk factors are more exposed to pDDIs.

Conclusions

Moderate and major pDDIs were common in cardiology ward. Patients with old age, longer hospital stay, male gender and taking more drugs were at higher risk to pDDIs. We recommend that healthcare providers should be quite vigilant about effects and management of pDDIs.

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Evaluation of the validity and reliability of the Turkish version of the quality of care parent questionnaire

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Abstract

Objective: This study was planned and implemented with the aim of testing the validity and reliability of the Turkish form of the Quality of Care Parent Questionnaire

Setting: The study was carried out in the pediatric clinics of 3 hospitals in the Denizli area in the West of Turkey.

Design and participants: The parents of 216 children receiving inpatient treatment at the Pediatric clinics at 3 hospitals were given the parents' characteristics specification form and the Quality of Care Parent Questionnaire. For the reliability study of the Quality of Care Parent Questionnaire, the Questionnaire's internal consistency reliability and Cronbach's Alpha coefficient were examined. Factor analysis was used for the structure validity.

Results: The questionnaire was found to be valid and reliable in Turkey. The questionnaire's Cronbach's Alpha value was determined to be 0.93.

Conlussion: Having been found valid and reliable, the Quality of Care Parent Questionnaire has been brought into the literature in Turkey.

Keywords: parent staisfaction, pediatric units, quality of care, validity and reliability.

Introduction

Parent satisfaction with care can be considered a good indicator variable for some important aspects of quality of care. Increased parent satisfaction associated with greater technical and interpersonel competence, more partnership building, more immediate and possitive nonverbal behaviour, more positive talk. (1)

Often illness and hospitalization are the first crisis children must face. The crisis of childhood ilness and hospitalization affects every member of the family. Almost all parents respond to their child's illness and hospitalization with remarkable consistent reactions.(2) Parents need to feel that nurses and other health care providers are there for the whole family's benefit and well-being.(3) Health professionals can positively influence the coping ability of the family through providing information and ongoing communication, and incorporating the needs of each individual family member into their care plan. While all individuals and families cope in different ways and have differing strengths, they can all be successful in their care of the child. (4)

In the field of children's healthcare, it may not be possible to precisely measure the assessment of children's satisfaction.(5) Parents are important collaborators in measuring satisfaction because of most children are unable to express their needs. (6)

Nursing of infants and children is intimately involved with care of the child and the family. (2) A reliable and valid standard must be present in the development of pediatric care quality. (7,8) In recent years, there has been an increasing number of studies focusing on parent satisfaction with pediatric care. (9,10) In children's hospitals, there is a great need for awareness of the patient's and family's satisfaction with the quality of care. (10)

Objective

This study was planned and implemented with the aim of testing the validity and reliability of the Turkish form of the Quality of Care Parent Questionnaire.

Method

Sample and Setting

The study was carried out in three hospitals in the region of Denizli in the west of Turkey. The population of the study was composed of the mothers/fathers of children receiving in-patient treatment at pediatric clinics between November 2007 and March 2008. The mothers/fathers of 216 children made up the sample. The determination of the size of the sample was based on the number of items found in the questionnaire. It was proposed that an absolute minimum of five participants per variable and no fewer than 100 individuals per analysis. (11)

Consenting parents of children receiving hospital treatment between November 2007 and March 2008 were chosen by the random sampling technique to be included in the study.

Instrument

The Child Receiving Pediatric Treatment Parent Characteristics Specification Form and the Quality of Care Parent Questionnaire were used in this study. The Parent Characteristics Specification Form is made up of 8 questions directed towards the child and the parents. The Quality of Care Parent Scale was developed by Ygge and Arnetz (2001). This questionnaire consists of a total of 8 subsections and 43 items concerning: information on the illness (3 items), information on routines (4 items), accessibility (3 items), medical treatment (4 items), caring processes (8 items), Staff Attitudes (8 items), participation (4 items), and staff work environment (9 items).

The questionnaire's items were scored on the 4 point likert scale. Only two of the questionnaire items ask the parent to express directly a certain level of satisfaction. These questions concern the adequacy of the child's pain treatment and include a fifth response altenative: "not applicable". The questionnaire was graded in the following way: 'yes, to a great degree ' (4 points), 'yes, to a certain degree' (3 points), 'no, not especially' (2 points), 'no, not at all' (1 point). The following items were reverse coded: 'Do you have problems reaching the hospital by telephone?', Do you have problems reaching your child's doctor by telephone?', Do you have problems reaching your child's nurse by telephone?', Do you think the staff work under stress?', and 'Do you think the staff have difficult working conditions?'. High subsection point averages indicate positive circumstances in terms of satisfaction. (12)

Ethical Consideration

Permission for the questionnaire to be used in the study was obtained by email from its writers. Before the research began, the necessary permission was obtained from the three hospitals to be used in the study, the aim of the study was explained to the parents and those parents who agreed to take part were given the questionnaire.

Translation Procedures

Standardizing the questionnaire according to the norms of individual speakers of the language into which it is translated forms the basis of adapting the questionnaire to a new culture. (13) The Quality of Care Parent Questionnaire was translated from English to Turkish by two nursing professors and one English language expert. This Turkish translation prepared by the researchers was translated back into English by a linguist who had not previously seen the questionnaire. After this new translated English version was compared with the original questionnaire and the necessary adjustments were made, the researchers then produced the final version of the questionnaire.

Three experts were asked for their opinions on the Turkish version of the questionnaire: two pediatric nursing experts and one public health nursing expert. The experts assessed each item in terms of its distinctness, comprehensibility and appropriateness to the aim and then the final version was prepared in line with their recommendations.

Data Analyses

In the data analysis the figure and percentage distributions of the specific information were conducted by coding the data in the SPSS 11.5 program. The questionnaire's reliability was evaluated by internal consistency tests. For this purpose, the split-half technique and Cronbach's Alpha coefficient were examined. Factor analysis was used for the construct validity.

Results

Distribution of Parents' and Children's Specifications

The mean age of parents taking part in the research was established to be 28.69 ± 6.80 . When the education levels were studied, it was found that

63.4% of the parents had received 5 years of education and 30.5% more than 5 years. It was determined that 57.9% of the children included in the study were in the 0-1 year age group and 45.4% of these children were receiving hospital treatment for the first time in their lives. Of the children who had previous hospital experience, it was ascertained that 58.5% came to hospital "from time to time". At the time of data collection, 53.2% of the children included in the research were staying in hospital for 48-96 hours. 63.4% of the parents indicated that the health status of their child was of 'moderate' level and 37.5% stated that they were very worried about their child's health.

Reliability Analysis

The split-half technique is used when the variance of each of the questionnaire's two halves was found to be equal or very similar. (14) The variance of both sections of the questionnaire were found to be very close. The variance of the first section was (167.13) and the variance of the second section was (168.77). The alpha value for the questionnaire's first section (22 items) was found to be 0.92 and for the second section (21 items) it was found to be 0.84. The Spearman-Brown coefficient for the whole of the questionnaire was determined to be 0.83.

The item total correlations were examined in order to assess the questionnaire's internal consistency reliability. It is recommended that where the correlation coefficient falls below 0.20, the item be removed from the scale. (15)

In the evaluation, 1 item from the staff work environment subscale (Item 36) 'Do you think that staff work under stress?' was found to have a correlation coefficient of under 0.20 and was therefore removed from the questionnaire. As item 36 from the scale's staff work environment subsection was removed, another item from the same subsection, item 38 'Do you think staff have a heavy workload?' was found to have higher 'a' value than the average and the decision was taken to remove this item too. As a result, the subsection cronbach alpha coefficient increased from .81 to .91 and the cronbach alpha coefficient for the whole scale increased from .92 to .93.

The Cronbach's alpha values for the questionnarie's subsections were found to be as follows: 0.95 for the information on illness subsection, 0.70 for the information on routines subsection, 0.85 for the accessibility subsection, 0.73 for the medical treatment subsection, 0.76 for the caring processes subsection, 0.95 for the staff attitudes subsection, 0.77 for the participation subsection and 0.91

		1	
Subscales	Number of Items	Item-Total Subscale Correlation	Cronbach Alpha Values
Information on Illness	3	.8593	.95
Information on Routines	4	.3360	.71
Accessibility	3	.6677	.85
Medical Treatment	4	.3773	.73
Caring Processes	8	.3470	.76
Staff Attitudes	8	.7887	.95
Participation	4	.3376	.77
Staff Work Environment	9	.6284	.91

Table 1. Item-Total Correlation Subscales' and Cronbach Alpha Values

Table 2. Comparison of Turkish Sample and the Original Sample Subsections' Cronbach Alpha Values

1 0	1 0 1	
Subsection	Turkish sample cronbach's alpha	Original sample cronbach's alpha
Information on Illness	.95	.86
Information on Routines	.70	.62
Accessibility	.85	.81
Medical Treatment	.73	.79
Caring Processes	.76	.80
Staff Attitudes	.95	.76
Participation	.77	.80
Staff Work Environment	.91	.79

for the staff work environment subsection. The questionnaire's item total correlation subscales and cronbach alpha values are shown in Table 1.

This study's cronbach alpha values and the cronbach alpha values of the original scale can be seen in Table 2.

Construct Validity

Factor analysis was performed in order to evaluate the construct validity of the questionnaire's. The calculated KMO (Kaiser- Meyer- Olkin) was .88; indicating that the sample was large enough to perform a satisfactory factor analysis.

KMO value approaching 1 is considered excellent, while a value of below 0.50 is unacceptable. (14) The factor analysis was evaluated according to 41 items and the basic components analysis was carried out according to the results of the varimax rotation. The scale consists of a total of 8 factors (Table 3).

Eight items in the staff attitudes subsection and three items in the caring processes subsection make up Factor 1, with a 17.26% variance. Seven items in the staff work environment subsection and two items in the medical treatment subsection, make up Factor 2, with a 15.36% variance. Three items in the information on illness subsection and two items in the information on routines subsection make up Factor 3, with a 9.20% variance.

Five items in the caring process subsection make up Factor 4, with a 8.15% variance. Four items in the participation subscection make up Factor 5, with a 6.63% variance, Three items in the accessibility subsection make up Factor 6, with a 6.01% variance, Two items in the medical treatment subsection make up Factor 7, with a 5.21% variance and two items in the information on routines subsection make up Factor 8, with a 3.65% variance. The tool explains 71.48% of the total variance.

Factor loads between 0.30 and 0.40 can be taken as cutting points in order to establish a pattern of factors. (18) The factor loads of the items in the scale vary between 0.36 and 0.93.

Items 4 and 5 in the 'information on routines' subsection appeared under the 'information on illness' subsection. Because the correlation between the items and their own subsection was significant, the items were placed back under their own subsection again. Item 4 r=.31 item 5 r=.39 P=0.000

Items 13 and 14, which should have been in the medical treatment subsection, appeared under the staff work environment subsection. Because the correlation between the items and their own subsection was significant, the items were placed back under their own subsection again. Item 13 r=.19 p=0.006 item 14 r=.16 p=0.002

Items 20, 21 and 22, which should have been included in the caring processes subsection, appeared under the staff attitudes subsection. Because the correlation between the items and their own subsection was significant, the items were placed back under their own subsection headings. Item 20 r= .59 p=0.000 Item 21 r=.68 p=0.000 item 22 r=.68 p=0.000

Discussion

The item total correlations were examined in order to to evaluate the scale's internal reliability. As a result of the evaluation 1 item from the staff work environment subsection item 36, 'Do you think the staff work under stress?' was removed as its correlation coefficient was under 0.20. It was determined that when the 36th item in the staff work environment subsection was removed, the 38th itemin the same subsection -'Do you think staff have a heavy workload?' rose above the subsection's alpha value. If the alpha coefficient rises when some items are removed from the questionnaire, the item reliability goes down and therefore they have to be removed from the scale. (15) It was therefore decided to remove item 38 from the questionnaire as well. The cronbach alpha coefficient rose to 0.93 for the whole questionnaire. The cronbach alpha coefficients of the questionnaire subsections vary between 0.70 and 0.95. The original questionnaire's Cronbach Alpha coefficient was found to be between 0.62 and 0.86. (12) The alpha value for the first part of the scale (22 items) was found to be 0.92 and for the second part (21 items) it was found to be 0.84. The Spearman-Brown coefficient for the whole scale was determined to be 0.83.

The alpha value is considered as to be a sign of the test's homogeneity. The internal consistency coefficient should be minimum 0.70. The scale is highly reliable if $0.80 \le \alpha < 1.00$. (14, 15) The alpha values are within this range for the entire questionnaire.

Items	Eigenvalue	Variance Explained	Factors	Factor load
20. Did staff offer support to your child when he/she needed it?				.58
21. Are staff attentive to your needs/wishes?	1			.70
22. Were staff responsive to your child's needs/requests?	1			.71
23. Were you treated kindly in your contact with staff at the hospital?	1	17.26	Factor	.63
24. Was your child treated kindly in contact with staff at the hospital?				.62
25. Were you well taken care of when you first came to the ward/clinic?	15.39			.75
26. Was your child well taken care of when you first came to the ward/clinic?]			.74
27. Did staff take you seriously?				.78
28. Did staff take your child seriously?				.74
29. Have you been treated with respect?				.76
30.Has your child been treated with respect?				.76
13. Do you have confidence in staff competence?				.55
14. Do you confidence in staff skill?				.60
35. Do you think that there is a positive work climate among staff?				.64
37. Do you think that staff find their work stimulating?			Factor	.70
39. Do you think that staff assume responsibility and are engaged in their work?	3.14	15.36	2	.77
40. Do you think that staff have a positive attitude toward their work?				.81
41. Do you think that the care is characterized by good cooperation among staff?				.77
42. Do you think that the care is efficient?				.69
43. Do you think that all staff work towards the same goal-good care for the patient?				.70
1. Have you recieved sufficient information concerning your child's illness/course of				81
illness?				.01
2. Have you recieved sufficient information concerning tests/examination/treatments				87
to be done?	2.45	9.20	Factor 3	.07
3. Have you recieved sufficient information concerning results of tests/ examination/				86
treatments?				.00
4. Have you recieved sufficient information concerning ward/clinic routines?	_			.56
5. Have you recieved sufficient information concerning to whom you should direct				59
your questions?				
15. Did you feel that staff had time for you?				.36
16. Did you feel that staff had time for your child?			Factor	.43
17. Have staff introduced themselves to you?	2.23	8.15	4	.86
18. Have staff introduced themselves to your child?	-			.85
19. Did staff offer support when you needed it?				.62
31. Did you have the possibility to ask questions about your child's illness?	-			.60
32. Have you understood the information you recieved about your child's illness?	-			.73
33. Did you have the opportunity to participate in discussions concerning your child's	1.89	6.63	Factor	.79
examinations/treatments?			5	
34. Have you had the opportunity to discuss the goals of your child's treatment with				.74
the child's physician?				00
8. Have you experienced problems contacting the hospital by telephone?	1.50	6.01	Factor	.82
9. Have you experienced problems contacting your child's physician by telephone?	1.59	6.01	6	.89
10. Have you experienced problems contacting a nurse by telephone?				.88
11.Do you think that your child received satisfactory pain treatment?	1 4 4	5.01	Factor	.93
12.Do you think that your child received satisfactory pain treatment within in a	1.44	5.21	7	.92
reasonable period of time?				
o. Have you recieved sufficient information concerning which physician was			Faster	.66
responsible for your child's care?	1.16	3.65	ractor	
for your child's care?			ð	.54

Table 3. Results of Varimax Basic Components Analysis of the Quality of Care Parent Questionnaire

The calculated KMO (Kaiser-Meyer-Olkin) was 0.88, indicating that the sample was large enough to perform a satisfactory factor analysis. The KMO is considered to be "perfect" when it approaches the value of "1". In this respect, the available data were found to be sufficient to perform a factor analysis. According to the results of the factor analysis, the questionnaire consists of 8 factors. All of the questionnaire's subsections revealed 71.48% of the entire variance. The revealed variance should be above 30% in multidimensional scales. (16) From this point of view, the questionnaire is considered to be adequate for the measurement of parents' satisfaction.

The 4th and 5th items of the information on routines subsection were in the information on illness subsection, the 13th and 14th items (which were supposed to be in the medical treatment subsection) were in the staff work environment subsection, and items 20, 21 and 22 (which were supposed to be in the caring processes subsection) were in the Staff Attitudes subsection. As the items' correlation with their own subsection is significant, the items were put back into their own subsections.

In this study, in which the validity and reliability of the The Quality of Care Parent Questionnaire were tested, the Quality of Care Parent Questionnaire was found to be reliable and valid in Turkey.

Conclusion

Parents' satisfaction is an important indicator for high quality pediatric care services. Parents' satisfaction often decreases due to hospital routines, lack of information about the child's health condition, or insufficient support during the child's hospitalization. It is suggested that parents be informed in pediatric clinics about the illness and about service routines, that they can reach doctors / nurses by telephone when needed, that competent personnel provide adequate medical treatment and that a standardised caring processes will increase parents' satisfaction.

It is important to measure parents' satisfaction with standard forms. Thus, with this study, an instrument measuring parents' satisfaction has been brought into the Turkish literature.

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Correlation of waist circumference and body mass index with VO₂max in Korean adults

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Abstract

This study examined whether the relationship between body mass index (BMI) and maximal oxygen consumption (VO₂max) was greater than that between waist circumference (WC) and VO₂max in Korean adults. This study included 310 Korean subjects aged 20-68 years. These subjects visited the Exercise Science Laboratory at the Seoul National University, Seoul, Korea, where the WC, BMI, and VO₂max were assessed via a graded exercise test (GXT) in 2010. Then, the association of WC and BMI with VO2max was assessed using partial correlation analysis adjusted for age. We found that, in both men and women, VO₂max had a significant negative correlation with BMI (r = -0.543, p < 0.001) and (r = -0.525, p < 0.001), respectively and WC (r=-0.650, p < 0.001) and (r = -0.555, p < 0.001), respectively. Thus, we concluded that, although both BMI and WC have a high inverse correlation with VO₂max (a measure of cardiorespiratory fitness) in Korean adults (both men and women), the correlation between WC and VO₂max was higher.

Key words: body mass index, waist circumference, VO_2max

Introduction

Recently, obesity has become a serious social and public health problem in Korea. In 2009, the Korea National Health and Nutrition Examination Survey-IV (KNHANES-IV) reported that 31.9% of adults aged \geq 19 are obese and that the prevalence of obesity is continually increasing over the years (1).

Obesity is a major risk factor for cardiovascular (CV) diseases, type-2 diabetes, strokes, musculoskeletal disorders, and aggravates chronic diseases, such as arthritis, cholelithiasis, hypercholesterolemia, and hypertension. Therefore, disciplined efforts are required to cure and prevent obesity (2-3). Obese people are commonly reported to have lower physical fitness levels as compared to normal-weight people (4). Furthermore, several studies have reported that if the physical fitness level is low, the prevalence of chronic diseases like obesity increases mortality (5-6).

The exact evaluation of obesity is important in order to prevent chronic diseases and efficiently establish management strategies (7). Body mass index (BMI) has been widely used to evaluate obesity. However, a high waist circumference (WC) has been correlated to increased prevalence of type-2 diabetes, hypertension, cardiovascular disease, and metabolic syndrome that includes obesity, notwithstanding a normal BMI (8-9). In addition, Indians and the Japanese have been reported to have more abdominal fat than Caucasians with the same level of BMI. Hence, WC, which gives an estimate of abdominal fat, would be a more accurate prognostic marker for obesity (10-11).

Therefore, the European Group for the Study of Insulin Resistance (EGIR) (12), the National Cholesterol Education Program-Third Adult Treatment Panel (NCEP ATP-III) (13), the American Heart Association/National Heart Lung, the Blood Institute (AHA/NHLBI) (14), and the International Diabetes Federation (IDF) (15) use WC, and not BMI, for classifying obesity in the metabolicsyndrome category.

Epidemiologic studies have shown a strong inverse relationship between cardiorespiratory fitness (in terms of maximal oxygen consumption [(VO- $_2$ max]), and obesity (4, 16). However, previous studies have assessed obesity by using BMI, and not WC. Therefore, this study examined whether the correlation between BMI and VO₂max was greater than that between WC and VO₂max (a measure of cardiorespiratory fitness) in Korean adults.

Methods

Subject

The study included 310 Korean subjects, aged 20-68. These subjects visited the Exercise Science Laboratory at the Seoul National University, Seoul, Korea, between 01/01/2010 and 08/31/2010 for the assessment of BMI, WC, and VO, max. All study procedures were approved by the Human Care and Use Committee of the Institute of Sports Science of Seoul National University, and all participants submitted a written consent form.

Experimental procedures

Height and weight were assessed using an Inbody 3.0 (Biospace, Seoul, Korea), and the BMI (kg/m^2) was calculated from the data obtained.

WC was measured at the part of the trunk located midway between the lower costal margin (bottom of the lower rib) and the iliac crest (top of the pelvic bone). The subject stood with his feet approximately 25-30 cm apart during the measurement. While taking the measurement, the tape was fitted snugly to the waist without compressing any underlying soft tissue. The circumference was measured to the nearest 0.5 cm, at the end of a normal expiration (17).

VO2max was determined from the graded exercise test (GXT) by using a treadmill (Quark-b2, Cosmed, Italy). The VO₂max was estimated by gradually increasing the exercise intensity, starting from 2.74 km/h and a gradient of 10%. At 3-min intervals, the treadmill was inclined by 2% as described in the Bruce Protocol (18).

Statistical analysis

All the results obtained from this study are expressed as mean \pm standard deviation. The partial correlation coefficient was used to adjust for age when analyzing the correlation between BMI and VO₂max and between WC and VO₂max in both males and females. Statistical significance was set at p < 0.05, and all the analyses were performed using SPSS ver. 12.0 (SPSS, Chicago, IL, USA).

Results

The characteristics of the subjects

The characteristics of the subjects are shown in Table 1. The male and female subjects had an average age of 36.35 ± 16.12 and 48.00 ± 12.60 years, respectively, average height of 173.20 ± 5.10 and 157.24 ± 5.64 cm, respectively, average weight of 72.33 ± 10.19 and 59.35 ± 6.91 kg, respectively, average BMI of 24.08 ± 2.99 and 24.05 ± 2.85 kg/m², respectively, average WC of 83.21 ± 8.41 and 81.06 ± 8.24 cm, respectively, and average VO- $_{2}$ max of 35.31 ± 8.27 and 31.49 ± 5.19 mL/kg/min, respectively.

Variables	Male (N = 85)		Female (N = 225)	
variables	Range	Mean ± SD	Range	Mean ± SD
Age (years)	20.00 - 68.00	36.35 ± 16.12	20.00 - 68.00	48.00 ± 12.60
Height (cm)	161.00 - 186.00	173.20 ± 5.10	143.00 - 173.00	157.24 ± 5.64
Weight (kg)	57.50 - 101.90	72.33 ± 10.19	43.10 - 84.80	59.35 ± 6.91
BMI (kg/m ²)	18.56 - 33.46	24.08 ± 2.99	16.85 - 34.23	24.05 ± 2.85
WC (cm)	66.70 - 107.00	83.21 ± 8.41	63.50 - 102.00	81.06 ± 8.24
VO ₂ max (ml/kg/min)	20.71 - 52.91	35.31 ± 8.27	14.76 - 44.58	31.49 ± 5.19
RMI. Rody Mass Indax WC.	Waist Circumforance			

Table 1. The characteristics of the subjects (N = 310)

BMI; Body Mass Index, WC; Waist Circumference

Table 2. Partial correlation of waist circumference, body mass index and VO, max (N = 310)

Variablas	Vo ₂ max (ml/kg/min)				
variables	Male (N = 85)		Female ((N = 225)	
	r	<i>p</i> -value	r	<i>p</i> -value	
BMI (kg/m ²)	-0.543	<0.001***	-0.525	<0.001***	
WC (cm)	-0.650	<0.001***	-0.555	<0.001***	

BMI; Body Mass Index, WC; Waist Circumference

***p<0.001, tested by partial correlation analysis (adjusted for age)

The partial correlation coefficient analyses

The partial correlation coefficient analyses that were used to adjust for age when analyzing correlation between WC and VO₂max and between BMI and VO₂max are shown in Table 2. The analyses revealed that, in both men and women, VO₂max has a significant negative correlation with BMI (r=-0.543, p<0.001 and r = -0.525, p < 0.001) and WC (r = -0.650, p<0.001 and r = -0.555, p<0.001), respectively.

Discussion

This study examined whether the relationship between BMI and VO_2max was greater than that between WC and VO_2max in Korean adults. This study indicates that, although both BMI and WC have a high inverse correlation with VO_2max in Korean adults, the correlation between WC and VO_3max is higher, even after adjusting for age.

The most commonly used indicator of body fat percentage (%BF) is BMI though it is a wellknown fact that it is not perfectly associated with %BF (19); our results show that the relationship between BMI and %BF is not strong but shows a (curvilinear association (20). On the other hand, measures of central obesity, such as WC and waist-hip-ratio (WHR), also have been reported. These measures give a more accurate description of the %BF distribution, as compared to BMI, more closely associated with CV, morbidity, and mortality (21). For this reason, WC was measured as an independent variable that prevents CV and metabolic syndrome including obesity (12-15).

Williams (2001) reported that physical fitness level is also an important risk factor related to public health outcomes like obesity (22). Although physical fitness variables consist of cardiorespiratory endurance (measured in terms of VO₂max), muscular strength, muscular endurance, flexibility, power, agility, and balance, there are many studies that report the relationship between VO₂max and public health outcomes only because VO₂max is an indubitable gold standard for assessing physical fitness (23-24). However, previous studies assessed obesity by using BMI, and not WC (4, 24). For this reason, our study focused on examining whether the relationship between BMI and VO₂max was greater than that between WC and VO₂max.

The results of this study showed that VO_2max showed more significant inverse correlation with WC than with BMI in both males and females. This finding suggests that abdominal fat, which was measured using (WC, is a more accurate prognostic marker and gives a better relationship with VO_2max for physical fitness levels than does BMI. Therefore, we suggest that WC is a better indicator than BMI for prediction of physical fitness levels.

However, this study has some limitations because it only gives a correlation; it does not give either a cause or an effect. In addition, the study does not represent the entire Korean population because the study only included subjects that were recruited at the Seoul National University, Seoul, Korea.

Conclusion

We concluded that, although both BMI and WC had high inverse correlation with VO_2max (a measure of cardiorespiratory fitness) in Korean adults (both men and women), the correlation between WC and VO_2max was higher.

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Self esteem, physical activity and sedentary lifestyle associated with physical performance among Turkish elemantary school children

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Abstract

This research was conducted in order to determine the relationship between Physical performance and self esteem among the children aged between 12-14 in terms of age, gender and participation in sports and exercises. The research was conducted with 865 students from Izmir city center who participated voluntarily (407 females, 458 males; 270 active and 595 not active sports participants). Some anthropometric and Physical tests were administered to determine the students' Physical performance. The motor performance tests used were as follows: right-left hand grasp strength and standing long jump for muscle strength, 30 second shuttle test for muscle endurance, sit-reach test for flexibility, 30 meter run test for speed, and 1 mile (1609 meters) run test for cardiovascular endurance. To determine self esteem level, the short school form of the Coopersmith Self Esteem Inventory (1967) was used. The characteristics of Physical performance and self esteem were investigated among the groups (in terms of age, gender and status of sports participation) using variance analysis at 3x2x2 level and Bonferroni test. The anthropometric measurements, physical performance and self esteem scores of the female students and male students who participated in physical activity were higher than those of the female students and male students who did not participate in sports. Statistically significant relationships were found between self esteem of the children aged between 12-14 who actively participated in physical activity and their strength, speed and cardiovascular endurance.

Key word: Adolescence, Physical activity, Physical performance, Self Esteem, Physical Fitness,

Introduction

Adolescence is a particular period during which physical growth improves and hormonal, sexual, social, emotional, personal and cognitive changes occur and is thought to begin with puberty and to stop with the end of physical growth (1). Chronologically, it is a transition period from childhood to adulthood. Adolescence has different biological, psychological and social characteristics as in other periods. Adolescence is said to be a transformation and change period and individuals undergo physical, psychological and social changes and transformations. Adolescence is described as the period of changes in behavioral and cognitive skills. Again, it is thought that the adolescent are educable and trainable (2, 3).

Adolescence is a critical as a transition period from childhood to adulthood and it is very important for physical and mental development. Physical growth during adolescence provides –in a sense- a basis for emotional and cognitive maturity. Therefore, it is emphasized that basis of a happy and healthy adulthood will be established if optimal growth and development are ensured during adolescence (4).

Self esteem is the people's appreciation and confirmation of the self attained by the fact that they accept and thus evaluate, trust in and respect themselves. Self esteem plays an important role in the lives of the people –especially in the adolescence period-. Sense of identity received during adolescence period grows in relation with self esteem (5). In other words, self esteem is people's satisfaction with themselves (6) and their acceptance, appreciation, trust and respect for themselves and is one of the basic determinants that enable the individuals to be psychologically active. It is true that sports and physical activities make huge contributions to creating healthy individuals and societies. it is know that childhood and the young hood is the period of life in which by proper process of exercise and PA can significantly influence the physical and psychological development(7). Some researches reported that the positive effects of routine sports and physical activities performed –especially- during the adolescence period are very important in points of muscle dynamics, good general health status and self confidence (8, 9, 10).

Also, rapid physical growth and hormonal structure during adolescence period may cause some certain changes in social characteristics and personality structure of this age group. It is an important issue emphasized in literature that self esteem plays an important role so that the individuals can become effective members in the society and establishes the base of the healthy personality (11, 12). Moreover, the research conducted by Marsh and Kleitman (2003) and Tucker (2007) points out that those who performed physical activities had higher self worth and self esteem compared to their sedentary peers(13,14). Besides, according to Heitzler et all (2006), PA habits that are developed early in life and carried over into adulthood through regular participation in PA during childhood and adolescence may be critically important in the promotion and maintenance of healthy body weight, risk factor reduction, and chronic disease prevention throughout the life span(15). On the other hand the lack of PA causes many of cardiovascular diseases(16) Also, some researches that investigated the correlation between physical activity and self esteem revealed that physical activities soon increased self esteem and there was a positive correlation between physical activity and self esteem (17, 18, 19, 20,21).

The present research aimed to determine physical performances and self esteem of the children aged between 12-14 and to evaluate the relation between physical performances and self esteem.

Materials & Methods

Participants

This is a comparative and descriptive study. Study sample was composed of 865 voluntary students (407 female and 458 male) aged between 12-14 and studying at 6 randomly selected public primary schools in Izmir. 270 participants were chosen among individuals who regularly participate in physical activities at least five days a week. On the other hand, 595 participants were chosen among individuals who led a sedentary life and took only physical education and sport class one hour a week. In addition, official consents of provincial directorate for national education and schools were obtained and those who did not prefer to participate were not included in the study.

Data collection

Necessary permissions were obtained before the study, and the test batteries applied to students during data collection were performed in the classrooms and schoolyards. Students were informed about each measurement tool and test procedure before the application of tests, and tools used in tests were presented and their motivation was provided. Participants were informed at least one week before the tests, and necessary information was obtained about their health conditions. Participants were not allowed for any warm-up movement before the test in accordance with the application procedures of test batteries. Study group was composed of students who were not sportive and did not participate in any physical activity except for physical education and sport class.

Instruments

Physical performance tests: Physical performance parameters of students were evaluated with tests selected from Fitnessgram, American Alliance for Health, Physical Education, Recreation and Dance (AAHPERD) and Eurofit Test Battery (Muscle Strength: hand grip strength, standing long jump; Muscle Resistance: pull-up; Flexibility: sit and reach test; Cardiovascular Endurance: 1 mile running test (1609 m endurance running); Speed: 30 m sprint).

Coopersmith Self Esteem Inventory-CSEI: The Turkish validity and reliability study of the survey developed by Coppersmith (1967) was performed by Turan et al. (1987)(22). It is a measurement tool used in the evaluation of individuals about themselves in various areas. The survey is composed of 25 sentences which include statements related to individuals evaluating themselves, their view of life

and social relations and the statements can be marked in the form of "like me" or "not like me". Four points are given to the appropriate choices when calculating the total points obtained in the survey. The highest total point that can be obtained from the scale is 100. There is no cutting point of the scale. There is a positive correlation between the high points obtained and self-esteem. An evaluation will be made according to the self-esteem points of the group being low or high when examining the findings related to self-esteem

Data analysis

Data obtained in the study were analyzed in Biostatistics and Medical Informatics Department of Medical Faculty of Ege University by using Statistical Package for the Social Sciences (SPSS) for Windows 15.0 packet software. The mean and standard deviation of data were calculated as descriptive statistics. Two-Way Variance Analysis and Further Bonferroni Analysis for age were used. 0.01 and 0.05 were chosen as significance level.

Results

As seen in Table 1 and 3, there was a statistically significant difference between the students aged between 12-14 who played sports and not in terms of self esteem scores (F=22.009, P=.000). Yet, there was not any statistically significant difference between self esteem scores of the female students and male students aged between 12-14 age group who played sports and not (F=2.157, P=.142) (Table 3).

As a result of variance analysis, the joint effect of age and sex was also found to be significant on self esteem scores (F=3.488, P=.031) (Table 2). It was thought that this joint effect was due to the fact that the difference between females and males increased with the advancement of age and self esteem scores of the females decreased whereas self esteem scores of the males increased (Graphic 1). Other joint effects (playing sports and age, playing sports and sex, playing sports, age and sex) were not found significant (p>0.05).

Table 1. Results Of Self Esteem Of The Female Students And Male Students Who Played Sports Or Not According To Age Groups

	athletes			Nen athletes			
	females	males	total	females	males	total	
	(N)	(N)	(N)	(N)	(N)	(N)	
	x±sD	x±sD	x±sD	x±sD	x±sD	x±sD	
12 years	(33)	(24)	(57)	(87)	(77)	(164)	
12 years	72.73±13.98	74.00±17.65	73.26±15.49	67.08±17.40	62.08±18.09	64.73±17.85	
12 yoorg	(38)	(49)	(87)	(111)	(124)	(235)	
15 years	64.63±20.72	67.35±14.95	66.16±17.64	63.64±15.00	63.29±17.15	63.45±16.14	
14	(38)	(88)	(126)	(100)	(96)	(196)	
14 years	65.68±13.62	71.00±15.69	69.40±15.24	57.40±19.58	65.00±15.74	61.12±18.16	
total	(109)	(161)	(270)	(298)	(297)	(595)	
	67.45±16.76	70.33±15.83	69.17±16.25	62.55±17.73	63.53±16.95	63.04±17.33	

Table 2. Self Esteem Anova Results In Terms Of Main Effects And Joint Effects

	main effect	ts	joint effects			
status of	age	Sex	Status of	status of sports	age	status of sports
sports	age	SCA	sports age	sex	sex	age sex
F:22.009	F:3.966	F: 2.157	F: 2.057	F: .805	F: 3.488	F:.917
P:.000*	P:.019*	P:.142	P:.129	P:.370	P:.031*	P:.400

Table 3. Multiple Comparison Tests In Terms Of Self Esteem According To Age Groups

variabla	groups		igint factors (i i)	standard doviation	n valua	
variable	(i) age	(j) age	Joint factors (I-J)	stanuaru ueviation	p value	
self esteem	12 age	13 age	4.244	1.685	.036*	
		14 age	4.200	1.654	.034*	
	13 age	14 age	044	1.469	1.000	

		variables	right-left-hand grasp strength	flexibility	number of sit and reach test	standing long jump	30 meters running	1609 meters running	VO ² max
es athlete	athlete	12 age male	517*					-410*	.450*
m scol		14 age male					-267*		
lf estee		12 age female				.369*			
Se	non athlete	14 age female			.281*				
		14 age male		.235*					

Table 4. Comparison Of Self Esteem Scores And Motor Performances Among Female Students AndMale Students Who Played Sports And Not According To Age Groups



Graphic 1. Graphical Presentation Of The Joint Effect Of Age And Sex Found Significant In Terms Of Self Esteem

According to the Table 4, there was a significant correlation between self esteem scores and body weight (r=-.408, p=.048), right-left hand grasp strength (r=-.517, p=.010), 1609 meters run test v and maximal aerobic power (r=.450, p=.027) among males aged between 12-14 while there was a significant correlation between self esteem scores and standing long jump (r=.369, p=.000) among the females who belonged to 12 age group and did not play sports.

We could not find any significant correlation between self esteem scores and performance parameters of females and males aged 13 who played sports and not (p>0.05). There was a significant correlation between self esteem scores and 30 meters run test (r=-.267, p=.012) among the males aged 14 who played sports whereas a significant correlation was detected between self esteem scores and flexibility (r=.235, p=.021) among the males aged 14 who did not play sports. Also, there was a significant correlation between self esteem scores and number of sit and reach test (r=.281, p=.005) among the females aged 14 who did not play sports.

Discussion and Conclusion

This research was conducted in order to determine the relationship between physical performance and self esteem levels among the children aged between 12-14 and studying at the state schools of İzmir province in terms of age, gender and participation in physical activity and exercises and to find out the correlation between physical performance and self esteem.

According the results of the present research, there was a statistically significant difference between self esteem scores of the students aged between 12-14 who played sports and not (P<0.05). Besides, there were also statistically significant differences between the self esteem scores of the female students and male students who played sports and not in terms of age groups (P<0.05) (Table 3). The multiple comparison tests revealed that the difference was significant both for 12-13 age group and 12-14 age group (p<.05). On the other hand, the joint effect of age and sex was found significant on self esteem scores (P=.0.05) (Table 3).

We are of the opinion that this joint effect was due to the fact that the difference between females and males increased with the advancement of age and self esteem scores of the females decreased whereas self esteem scores of the males increased. Tiggerman and Williason (2000), Browker (2006) reported in their studies that there was a positive correlation between exercises and self esteem on behalf of males(23,24). Meanwhile, studies in literature indicated that the correlation between physical activities and self esteem was positive and physical activities increased the improvement of self esteem soon (17,18,19,21). On the other hand, the results of the studies conducted by Marsh (1998), Gruber (1986), Findlay and Coplan (2007), Marsh et al., (1995) demonstrated that adolescents who played elite sports had higher self esteem levels compared to their sedentary peers and this resulted from the positive correlation between physical activity and self esteem and self concept(25,26,27,28). It is proved that participation of the children in sports affects the relation between their self esteem and behavioral character positively.

The results associated with the relation between physical performances and self esteem of the children who played sports and not showed that the females who belonged to 12 age group and did not play sports presented a statistically significant correlation between their self esteem scores and physical performances in terms of standing long jump (P<0.05). Standing long jump are among the parameters of explosive power and muscular power. Self esteem scores of the females whose standing long jump points were higher turned out to be higher, too. Also; among the females who were aged 14 and did not play sports, a statistically significant and positive correlation was discovered only between self esteem scores and number of sit and reach test (p < 0.05). As for the males who were aged 14 and did not play sports; a statistically significant and positive correlation was detected only between self esteem scores and flexibility test (p<0.05). Browker (2006) reported in the study which investigated the relation between those who participated in sports in the early adolescent period and self esteem that the relation between self esteem of both female students and male students who participated in sports was positive (24). The study of Schneider (2008) which investigated the relation between self esteem and physical activity in terms of 9 week physical activity programme administered to sedentary females who did not play sports revealed that a positive effect occurred among those who took part in the programme in points of strong activities and cardiovascular fitness and that cardiovascular fitness level as well as general physical self esteem improved better (29).

The age of 14 corresponds to a period during which males undergo a rapid physical growth after the transition period. Males excel females in physical growth at 14 years of age when height of males becomes maximal. Self esteem of the male adolescents aged 14 is affected positively by the fact that they have obtained higher speed and flexibility points. It is suggested in the studies conducted that speed and flexibility programmes that will be held for males especially during this age will make positive contributions to their self esteem.

The study of Crocker et al. (2000) conducted in order to assess the relation between self esteem perception of Canadian children aged between 10-14 and their physical condition, strength, body image and general physical self esteem values reported that physical self esteem perception and sportive skills strongly related to activity(30).

The study of Özdemir et al. (2007) which investigated the effect of different types of exercise programmes on physical self esteem perception and some physiologic parameters pointed out that aerobic exercises were effective upon decrease in body fat percentage and physical self esteem perception and that swimming exercises increased more maximal oxygen consumption than other groups(31).

Enhancement of self esteem levels and self sufficiency of the individual make an important contribution to the protection of physical and psychological health and prevention of diseases.

It is explicitly emphasized in literature that exercises contribute to improvement of self esteem. It was clearly seen in the present study that strength, speed and cardiovascular endurance of physical performance parameters affected self esteem level positively. It is stated in literature too that self esteem levels of the individuals who take part in physical activity and exercises programmes increase whereas depression and anxiety levels decrease. Our research concurred with the literature in this sense. Moreover, it drew our attention during our observations that children were reluctant while they were doing physical performance tests and they quitted in case of any difficulty and tended to stop the tests. Especially, very low performance results of female students were one of the factors that did not escape our notice. All of these results may imply that females socio culturally abstain from sports and physical activities in our country during this critical period when growth and development get faster.

Conclusion

In light of the study results, to determine current physical performances and self esteem levels of the children aged between 12-14 will contribute to their physical and psychological development. Children should be made to adopt sports and physical activity habits with enjoyable games since younger ages through the spread of new school concepts. Meanwhile, strength and general endurance programmes added in Physical Education and Sports Courses will contribute to children's physical performances and thus will help a healthy society with high self esteem and self confidence to grow.

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Internet use and its relation with the academic performance for a sample of high school students

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Abstract

This study was conducted to determine the general characteristics of Internet use among high school students in Turkey and to examine the relation between the Internet use and the academic performance of the students. The population of the research consisted of 1100 randomly chosen high school students, studying at 4 state high schools during the academic year of 2008-2009 and the sample of the study included 804 high school students willing to participate in the research and studying at these schools during the same period. Data were collected by the investigators using the survey form prepared in accordance with the literature. The data were assessed using percentage, average, standard deviation, chi-square and correlation analyses using SPSS 15.0 program package on computer. It was found that as the time the students used computer and internet increased, their success at school was more adversely affected, that the male students more actively used computers and internet, and negative opinions on use of computer and internet were at higher rates among students with low academic success levels. It was concluded that it will be useful if families keep the time for internet use by students under control, social activities are increased and group works are emphasized at schools, and thus social relations of teenagers are strengthened.

Key words: High school students, Internet Use, Computer Use, Academic Success

Introduction

Academic failure is one of the important concerns of families and education experts. Every year a great number of students in different countries encounter academic failure. Therefore, this case should be analyzed carefully as one of the important social and educations problems¹.

While internet and computer use is considered a technological miracle that supports children and teenagers in accessing information, making search and for their personal development such as problem solving, creativity and critical thinking,^{2,3} it also causes concerns with its aspect of being used excessively, out of control, out of purpose and unconsciously, and is thought to adversely affect the development of personal skills.^{4,5} Chisholm (2006) ⁶ reports that children and teenagers aged between 8 and 18 spend eight hours on average every day, using informative and communicative technological means.

Adolescence is an important period during which teenagers start to form their identity and determine their future objectives. During this period, teenagers want to use their autonomy and make decisions independent from their family, and experience difficulties in managing and maintaining their emotions. Information they get from, and the relations they have in virtual environment adversely affect the safety and normal development of the teenagers in getting familiar to the real world and building their identity. Knowledge and maturation to be acquired from family and environment are replaced by relations established in virtual environment. A study reveals that 74% of teenage girls particularly between the ages of 12 and 18 spend most of their time messaging in chat rooms or e-mailing. It is emphasized that children and teenagers who are unable to use computers at home tend to go to internet cafes and the latter have become localities in which children and teenagers show intensive interest⁷. Berson and Berson² reported that 92% of 10800 teenagers with ages ranging between 12 and 18 had internet access at home and most of those teenagers spent most of their time with messaging with people they met in chat rooms in virtual environment, surfing across websites and playing games and only 1% of them use internet for making searches and studying. Kubey et al.² found that school performances and academic successes of university students who use internet for more than 11.18 hours weekly are lower than that of those using internet for 3.84 hours or less weekly in a study they performed.

Due to the potential of unconscious use, teenagers living in developing countries are more vulnerable to risks posed by computer and internet use. In recent years, computer and internet use rapidly increased in Turkey and teenagers began to spend long hours in front of computers. However, there are only few studies evaluating the effects of prolonged computer use on the lives of teenagers. High school is the period during which computer and internet use is the most intensive. No comprehensive study examining the effects of computer and internet use on academic success of high school students is available in our country. Therefore, this study was planned as a definitive study for determining the effects of computer and internet use by high school students on their academic success.

Materials and methods

Collection of Data

The study was carried out with 804 high school students aged 15-18, studying at 9th, 10th and 11th grade at randomly chosen 4 high schools in Istanbul city between May and October 2008. Data was collected using a survey form consisting of 48 questions; 14 out of which were open ended and 34 were closed ended, developed by the investigators based on the literature knowledge. Collection of data was carried out collectively in classroom environment under surveillance. The students were seated so that they would not be influenced by each others' answers. The students willing to participate in the study were given survey forms and requested to answer the questions on them. The surveys were completed within around 15 minutes. Surveys were collected after being completed.

Statistical Assessment

The data were assessed using percentage, average, standard deviation, chi-square and correlation analyses with SPSS 15.0 program package on computer.

Population-Sample

The population of the research consisted of 1100 randomly chosen high school students, studying at 4 state high schools located in Istanbul during the academic year of 2008-2009 and the sample of the study included 804 high school students willing to participate in the research, studying at the same schools during the same period.

Study questions

Do computer and internet using periods of high school students adversely affect their success at school?

Does gender factor have any effect on the computer and internet use of high school students?

Is there any relation between the opinions of high school students on computer and internet use and success at school?

Ethical issues

In order to conduct the study, written consent was obtained from the Istanbul Provincial National Education Office and school directorates, and oral consents of all the students who participated in the research were received.

Constraints of the Study

Study data were collected using the survey form developed by the investigators. Because the sample was large in numbers, face to face interview method was not used in implementation of the surveys. Survey forms were distributed among the students under surveillance and then collected back. This method may have caused incorrect answering of some questions due to misunderstanding. In order to eliminate this constraint, the investigators stayed in the classroom and encouraged the students to ask questions about the parts they didn't understand properly before they answered them.

Because the number of students studying at high school in Istanbul city is very large, data were collected from students studying at randomly chosen 4 schools. A new study was planned with a larger sample. The results of the study were only applicable to the schools covered by the study and could not be generalized to cover the entire Istanbul city.

Results

The average age of the students included in the study was $16.13\pm.88$ (youngest 15, oldest 18). Table 1 shows the socio-demographic and the family-related characteristics of the students. According to this, the ratio of female and male students was F:49.5% and M: 50.5%. Out of the students, 33.7% studied at 9th grade and 64.3% defined their success at school as "partially successful". Most of the students (91.9%) had nuclear families; 46.7% of the mothers and 31.8% of the fathers were primary school graduates and 60.6% reported their economic status as good.

It was determined that average points of the students were 3.5 ± 0.6 , average period of absence was 5.2 ± 3.7 days, computer using periods were 2.07 ± 1.5 hours and internet using periods were 1.8 ± 1.5 hours (Table 2).

Out of the students, 76.6% had their own rooms, 98.1% were familiar to computers, 82.2% had a computer and 69.9% had internet access at home, 64.6% had their computer in their own rooms. It was found that 61.3% of the students who had their own rooms used computer for 2 hours or more. It was further determined that the students connected to internet mostly between 16.00 and 17.00 (24.4-17.9%) and they mostly connected *haracteristics of Students* (N=804)

Socio-Demographic Characteristics	Number (n)	Percentage (%)
Gender		
Girl	398	49.5
Boy	406	50.5
Grade		
9	271	33.7
10	267	33.2
11	266	33.1
School standing (as per own expression)		
Successful	229	28.5
Partially Successful	517	64.3
Unsuccessful	58	7.2
Family Type		
Nuclear Family	739	91.9
Large Family	51	63
Divided Family	14	1.7
Mother's educational background		
Illiterate	31	3.9
Primary School	373	46.4
Secondary School	158	19.7
High School	168	20.9
University	74	9.2
Father's educational background		
Illiterate	6	0.7
Primary School	255	31.8
Secondary School	154	19.2
High School	258	32.0
University	131	16.3
Economic status (as per own expression)		
Good	280	34.8
Medium	487	60.6
Bad	37	4.6

Table 1. Socio-Demographic and Family-Related Characteristics of Students (N=804)

Variables	Average. ±SD	Lowest	Highest
Average points of students	3.5±0.6	1	5
Absence period	5.2±3.7	0	40
Computer using period	2.07±1.5	0	15
Internet access period	1.8±1.5	0	10

Table 2. Average, Standard Deviation, Lowest, Highest Values of Some Characteristics of Students

Table 3. Comparison of Characteristics of Students With Respect to Computer and Internet Use Depending on their Gender (N=804)

Gender Characteristic	Girl (n=398) n (%)	Boy (n=406) n (%)	Total n	Statistical analysis χ ²
Availability of computer at home				
Yes	333(83.67)	328(80.79)	661	1.140
No	65(16.33)	78(19.21)	143	p=0.165
Availability of internet access at home				
Yes	288(72.36)	274(67.49)	562	2.269
No	110(27.64)	132(32.51)	242	p=0.076
Regular internet café visits				
Yes	65(16.33)	177(43.60)	242	71.008
No	333(83.67)	229(56.40)	562	p=0.0001

Table 4. Comparison of the Academic Success and Some Characteristics of Students (N=804)

Average Points Characteristic	3 and below (n=157) n (%)	Above 3 (n=647) n (%)	Total n	Statistical analysis χ ²
Availability of computer at home				
Yes	112(71.34)	549(84.85)	661	15.783
No	45(28.66)	98(15.15)	143	p=0.0001
Availability of computer in private room				
Yes	77(69.37)	350(63.64)	427	1.327
No	34(30.63)	200(36.36)	234	p=0.249
Regular internet café visits				
Yes	69(43.95)	173(26.74)	242	17.786
No	88(56.05)	474(73.26)	562	p=0.0001
Time spent in front of computer				
2 hours and less	31(19.75)	335(51.78)	366	52.273
More than 2 hours	126(80.25)	312(48.22)	438	p=0.0001

for searching (50.5%) and chatting (18.1%). These were followed by playing games (12.7%), listening to music (9.7%), sharing content in forum sites (6.6%) and accessing websites with sexual content (2.4%). It was found that 16.5% of the students visited internet cafes even though they had internet access at home.

Characteristics of the students with respect to computer and internet use according to their gender are given in Table 3. Accordingly, it was determined that boys more frequently visit internet cafes. The difference between genders was statistically significant (p<0.05). No difference was found between the genders with respect to availability of computer and internet at home (p>0.05).

When we compared the repeated grades, one of the indicators of the academic success of the students, with the period spent in front of the computer, it was found that 93.9% of the students who repeated grade and 56.7% of those who didn't spent 2 hours or more in front of the computer. The difference between them was significant (χ^2 =34.685, p=0.0001).

Results of the comparison between the academic standings and some characteristics of the students are given in Table 4. According to this, a significant difference was found between the average points and availability of computers at home, visiting internet cafes and the time spent in front of the computer (p<0.05). It was determined that 71.34% of the students with a average points under 3 and 84.85% of the students with average points over 3 had computers at home. This difference was found statistically significant. It was found that points taken at school were affected by whether the computer was located in their own rooms or another room

in the house. It was determined that 43.95% of the students with average points under 3 and 26.74% of the students with average points over 3 visited internet cafes. This difference was found statistically significant (p<0.05). It was also found that 80.25% of the students with average points under 3 connected to internet for more than 2 hours daily and the percentage of those using internet for more than 2 hours daily among those with average points over 3 was 48.22% in the group. This difference was statistically significant (p<0.05).

Results of the comparison between the opinions of the students on computer games / internet

Table 5. Comparison of the Opinions of Students on Computer Games / Internet According to Their Academic Standings (N=804)

Average Points	3 and below (n=157)	Above 3 (n=647)	Total	Statistical analysis
Playing computer games/accessing internet	n (%)	n (%)		χ^2
Better than being with people				
Yes	47(29.94)	139(21.48)	186	5.076
No	110(70.06)	508(78.52)	618	p=0.017
It is more enjoyable than the times I spend with my friends				
Yes	25(15.92)	107(16.54)	132	0.035
No	132(84.08)	540(83.46)	672	p=0.480
It helps me forget my isolation				
Yes	61(38.85)	216(33.38)	277	1.673
No	96(61.15)	431(66.62)	527	p=0.116
It makes me feel more active and alive				
Yes	64(40.76)	199(30.76)	263	5.748
No	93(59.24)	448(69.24)	541	p=0.011
It calms me down				7.400
Yes	41(26.11)	108(16.69)	149	7.429
No	116(73.89)	539(83.31)	655	p=0.006
Best way of spending time				
Yes	62(39.49)	203(31.38)	265	3.765
No	95(60.51)	444(68.62)	539	p=0.033
When necessary, I can lie to my family for it				
Yes	20(12.74)	55(8.50)	157	2.683
No	137(87.26)	592(91.50)	647	p=0.072
I can be absent for it				
Yes	10(6.37)	14(2.16)	24	7.716
No	147(93.63)	633(97.84)	780	p=0.010
More interesting than being with people				
Yes	23(14.65)	81(12.52)	104	0.509
No	134(85.35)	566(87.48)	700	p=0.276
It takes most of my time compared to other activities				
Yes	69(43.95)	258(39.88)	327	0.868
No	88(56.05)	389(60.12)	477	p=0.200

	Academic success	Absence	Time spent on internet
Academic success			
r			449
р			0.0001*
Absence			
r	309		
р	0.0001^{*}		
Time spent on internet			
r		.209	
р		0.0001*	

Table 6. The relation between the academic final points as well as absence from school and the time they spent on internet

*Correlation is significant at the 0.01 level.

depending on their academic standings are given in Table 5. According to this, compared with the students with average points of 3 or higher, the students with average points under 3 agreed with higher percentages on the opinions such as "playing computer games is better than being with people" (29.94%), "I feel myself more active and alive when playing computer games" (40.76%), "playing games on computer calms me down" (26.11%), "playing computer games and connecting to internet are the best ways for spending time (39.49%), "I can be absent from school for playing computer games and connecting to internet" (6.37%). This difference between them was statistically significant (p<0.05).

The relation between the final academic points as well as absence from school and the time they spent on internet is given in Table 6. As seen in the Table, as the time students spent on internet increased, their academic standing decreased (p<0.05).

Discussion

In the study planned in order to determine the relation between the high school students' computer/internet use and their academic successes, it was determined that the average age of the students was $16.13\pm.88$, ratio of girls and boys was F: 49.5% and M: 50.5%. The students' average computer using periods were 2.07 ± 1.5 hours daily and their average internet access periods were 1.8 ± 1.5 hours daily. Chisholm⁵ reports that children and teenagers between the ages of 8 and 18 spend eight hours on average for using technologic information and communication means every day. Com-

puter use and internet connection period is proportional to access. Thus, in a research performed on children aged 3-18, it was found that 35.7% of them had computers and 21.7% of them had internet access at home.8 Wartella and Jennings9 reported that 60% of the children aged between 8 and 17 had computers at home and most of them had internet access. Zboralski et al.¹⁰ reported that 30% of children started using computers before the age of 7 and 60% of them accessed internet every day. It was determined that out of the students in the study group, 76.6% had their own rooms, 98.1% were familiar to computers, 82.2% had a computer and 69.9% had internet access at home, 64.6% had their computer in their own rooms. 61.3% of the students who had their own rooms used computer for 2 hours or more. It was interesting that percentages were higher when findings of the study were compared with the literature. Considering that the literature was related to past years, it can be concluded that use of internet and computers in daily life has gradually increased in years. Furthermore, we can say that the low level of internet connection fees in our country facilitates access.

According to the studies conducted, the first three reasons of teenagers studying at high schools for connecting to internet were respectively chatting, checking e-mail messages or sending e-mails and playing online games.¹¹⁻¹³ In a study performed by Berson and Berson,² it was found that 92% of 10800 teenagers aged between 12 and 18 spend most of their time by messaging with people they met in chat rooms in virtual environment, surfing across websites and playing games, and only 1% of them use internet for making

searches and studying. Contrary to the literature, it was determined that half of the teenagers (50.5%)in the study group connected to internet for searching purposes, but other reasons for connecting to internet were chatting (18.1%), playing games (12.7%), listening to music (9.7%), sharing content in forum sites (6.6%) and accessing websites with sexual content (2.4%). Today, of the fact that secondary education is based on the student's performance requires teenagers to make researches and consequently connect to internet. Moreover, spending long time on internet causes problems in interpersonal relations. In a study conducted by Suhail and Bargees¹⁴ on 200 students, it was found that internet use resulted in difficulties for teenagers in interpersonal relations. Kraut et al.¹⁵reported that children and teenagers who spent excessive time on internet gradually became isolated and suffered from difficulties in establishing face to face relations. In parallel with the literature, when we analyzed the opinions of students with average points under 3 on computer games / use, it was found that they agreed with higher percentages on opinions such as "I feel myself more active and live when playing computer games" (40.76%), "it is the best way of spending time" (39.49%), "it is better than being with people" (29.94%), "it calms me down" (26.11%), "I can be absent from school for this" (6.37%). On the other hand, in some studies, it was reported that as the period of internet use increased, emotional and behavioral problems such as solitude, social isolation and aggression were more widely observed in children and teenagers, their general health levels decreased, and percentage of finding depressive symptoms increased. 3,4,16-21 Prolonged internet use not only causes disorders in interpersonal relations, but adversely affects performance at school as well. Kubey et al.³ found in a study they conducted that school performances and academic successes of university students who used internet for more than 11.18 hours weekly were lower than that of those using internet for 3.84 hours or less weekly. It was determined that out of the students with average points under 3, 43.95% visited internet cafes and 80.2% spent time in front of the computer for more than 2 hours daily. On the other hand, when we compared repeated grades, one of the indicators of the academic success of the students, with the period spent in front of the computer, it was found that 93.9% of the students who repeated grade, and 56.7% of those who didn't, spent 2 hours or more in front of the computer. Furthermore, it was demonstrated that more of the students with average points over 3 had computers at home, but the duration they used computer was usually below 2 hours. These results make us consider that when the duration of computer use at home is kept under control, academic success will be positively affected accordingly. Also in a study supporting the results of our study, it was found that as the period they spent on internet increased, the academic success of students decreased, and they encountered with difficulties in learning.²²

Out of the male students in the study group, 67.49% had internet access at home, but 43% of them visited internet cafes. It is emphasized in the literature that children and teenagers who are unable to use computer at home environment tend to go to internet cafes and the latter have become localities in which children and teenagers show intensive interest.⁷ Furthermore, the literature also reports that male gender is a risk factor in internet use and addiction.²³⁻²⁷

Conclusion

It was found that the students' computer and internet using periods adversely affect their success at school, males were more active in using computer and internet, computer using periods were longer and higher level of negative opinions on internet use was seen in students with lower level of academic success. It must be ensured that families keep the period of internet use by students under control, social activities are increased and group works are emphasized at schools, and thus social relations are strengthened. It is considered that the interest in internet may decrease if various sport activities are provided and scientific and cultural clubs from which students can benefit are established at schools. In addition, implementation of study hours apart from class hours can positively affect academic performance.

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A work related stress among nurses of public hospitals of AJ&K" - Cross-Sectional Descriptive Study

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Abstract

Introduction/background: Stress is pandemic nowadays and is part of everyday life for health professionals like nurses whose main responsibility is to provide help to patients who are facing life crises. Stress at work is perceived at individual level and when it exceeds the persons coping capacity it presents in form of physiological, emotional, cognitive and behavioral reactions.

Aim & objectives: Objective of study was to assess the levels of stress and identify the factors of stress among nurses in public hospitals of AJK.

Methods/study design: A cross section study was carried out. 100 nurses were included from 3 hospitals of AJK and they were administered a questionnaire regarding socio-demographic, work characteristics and Expanded Nursing Stress Scale.

Results/findings: More experienced and less educated nurses perceived more stress. 48% of the nurses reported high and 52% reported low level of stress. Blaming the nurses for wrong things is the most stressful situation, found in study (Mean=3.49±0.829). Regarding problems with other health care personnel, nurses rated "problems with supervisors" as second most stressful subscale (Mean=3.01±0.763). Older Nurses having more experience and low education had more stress as compared to their counterpart. The findings indicates that the most stressful subscale for nurses is the patient and family stress as indicated by (Mean=3.11±0.503). Items included in subscale are: Being blamed for wrong things (3.49), Abuse from patients' families (3.48), Dealing with violent situations created by a patient (3.08), Meeting unreasonable demands of patient's family (3.06), Dealing with abusive patients (2.98) and Meeting unreasonable demands of patients (2.62)

Discussion/conclusion: Nurses working in hospitals encounter a variety of stressors, which

can affect their professional capabilities. There is need to recognize the stress causing issues by administrators of healthcare setups to incorporate them in teaching and improving working conditions to reduce perceived work stress.

Introduction

Stress is pandemic nowadays and is part of everyday life for health professionals like nurses whose main responsibility is to provide help to patients who are facing life crises. Stress at work is perceived at individual level and when it exceeds the persons coping capacity it presents in form of physiological, emotional, cognitive and behavioral reactions. [1].

Pressure at work can be positive leading to increased productivity. However, when this pressure becomes excessive it has negative impact in form of high staff turnover, absenteeism because of sickness, decreased quality and quantity of care, decreased job satisfaction and increased costs of health care. [2,3] . According to American Institute of Stress, american industry's estimated cost of worth more than \$300 billion due to work stress. [4]

Long-lasting stress can interfere with one's physical and mental well-being.[5] Job stress has been found to be associated with minor psychiatric disorders among hospital nurses. [6] Suicide rate is also higher among nursing profession.[7] Also nurses working in public hospitals are more stressed than those working in private hospitals.[8,9] If nurses remain in stressful condition for long duration without any effective measures to deal with,then it can have detrimental effects upon nurses and, subsequently, upon their performance in the workplace.[10,11,12] Generally females are found to have a significantly higher level of stress than males .This is due to the severe hardships experienced by wo-
men in underdeveloped regions and the strong patriarchal influence on the society. [13] According to the Labour Force Survey (LFS), in 2007/08 an estimated 442 000 individuals in Britain, experienced work-related stress at a level that was making them ill, giving an annual incidence rate of 780 cases per 100 000 workers.Estimates from the LFS indicate that self-reported work-related stress, depression or anxiety accounted for an estimated 13.5 million lost working days.[14]

In Pakistan data about occupational health and safety (OHS) is not available.[15] In AJK (Pakistan), the health care system is facing a shortage of nurses in most of the hospitals as the nurse population ratio is 1;12102.[16] Stress exacerbates the situation of nurse force shortage when they leave the profession as a result of stressful working conditions.

This study is aimed at improving working environment in public hospitals of AJK. It will allow the better understanding of the factors resulting stress in nursing and will help in identification of stress management strategies to improve the working conditions for nurses with resulting benefits for the better health care delivery to entire population.

Methodology

A cross sectional descriptive study was conducted in 3 hospitals of AJK (DHQ Hospital in Mirpur, Bhimber and Kotli) from May to July 2009. 100 nurses of the above mentioned hospitals, who had been working at the hospital for more than 6 months, were chosen so as to exclude participants not fully oriented and adjusted at their new working place. While those who refused and belonged to managerial work were excluded as the nature of work related stress factors differed from those dealing with patients. Study was approved by Ethical review committee of Health Services Academy Islamabad. Informed Consent was obtained from nurses, after explaining them purpose of study. They had the right to withdraw from study anytime and were assured about the confidentiality of data.

The Expanded Nursing Stress Scale (ENSS) questionnaire, used to assess perceived stress. [17]. The ENSS mentioned in the preceding section consisted of 39 items with response options in a 4 point Likert-like format (1=never stressful,

2=occasionally stressful, 3 = frequently stressful, 4 = extremely stressful). Cronbach's alpha was used to assess the internal consistency of the questionnaire. The alpha coefficient for this scale in the present study was 0.883. Data was entered, cleaned, and analyzed by using SPSS version 17.

Results

The socio-demographic and work characteristics of the respondents are shown in table 1.

Age Of the nurses was ranged 22 to 56 and majority of them were less than 30 years old. (50%) of the respondents were married, (46%) were single and (4%) were either widow or divorced. More than half of the respondents (55%) had diploma in nursing, while (22%) had bachelor in nursing qualifications. (63%) of the respondents were living in urban area.

At the time of data collection, (50%) of the nurses were working on morning shift, (31%) of the nurses were on evening shift, and (19%) of the nurses were on night shift.

Regarding the work related factors, majority (72%) of the respondents had less than 10 years of working experience. 56% of the nurses were responsible to provide care of more than 20 patients during her duty hours. Majority of nurses (91%) were having permanent job.79% of the respondents were working for 6 hours in a day while 21% were working 12 hours in a day. only 12% were working in a private setup to supplement their income from the hospital.

Stress is operationally defined as the score of individual on "Expanded Nursing Stress Scale (ENSS) which consists of 9 subscales i.e. workload, conflict with physician, problems with supervision, problems with peers, inadequate emotional preparation, patient and family, uncertainty concerning treatment, discrimination and death and dying. Higher scores on the ENSS indicate more frequently experienced stress.

Tables 2.1 and 2.2 indicate the levels of stress caused by each situation, encountered by nurses in their work place. The answer for each question was scored from one to four according to the Likert rating scale. Maximum score of individual on scale is 4 (extremely stressful) and lowest score on scale is 1(not stressful).

Variables	Categories	n (%)
	1) Less than 30 years	63 (62)
Age	2) 30-45 years	38 (37)
	3) 45-60 years	01 (01)
Marital status	1) Married	51 (50)
	2) Unmarried	47 (46)
	3) others(widow, divorced, separated)	4 (04)
Place of residence	1) Urban	64 (63)
	2) Rural	38 (37)
	1) Diploma in nursing	56 (55)
Education level	2) BSc	24 (23)
	3) BSc nursing	22 (22)
Basic nav scale	1) 16	101 (99)
Dasie pay seale	2) 17	01 (01)
	1) 0	12 (12)
Number of Children	2)1-2	17 (17)
Number of Children	3) 3-5	20 (19)
	4) more than 5	5 (5)
	5) not applicable	48 (47)
	1) Less than 10 years	73 (72)
Total Work experience	2) 10-20 years	26 (25)
	3) More than 20 years	03 (03)
	1) Morning shift	51 (50)
Shift of working	2) Evening shift	32 (31)
	3) Night shift	19 (19)
Contract status	1) Permanent	92 (91)
Contract status	2) Temporary	10 (09)
	1) Ward	95 (93)
Name of Department	2) OPD	02 (02)
Name of Department	3) OT	04 (04)
	4) Other	01 (01)
Working hours per day	1) 06 hours	81 (79)
working hours per day	2)12 hours	21 (21)
	1) Less than 10	10 (10)
No. of patients allocated	2) 11-20	35 (34)
No. of patients anocated	3) 21-30	29 (28)
	4) More than 30	28 (28)
Warking in private sector	1) Working	12 (12)
	2) Not working	90 (88)
	1) Hospital	6 (6)
Name of Private health facility	2) Clinic	6 (6)
	3) not applicable	90 (88)

Table 1. Demographic and work characteristic findings

Subscales	Situations	Not stressful	Occasional stressful	Frequently stressful	Extremely stressful
			n	(%)	
	Shortage of time to complete all nursing work is	5 (4.9)	72(70.6)	16(15.7)	9 (8.8)
workload	Doing too much non-nursing work such as clerical work	14(13.7)	34(33.3)	28(27.5)	26(25.5)
	Shortage of staff in the unit is	04 (3.9)	31(30.4)	28(27.5)	39(38.2)
	Taking decisions under pressure	5 (4.9)	39(38.2)	12(11.8)	46(45.1)
	Unnecessary physician criticism	7(6.9)	38(37.3)	18(17.6)	39(38.2)
Conflict with	Disagreement to a doctor regarding the treatment of patient	11(10.8)	59(57.8)	16(15.7)	16(15.7)
Physician	Absence of physician when he desperately needed in unit	3(2.9)	28(27.5)	20(19.6)	51(50)
	Doing doctors' work in addition to one's own	17(16.7)	31(30.4)	30(29.4)	24(23.5)
	Problems to share work experience with colleagues	50(49)	38(37.3)	7(6.9)	7(6.9)
Problems with Peers	Working with a difficult team member	14(13.7)	43(42.2)	15(14.7)	30(29.4)
	Working with male members of the team	60(58.8)	30(29.4)	8(7.8)	4(3.9)
	Conflict with supervisor	10(9.8)	42(41.2)	14(13.7)	36(35.3)
	Lack of support from the supervisor	6(5.9)	32(31.4)	12(11.8)	52(51)
Problems with	Criticism by a supervisor	4(3.9)	36(35.3)	20(19.6)	42(41.2)
Supervision	Lack of support from the nursing administrator	8(7.8)	20(19.6)	24(23.5)	50(49)
	Being held accountable for uncontrollable things	2(2)	24(23.5)	36(35.3)	40(39.2)
	Harassment at the work place is	12(1.8)	43(42.2)	26(25.5)	21(20.6)
Discrimination	Discrimination because of race or ethnicity	17(16.7)	43(42.2)	21(20.6)	21(20.6)
Discrimination	Discrimination on gender basis	15(14.7)	43(42.2)	32(31.4)	12(11.8)
	Repeated shifting to other departments d/t shortage of staff	13(12.7)	17(16.7)	24(23.5)	48(47.1)

Table 2.1. Stress findings related to hospital system

The analysis indicates that being blamed for wrong things is the most stressful event perceived by the nurses in the public hospitals as 67.6% rated it as extremely stressful.(N= 69, Mean= 3.49). And working with male members of the team is the least stressful event perceived by the nurses in the hospitals as 58.8% rated it as not stressful.

In Table 3 Mean and Standard deviation of items of subscales are shown. Those perceived as causing highest stress in nurses are: Being bla-

med for wrong things, Abuse from patients' families, Any mistake regarding a patient's treatment, Absence of a physician in medical emergency, Absence of physician when a patient is dying, Absence of a physician when he/she is desperately needed in unit, Lack of support from the nursing administrator, Being held accountable for uncontrollable things, Meeting unreasonable demands of patient's family, Lack of support from the supervisor.

		Not	Occasional	Frequently	Extremely
Subscales	icales Situations		stressful	stressful	stressful
Inadequate	Inadequately prepared in fulfilling the emotional needs of a patient	19(18.6)	39(38.2)	34(33.3)	10(9.8)
Preparation	being asked a question by a patient for which there is no satisfactory answer	21(20.6)	53(52)	18(17.6)	10(9.8)
	Inadequate information from a physician regarding the medical condition of a patient	2(2)	46(45.1)	23(22.5)	31(30.4)
	Inappropriate physician's order regarding a patient	4(3.9)	45(44.1)	26(25.5)	27(26.5)
Levels of	Any mistake regarding a patient's treatment	1(1)	24(23.5)	20(19.6)	57(55.9)
Uncertainty	Performing tasks for which not trained	5(4.9)	33(32.4)	24(23.5)	40(39.2)
Treatment	Absence of a physician in medical emergency	4(3.9)	26(25.5)	12(11.8)	60(58.8)
	Inadequate experience to meet the patient's needs	19(18.6)	45(44.1)	22(21.6)	16(15.7)
	Facing sudden and uncertain situations	7(6.9)	34(33.3)	46(45.1)	15(14.7)
	Being exposed to health and safety hazards	8(7.8	26(25.5)	21(20.6)	47(46.1)
	Meeting unreasonable demands of patients	4(3.9)	46(45.1)	37(36.3)	15(14.7)
	Meeting unreasonable demands of patient's family	1(1)	28(27.5)	35(34.3)	38(37.3)
Patient and	Being blamed for wrong things	3(2.9)	13(12.7)	1716.7)	69(67.6)
Family	Dealing with abusive patients	6(5.9)	29(28.4)	28(27.5)	39(38.2)
	Abuse from patients' families	1(1)	15(14.7)	20(19.6)	66(64.7)
	Dealing with violent situations created by a patient	5(4.9)	27(26.5)	27(26.5)	43(42.2)
	Performing procedures on a dying patient	30(29.4)	41(40.2	15(14.7)	16(15.7)
Death and	Observing a dying patient	20(19.6)	51(50)	16(15.7)	15(14.7)
Dying	Absence of physician when a patient is dying	3(2.9)	27(26.5	19(18.6)	53(52)

Table 2.2. Stress findings related to patient dealing

In Table 4 mean stress levels of the nursing stress subscales are given. The results have shown that the most stressful subscale is the patient and family (Meeting unreasonable demands of patients, Meeting unreasonable demands of patients' family, Being blamed for wrong things, Dealing with abusive patients, Abuse from patients' families and Dealing with violent situations created by a patient) as indicated by the Mean (Mean= 3.118), and the least stressful subscale is the problems with peers (Problems to share work experience with colleagues, Working with a difficult team member and Working with male members of the team) as indicated by Mean (Mean= 1.96).

Total perceived job related stress among the staff nurses in the public hospitals in AJK has been calculated using the mean and the standard deviation measures and the result was (N= 102, Mean= 2.75 ± 0.399). This is an indication that the staff nurses in the public hospitals are occasional to frequently stressful according to their ratings of the listed items as stressful for them. At the cut off point of 2.75, 48% of nurses are lying above mean showing high work related stress as compared to 52% of low stress.

After applying independent sample t-test on different subscales of nursing stress scale as shown in Table 5, it was found that regarding death and dying, there was significant difference in stress level of nurses who were more than 30 years of age as compared to less than 30 years of age (P-Value = 0.018) in 2 tailed. Similarly significant difference was present in death and dying stress level among those having basic diploma educati-

Subscales	Stressors	Mean	S.D
	Shortage of time to complete all nursing work	2.28	0.695
XX7 11 1	Doing too much non-nursing work such as clerical work	2.65	1.011
Workload	Shortage of staff in the unit	3.00	0.923
	Taking decisions under pressure	2.97	1.019
	unnecessary physician criticism	2.87	1.012
Conflict with	Disagreement to a doctor regarding the treatment of a patient	2.36	0.876
Physician	Absence of a physician when he/she is desperately needed in unit	3.17	0.934
	Doing doctors' work in addition to one's own	2.60	1.027
Inadequate	Inadequately prepared in fulfilling the emotional needs of a patient	2.34	0.895
Preparation_	Being asked a question by a patient for which there is no satisfactory answer	2.17	0.868
Due 1, 1	Problems to share work experience with colleagues	1.72	0.872
Problems with Peers	Working with a difficult team member	2.60	1.055
1 0015	Working with male members of the team	1.57	0.802
	Conflict with supervisor	2.75	1.050
D 11 - 4	Lack of support from the supervisor	3.08	1.031
Problems with	Criticism by a supervisor	2.98	0.965
Supervision	Lack of support from the nursing administrator	3.14	0.995
	3.12	0.836	
	Inadequate information from a physician regarding the medical condition of a patient	2.81	0.898
	Inappropriate physician's order regarding a patient	2.75	0.898
Uncertainty	Any mistake regarding a patient's treatment	3.30	0.865
Concerning	Performing tasks for which not trained	2.97	0.959
Treatment	Absence of a physician in medical emergency	3.25	0.972
	Inadequate experience to meet the patient's needs	2.34	0.960
	Facing sudden and uncertain situations	2.68	0.810
	Being exposed to health and safety hazards	3.05	1.018
	Meeting unreasonable demands of patients	2.62	0.784
	Meeting unreasonable demands of patient's family	3.08	0.829
Patient and	Being blamed for wrong things	3.49	0.829
Family_	Dealing with abusive patients	2.98	0.954
	Abuse from patients' families	3.48	0.780
	Dealing with violent situations created by a patient	3.06	0.942
	Harassment at the work place	2.55	0.951
D	Discrimination because of race or ethnicity	2.45	1.001
Discrimination	Discrimination on gender basis	2.40	0.882
	Repeated shifting to other departments due to shortage of staffs	3.05	1.075
	Performing procedures on a dying patient	2.17	1.025
Death and	Observing a dying patient	2.25	0.941
Dying_	Absence of physician when a patient is dying.695	3.20	0.934

 Table 3. Mean and standard deviation of nurse stressors

on as compared to those having high education. Thus nurses of more than 30 years of age, with more work experience and having low qualification perceived more stress as compared to their counterpart. No statistical significant difference was found between married nurses versus of having other marital status.

Table 4.	Mean stress	levels	of nurs	ing s	stress	su-
bscales.						

Subscales	Mean	S.D
Patient and family	3.118	0.503
Problems with supervisors	3.014	0.763
Uncertainty concerning treatment	2.89	0.557
Conflict with physician	2.75	0.672
Workload	2.72	0.624
Discrimination	2.61	0.651
Death and dying	2.54	0.832
Inadequate emotional preparation	2.25	0.716
Problems with peers	1.96	0.622

Discussion

The present study was conducted to identify different levels of occupational stress among nurses in public hospitals of AJ&K. To our best knowledge this is the first study to investigate the work stress in nurses in AJ&K.

Stress is experienced by a nurse when expectations from her outweigh the resources. A moderate level of stress is considered as normal and nece-

Table 5.	Ind	ependent	sample	r T	' test
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ssary motivating factor. Continuously increasing population and limited resources in government hospitals has changed the working pattern of nursing as a whole. Stress levels are on the rise and little is being done about assessment of the problem and active management of its consequences. The pressures of different stressful conditions created a work-personal life imbalance, which begins to affect the health of the nurses. Also it affects the nurses' efficiency and effectiveness.

Statistically significant difference was found between age of two groups of nurses and death and dying stressor. Nurses aged more than 30 years had significantly higher stress as compared to those who are less than 30 years. Similarly nurses with more experience were found to perceive more stress as compared to less experienced. The findings of the effect of age and work experience on perceived stress are consistent with the finding of a study conducted in India to assess the occupational stress in nurses, in which perceived stress was high in the older and more experienced nurses. [18]. While findings are not compatible with findings of study in Taiwan in which stress was high in young nurses.[19]

The findings indicates that the most stressful subscale for nurses is the patient and family stress as indicated by (Mean= 3.11 ± 0.503). Items included in subscale are: Being blamed for wrong things (3.49), Abuse from patients' families (3.48), Dealing with violent situations created by a patient (3.08), Mee-

	Factors	Ν	Mean	S.D	P value
	Age of respondent				
Death and dring	< than 30	63	2.38	0.821	0.018*
Death and dying	> than 30	39	2.78	0.800	
	Education level				
Drohlom with poor	Diploma in nursing	56	2.11	.600	.006*
Problem with peer	Higher qualification	46	1.77	.604	
Death and dring	Diploma in nursing	56	2.69	.834	.035*
Death and dying	Higher qualification	46	2.34	.798	
	Work experience				
Death and dring	< than 10 years	73	2.39	.821	.006*
Death and dying	> than 10 years	29	2.89	.761	
	Work shift				
Disprimination	Morning	51	2.66	.785	.022*
Discrimination	Other(evening & night)	51	2.41	.865	

ting unreasonable demands of patient's family (3.06), Dealing with abusive patients (2.98) and Meeting unreasonable demands of patients (2.62). These findings contradicts majority of earlier studies conducted to find out the stressors in nurses, which reported workload and inadequate preparation stressors as highest one.[18,20]

The timing hours for visitors are usually fixed, particularly in evening to meet patient, since many come after work periods or according to their own suitability. Family and friends of patient provide much attention to the patient, as a part of our customs. Dealing with families and visitors in addition to their direct patient's care activities place increased pressures on nurses.[18]

Blaming the nurses for wrong things is the most stressfulsituation, found instudy (Mean= 3.49 ± 0.829). It is the usual practice in many hospitals and it decreases the morale of nurses and sometimes they react negatively to this in such manner, which affects the quality of care. Nursing administrators need a change in their behavior by finding out the root cause of the problem to solve them rather than assigning blame to the nurses.[21,22]

When doctors are not present then nurses have to face verbal abuse and misbehave from patients and relatives for issues that may not be directly connected to their work. Unnecessary demands by patients and their relatives results in disagreement and lead to more stress.[18,20] Patients' expectations from nurses are sometimes difficult to deal with and they tend to be violent. No training is given to them to deal with such situations.

Regarding problems with other health care personnel, nurses rated "problems with supervisors" as second most stressful subscale (Mean= 3.01 ± 0.763). It is proposed that supervisors are considered in a position of authority so they have more power to alter stressors in the work environment. Alternatively, it could be that a supervisor is able to provide the necessary resources or support to assist nurses to cope with the situation. Also the nursing supervisor may encourage them to engage in problem-focused coping, rather than emotion-focused coping.[23,24]

When such support from supervisors is unavailable or perceived as inadequate, the level of stress may be perceived higher by the nurses. On other side this lack of support may have been due to increased demands placed on managers and supervisors in hospitals. Their different role from those nurses involved in direct patient care moved them away from the wards and patients, which may have contributed to a sense of lack of support.

In this study the least stressful stressors are related to Peers. It is interesting finding that majority of nurses do not felt any stressful situation related to work with their colleagues.

A nurse requires the cooperation of other colleagues to accomplish her work. They also require effective working relationships and communication with others. Results did not meet the findings to study conducted in USA in which high stress due to colleagues was perceived. [25]

Regarding uncertainty concerning treatment factor, reason of high level of stress among nurses is lack of autonomy and independency in making decisions. Mainly Physicians are responsible to manage urgent health problems of patients and they have to make decisions on patient's health. In case of their absence in medical emergency, majority of the nurses feel themselves unable to make decisions in emergency. They also feel powerless to change perceived unsatisfactorily situations. Although some of the nurses felt inadequately trained or equipped for their job.

Nurses rated inadequate emotional preparation as less stressful subscale. Lack of provision of emotional care is not felt stressful by the nurses. The results clearly suggest that nurses are avoiding emotional demands of the patients as indicated by (Mean 2.34, 2.17). Might be the nurses ignoring this perspective unconsciously to reduce stress as a coping mechanism. It looks so as they have set their nursing objective only as physical objective and avoiding the emotional objectives in their job.[26] This situation is against the concept of holistic care in nursing profession (the physical, emotional, social and spiritual aspect of care) and showing the conversion of the nurses into machines i.e., without emotions.

This was first study to be conducted in AJ& K to assess the stress level in nurses. A limitation of the study was the use of limited sample confined to limited geographical area. There is a need to replicate the study using a larger number of nurses with a wider geographic distribution, and random sampling methods. This replication should be

done to assess stress in nurses among hospitals of varying sizes.

Secondly, data accumulated through a self-rating Likert like scale might impose a limitation on participants' responses in this study, even though an explanation regarding rating was given to the participants as clearly as possible.

Conclusion

Patient and family issues and problems with supervisors were major stressors identified in this study. Attention to these stressors is needed in order to maximize the quality of nurses working lives. Nurses working in hospitals encounter a variety of stressors, which can affect their professional capabilities. Their stressors should be relieved to enable them providing the emotional aspect of care which is as important as the physical aspect of care.

Stress reflects the impact of the hospital system and its administration on the staff. The hospital authorities needs to recognize the issues of excessive work load, poor working conditions, organizational constraints, and interpersonal conflicts to reduce the perceived work related stress. Unless the various work stressors are recognized and properly dealt with, it may lead to poor morale and uncooperative behavior of nurses towards patients. If left unattended, the end results could turn the hospital into a dysfunctional system.

Recommendations

Interventions should be targeted at sources of stress and more support should be given to nurses at individual level. It is not possible to expect any individual to separate the workplace from their personal lives. So research is needed to identify the personal circumstances which exacerbate workplace stress, and how they may possibly be used to reduce stress. Results of the study can be implicated at nursing administration, practice and education levels.

They should provide environment conducive for the social support and should focus on those stressors over which they have the most influence to change. They should arrange frequent staff meetings with the purpose of improved nurse training regarding early identification of stressors and the ways to deal them. There is a need to teach skills in areas like improving communication, conflict management and also emotional preparation for difficult patient and family interactions. This will help to minimize the emergence of probable stressful situations.

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Do physicians & allied health workers have same believe in complementary and alternative medicine (CAM)?

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Abstract

Aim: The purpose of this study was to assess whether family physicians and allied health workers are aware with and have positive attitudes about complementary and alternative medicine (CAM).

Methods: It is a cross-sectional study conducted during April to June 2011 at family medicine health care clinics in Erzurum, Turkey. There were 231 family physicians in 72 family medicine health care clinics working together with an allied health professional (nurse, midwife or health technician). Out of 462 participants invited, 333 (72.0%) accepted to join. The structured and pre-tested questionnaire was self-completed by all participants.

Results: The main finding was that two groups differed significantly (p=0.001) as regard to their level of knowledge. The other variables like gender, age or working experience did not show any significant affect to knowledge level. The comparison in between the groups shows that out of six questions related to attitudes, only two questions have significant (p=0.001) difference otherwise there was no significant difference among agreements. Whereas physicians have suggested CAM to their patients more (p=0.004) as compared to allied health professionals during last one year.

Conclusions: Both groups have limited knowledge but positive attitude and shows significant difference. However both groups are ready to learn more about CAM and want to improve their knowledge.

Key words: Complementary and alternative medicine, health workers, family physician

Introduction

Complementary and alternative medicine (CAM) refers to a group of medical and health systems, practices, disciplines and products that are not considered as a part of conventional medicine [1,2]. According to estimates, more than 80% of the developing world and half of the developed world utilize CAM [3,4]. There are several reasons for using CAM including dissatisfaction with conventional medicine via failed treatments and high costs as well as high expenses incurred from conventional medicinal treatments [5]. Eventually, people turn to CAM because they believe mind/ body therapies are important for health maintenance or simply because they find it an interesting concept worth experimentation [6,7].

Turkey is different from other developed countries in that there are no official regulations for many CAM modalities. There are several reasons for this including having no complementary practitioners as the curricula in medical and allied sciences colleges do not have enough CAM-related content. Therefore, in Turkey there is limited information about the general approaches among family physicians and allied health workers regarding CAM [8].

Since it is important that health workers should be aware of CAM in order to practice it appropriately, this study is an attempt to assess the knowledge, attitude and behavior of family physicians and allied health workers regarding CAM.

Materials and methods

Study Design and Setting

We conducted a cross-sectional knowledge, attitude and behavior survey. The study was conducted during April to June 2011 at family medicine health care clinics in Erzurum, Turkey. There were 231 family physicians in 72 family medicine centers serving to a population of around 790 000 people on a list based manner. Each family physician was working together with an allied health professional (nurse, midwife or health technician).

Study Sample and Data Collection

All family physicians and allied health workers in the city were invited to participate in the study. The invitation letter and questionnaire were sent through the health directorate and again collected back through the same route utilizing the official postal system. Out of 462 participants invited, 333 (72.0%) accepted to join. The structured and pre-tested questionnaire was self-completed by all participants.

Questionnaire

a. Preparation

The researchers have developed a questionnaire. It was based on the prior experience of authors, input from colleagues, peers as well as from previous published papers. The draft so prepared was then pre-tested on 10 respondents and modified according to the pre-tests results. The results of the pre-testing were not included in the final analysis of the data.

b. Segments

The questionnaire was divided into four sections.

Section 1: General Information

The first section comprised socio-demographic information such age, gender, and educational level.

Section 2: Knowledge

This section assesses the knowledge of the respondents regarding CAM. It contains total 7 questions. The first three questions are comprised of pictures of different plants (linden, thyme, and daisy) while other questions have some answers to be ticked by respondents.

Section 3: Attitude

This part of the questionnaire comprised of questions related to attitude of health workers towards CAM. This segment contains 6 questions based on a five point Likert scale [9] from strongly agree to strongly disagree.

Section 4: Behavior

This section comprised of 5 questions related to the behavior of health workers such as "Have you ever suggested any CAM to your patients in last one year?"

Statistical Analysis

The data was analyzed using Windows SPSS version 18.0. As part of descriptive statistics, n (%) and mean \pm standard deviations were given where appropriate. Associations were assessed using Chi-square and independent samples t tests. Socio-demographic variables with a significant p value were subjected to a multiple logistic regression analysis to determine which factors were independent predictors of knowledge, attitude and behavior. A p<0.05 was considered significant. All odds ratios were recorded with a 95% confidence interval.

Ethical Considerations

All efforts were made in this study to fulfill the ethical considerations in accordance with the Declaration of Helsinki. The confidentiality of each participant was strictly ensured throughout the project. The Local Ethics Committee at the Faculty of Medicine, Ataturk University, has approved the study.

Results

Results for 333 participants were analyzed. Mean age was 32.3 ± 6.2 years. 193 participants (58.3%) were females while 138 participants (41.7%) were males. A total of 158 family physicians (47.7%) and 173 allied health professionals (52.3%) have participated in the study. Participants' mean working experience was 8.7 ± 5.1 years.

The majority (n=53; 36.6%) had knowledge about herbal treatment followed by 47 participants (32.4%) who were aware about acupuncture. The most recognized herb was daisy (n=83; 24.9%). Two hundred twenty nine participants (89.8%) knew the method for applying acupuncture (Table 1).

When compared the knowledge level with different demographic features (Table 2), significant difference (p=0.001) was found only in between physicians and other health workers. The other variables like gender, age or working experience did not show any significant difference.

We combined the responses of the participants as A is equal to strongly agree and agree and B is equal to strongly disagree and disagree. Table 3 depicts that there is a significant difference (p=0.043) in physicians and health workers, opinion. The majority (n=98; 80%) strongly agreed to take part in any course related to CAM. Very less number (n=36; 32.7%) of physicians expressed that CAM is a thread for public health; allied health workers also had similar opinions. However majority physicians (n=90; 76.3%) strongly agreed plus agreed that unproven treatments should be prohibited;

allied health workers had similar opinions in this regard too. Regarding the question about usage of CAM and benefits of CAM on placebo effects, the two groups had different opinions (p=0.001).

Table 4 shows that almost one third (n=96; %28.8) of participants had advised diet therapy

Table 1. Overall knowledge about CAM

Itoms for shosking of knowledge	Unkı	nown	Known		
items for checking of knowledge	n	%	n	%	
Picture of linden	294	88.3	39	11.7	
Picture of thyme	325	97.6	8	2.4	
Picture of daisy	250	75.1	83	24.9	
Laxative effect of Senna	166	49.8	167	50.2	
Knows at least one CAM	258	77.5	75	22.5	
Knows Method for Acupuncture (MCQ)	34	10.2	299	89.8	
Knows Ginko is an Herbal extract (MCQ)	189	56.8	144	43.2	

CAM: Complementary and alternative medicine, MCQ: Multiple choose question.

Table 2.	Comparison	of Ki	iowledge	scores with	demograp	ohic featur	es
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		-	Knowle	D	
		п	Mean	SD	r
Groups of Participants	Physicians	158	2.80	1.29	0.001
	AHW	173	2.14	1.45	0.001
Gender	Males	193	2.35	1.38	0.100
	Females	138	2.60	1.30	0.108
Warking experience	≤ 10 year	176	2.44	1.29	0.610
working experience	\geq 11 year	73	2.53	1.36	0.019
Age groups	\leq 40 year	295	2.41	1.34	0.002
	\geq 41 year	33	2.85	1.54	0.085

SD: Standard Deviation, AHW: Allied health workers.

Table 3. Comparison of attitudes of Physicians & Allied health workers

		Groups					
		Phys	icians	AI	IW	Total	P
		n	%	n	%		
Interested to take part in an equire of CAM	Α	98	79.7	94	68.6	192	0.042
Interested to take part in an course of CAM	В	25	20.3	43	31.4	68	0.045
CAM is a thread for public health		36	32.7	45	33.6	81	0 000
		74	67.3	89	66.4	163	0.888
	A	90	76.3	91	71.1	181	0.259
Onproven treatments should be promoted	В	28	23.7	37	28.9	65	0.338
CAM should be used together with modern	A	95	79.8	99	87.6	194	0.110
medicine	В	24	20.2	14	12.4	38	0.110
CAM can be used sometimes instead of	A	56	45.9	77	66.4	133	0.001
modern medicine	В	66	54.1	39	33.6	105	0.001
Departite of CAM depends on pleashe offects	A	52	50.5	55	76.4	107	0.001
Benefits of CAW depends on placebo effects	В	51	49.5	17	23.6	68	0.001

A: Strongly agree + agree, *B*: Strongly disagree + Disagree, *AHW*: Allied health workers, *CAM*: Complementary and alternative medicine.

followed by 19.6% (n=65) herbal treatment and massage advised by 15% (n=50) during last one year. However about the utilization, around 20% (n=53) had utilized mainly diet, herbal treatment and praying (n=53, 21.9%; n=53, 21.9%; n=50, 20.7%, respectively) followed by massage (n=42; 17.4%) and acupuncture (n=9; 3.7%).

Table 4.	Comparison	between	advised	and	utili-
zed of CA	M by health	workers			

Tumor of CAM	CAM sı	iggested	CAM utilized		
Types of CAN	n	%	n	%	
Diet therapy	96	28.8	53	21.9	
Herbal treatment	65	19.6	53	21.9	
Massage	50	15	42	17.4	
Praying	40	12	50	20.7	
Acupuncture	39	11.7	09	3.7	
Meditation	08	2.4	06	2.5	
Hypnosis	07	2.1	00	00	
Yoga	06	1.8	5	2.1	
Bio-energy	05	1.5	00	00	
Leach therapy	05	1.5	00	00	
Cupping	00	00	05	2.1	
Others	12	3.6	19	7.9	
Total	333	100	242	100	

CAM: Complementary and alternative medicine.

There was no significant difference (p > 0.05) between males and females regarding the use of CAM as a suggestion. Whereas physicians have suggested CAM to their patients more (p=0.004) as compared to allied health professionals during last one year (Table 5).

Discussion

This study demonstrated that primary care health workers and allied health workers have significant differences in their knowledge regarding CAM and indeed both groups show insufficient knowledge however they utilize and suggest complementary and alternative methods frequently.

Although the trend shows an upsurge of the number of physicians in the last 40 years [10] however still the requirements of the patients are not fulfilled with full satisfaction, one reason why peoples are still searching for alternative methods. There are always some alternative methods [11] present since the medicine has evolved but it's practices are always in question. Although some neighbor countries use CAM widely [12], however the situation in Turkey is different and the

Table 5. CAM-related behavior of health workers by gender and profession

		Gender				
		Fema	ale	Ι	Male	P
		n	%	n	%	
Have you ever suggested any CAM to your	Yes	70	36,3	62	44,9	0.112
patients in last one year?	No	123	63,7	76	55,1	0.115
Have you ever tried any CAM on you in	Yes	69	35,8	40	29,0	0.107
last year?	No	124	64,2	98	71,0	0.197
Do you ask your patients about their use of CAM?	Always	13	6.7	12	8.7	
	Sometimes	123	63.7	101	73.2	0.058
	Never	57	29.5	25	18.1	
			Gi	roups		
		Physic	Gi ians	oups A	AHW	
		Physic n	Gi ians %	roups A n	AHW %	-
Have you ever suggested any CAM to	Yes	Physic n 76	Gi ians % 48,1	roups # n 56	AHW % 32,4	0.004
Have you ever suggested any CAM to your patients in last one year	Yes No	Physic n 76 82	Gi ians 9% 48,1 51,9	roups	AHW % 32,4 67,6	0.004
Have you ever suggested any CAM to your patients in last one year Have you ever tried any CAM on you in	Yes No Yes	Physic n 76 82 52	Gi ians 9% 48,1 51,9 32,9	roups n 56 117 57	AHW 32,4 67,6 32,9	0.004
Have you ever suggested any CAM to your patients in last one year Have you ever tried any CAM on you in last year?	Yes No Yes No	Physic n 76 82 52 106	Gi ians 9% 48,1 51,9 32,9 67,1	roups <i>n</i> 56 117 57 116	AHW % 32,4 67,6 32,9 67,1	- 0.004 - 0.994
Have you ever suggested any CAM to your patients in last one year Have you ever tried any CAM on you in last year?	Yes No Yes No Always	Physic n 76 82 52 106 13	Gi ians 48,1 51,9 32,9 67,1 8.2	Proups n 56 117 57 116 12	% 32,4 67,6 32,9 67,1 6.9	- 0.004
Have you ever suggested any CAM to your patients in last one year Have you ever tried any CAM on you in last year? Do you ask your patients about their use of	Yes No Yes No Always Sometimes	Physic n 76 82 52 106 13 112	Gi ians 48,1 51,9 32,9 67,1 8.2 70.9	Proups n 56 117 57 116 12 112	% 32,4 67,6 32,9 67,1 6.9 64.7	- 0.004 - 0.994 - 0.288

CAM: Complementary and alternative medicine, AHW: Allied health workers.

use of CAM is still a debatable topic. This study showed the knowledge, attitudes and behavior of family physicians and allied health workers that play a pivotal role in delivery of health care. The overall trend is almost same as it is mentioned in different published studies in Turkey [8].

Despite of the claim [3] of the policy makers that during last 10 years the traditional medicine awareness is increased among modern physicians or health workers, this study shows that only one third of the sample was aware about the herbal treatment followed by almost 30% who knows about acupuncture. Which is different from the results of another Turkish study [8] that shows a higher level of knowledge i.e., 61% were aware about CAM fully. In fact, other studies [13,14] rather reinforced our results and show low level of knowledge. In addition to these studies, another study [15] shows the low level of knowledge for acupuncture with 40% unable to answer even one question (of eight) correctly however it differs from our results that shows almost 90% were aware about the method of acupuncture. The literature also depicts that this method is practiced more [16] among the general practitioners (GPs).

Our data shows that there is a significant difference in the level of knowledge in between physicians and other allied health workers. In deed the physicians were more able to give the answers of MCQs present in the questionnaire. Yet there is no study present in Turkey to compare these results so it is difficult to generalize the results or get any inference. Nonetheless some international studies [17,18] also showed that doctors are more aware than students and it is also second by another study on nursing students [19] shows a limited knowledge regarding CAM.

In spite of low level of awareness, the participants had a positive approach towards CAM as almost 60% are interested to attend a course related to CAM, which is comparable to the results of other Turkish study [8]. Therefore it is understood that in Turkey the health workers are likely to apply and practice CAM if they are fully trained. Further, a study [17] in Germany shows that doctors and students both recommended that CAM should be a part of medical curriculum. Though it doesn't mean that are ready to practice even unproven treatment as our study shows that more than 50% participants of the study are in a favor to practice evidence based medicine (EBM). A survey of medical students in USA also favors the EBM practice of CAM [20]. Additionally they prefer to give CAM with modern medicine.

Sometimes there is a difference in believing and practicing. In our study the health workers are not only advising CAM frequently but also using for themselves. A study in New Zealand showed that the most common CAM therapy practiced by GPs was acupuncture, and chiropractic manipulation was the most common GP-referred therapy for patients [16]. However usage rate of CAM by patients was not a part of our study so we cannot conclude that after receiving advice from health workers which therapies were commonly used during last one year.

In order to appropriately counsel the patients, health workers should have information on CAM and need to practice it for them, if it is indicated. Our study showed that almost all participants have used CAM during last year. Diet (22%), herbal treatment (22%) and prayer (21%) are among the most commonly used CAM by health workers. Certainly it is matching with their advise to patients however not comparable to a study done in Turkey in 2007, which shows only 29% of GPs were using some type of CAM for themselves [8].

As one study in USA highlighted, prayer specifically for one's own health (43.0%) was on the top [1] similarly this study shows that praying is one of three most commonly advising and using CAM among the participants. Actually, herbal therapy has an important position as a complementary part of pharmacotherapy in modern medicine [21].

Conclusion

Both health workers have limited knowledge with significant difference however ready to enhance their knowledge that shows their positive attitude towards CAM. They are not only advising it to patients but having believed so also utilize for themselves. Therefore it is recommended to provide training opportunities for health workers to learn more about CAM or perhaps including in curriculum will enhance the standardization of the training and provide chances to learn and practice it more and more for effective use for patients.

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Effects of a 12-week aerobic exercise on back spine and thigh bone mineral density in heavy women after menopause

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Abstract

The purpose of this study was to investigate the effect of a 12-week selective aerobic exercise trial in water on bone density in obese postmenopausal women. Twenty obese post-menopausal women as subject to participate in this study. Subjects randomly divided into an experimental and control group. The experimental group performed selective aerobic training in water for 3 month, first month: 3sessions/wk, second month: 4 sessions/wk and last month: 5 sessions/wk. Each session lasted 90 min with the exercise intensity 65-75% of HRmax in all of sessions. Control group did not participate in any physical activity program during study period. Bone density of lumbar spine and femur were measured in both groups in before and after exercise training period by densitometry method. Also, calcium and phosphorus was measured in same times. Data analyzed with paired and independent samples T-Test. The results of this study indicate that there was a significant increase in femoral bone density in experimental group compared with control group in end of study period (P<0.05). Also, the lumbar spine bone density was increased moderately, but not significantly, in experimental group. On the other hand, calcium and phosphorus levels were not different significantly between experimental group and control group in end of study period (P<0.05). The results of this study indicate that one period of selective aerobic exercise trial in water enhanced femoral and lumbar spine bone density in obese postmenopausal women.

Key words: Osteoporosis, Menopause women, Aerobic exercise, Thigh bone

Introduction

As life expectancy has increased, osteoporosis has been more frequently diagnosed in women

and men worldwide [1,2]. Osteoporosis is the most common bone disorder in the world [3]. It is defined as "a skeletal disease, characterized by low bone mass and micro-architectural deterioration of bone tissue, with a consequent increase in bone fragility to fracture" [4]. Pursuant to the International Osteoporosis Foundation (IOF), 40% of women have fracture due to osteoporosis during their lifetime [5]. The impact of osteoporosis and fragility fractures increases as the population ages. The lifetime risk of any osteoporotic fracture is high and can be as high as 40-50% in women and 13-22% for men [6]. Osteoporosis is still afrequently under-recognized disease and considered to be an inevitable consequence of ageing [7]. As a disease of the elderly, the prevalence will increase as the population ages. Currently every third post-menopausal woman and every fifth man older than 50 years, suffer from osteoporosis [8].

Osteoporosis as a multi-factor disease of skeletal system, is the major cause of reductioninguality of life, fracture and death of old people especially women aftermenopause [9]. The menopause is a time when many women seek advice about bone health and their risk of osteoporosis. In the majority of early postmenopausal women, fracture probability is low and intervention to prevent bone loss is not indicated [10]. Menopause, whether it occurs naturally or surgically, is characterized by the loss of hormones produced by the ovaries. In natural menopause ovarian function decreases slowly over several years until menstruation ceases [11]. Osteoporosis is most common among women than men and increases as the levels of estrogen decrease. From the other side, preventing the reduction of bone mineral density or attempts to maintain it is the best way to deter its occurrence in elderly women after menopause. Different treatments to prevent the reduction of bone mineral density including estrogen therapy, skeletal anti-reabsorption drugs and physical activities have been tried [12]. But results of studies on medical methods to stoposteoporosis indicate that, in spite of their preventive efficiency, these methods in the long run may induce heart diseases, breast cancer and heart attack, while physical activities have positive effects on preventing the reduction of bone mineral density with no side effects. Thus, exercise therapy has been recently considered by a great number of researchers[9]. But from among different exercises, water exercises have been given less examination. Water is a medium that forces resistance appropriate to every individual's bodily requirements and so enhances physical activities and competition between muscular groups to suppress resistanceand also can be effective to increase mechanical strain on bones and bone formation [13]. Unlike other exercises, water exercise can also increase competition between upper and lower organs in an appropriate domain of movement; thus in these activities the jointsendure less strain. From the other side, water exercises enhance old people's capability to keep their balance and this way decreases the risk of falling and fragility fracture [13].

Considering the developing approaches of treatment to stop osteoporosis in old people, especially heavy women after menopause, and the importance of water exercises as an appropriate and less-risky approach, we tried to study the effect of a 12-week aerobic exercise on back bone and thigh bone mineral density in heavy women after menopause.

Materials and methods

Candidates

the data were gathered from 20 heavy women after menopause from Urmia(50-55 years) with BMI≥30 that wanted to use swimming pool for the first time and,according to the health questionnaire and the physician, possessed the requirements to take part in the study.They had no experience in sport exercises in the past. They were divided randomly in two groups, the exercise group and the control group. The exercise group did aerobic exercises in water for 12 weeks while the control group had no physical activities during the study.

Exercise Protocol

In the present study all the exercises were practiced in a pool with 120 cm depth, in the way that candidates had their heads and necks above the water. The procedure included: warm up, stretching exercises, jumping exercises, aerobics, flexibility and then cooling down to return to the primarycondition. During the exercises, heart beat started from the estimated maximum 65 percent and increased to 75 percent at the end and the candidates did the exercises in the range of 110-130 beat per minute. The duration of each exercise session was 90 minutes. To control the intensity of exercises, heart beat was measured by a pulsometer3 times during the exercise: before and after aerobic exercises and after cooling respectively. To consider the principle of extra load during exercises, first the repetition of the movements were increased, then break time shortened and then weight was increased by water bottles and speed increased by music. During the exercises, variety was brought into account. The frequency of sessions in the first month was 3 sessions a week and for the second month was 4 that increased to 5 sessions in the third month.

Data-gathering method

In the first place candidates were asked not to do physical activities of any sort two days before the experiment. To measure research variables, bloodsampling was done between 8 to 10 in the morning, 12 hours hungry a day before the experiment. So from the vein of each candidate left hand in sitting and resting positions 10 mL blood was taken. Parathormone measurements were done in vitro after providing serum exploiting DiaSorinInc N-tact PTH IRMA kit by Immunoradiometric Assay method using the Minineph device made in US. 25 hydroxy vitamin D3serum values were analyzedby Immunoassay method. Calcium and phosphor plasma values were measured by PX Daytona automated chemistry analyzer. At the end of exercise period and 48 hours after the last session, the control and the exercise groups were collected again in vitro and their blood and urine samples were taken. All the experiments were done in biochemistry laboratory of Urmia University. Bone mineral density values in back and thigh bones before and after the exercise period in both groups were measured in the density measurement and osteoporosis diagnosis center by a

radiograph with the maximum raypower 3 M REM using DEXA device in the density measurement and Osteoporosis diagnosis center.

Statistical analysis

To determine the measured values of variables in groups we used descriptive statistics and to determine the differences in each group and between the two groups we used correlated and independent t test respectively. A significant level of alpha error (p<0.05) was also considered.

Results

Results of correlated t test to compare values before and after exercise period in groups indicate that performing exercise protocol significantly increased the average of thigh bone mineral density, level of parathormone, 25 hydroxy vitamin D3 and calcium serum in the exercise group in a way that the average of results after the test were greater than those before the test (p<0.05). However, there was no change in values of the control group before and after the test. (Figures 1, 2, 3, 4, 5)

Results of independent t test also indicate that there are significant differences in the average of thigh bone mineral density, level of parathormone and calcium serum between the groups (p<0.05). The average of density changes of these indexes in the exercise group after exercises was significantly greater than the control group (Fig. 5).



*Significance at error level of Alpha 5% Figure 1. The histogram of the average changes before and after thigh bone mineral density test in research groups



*Significance at error level of Alpha 5% Figure 2. The histogram of the average changes before and after parathormone serum test in research groups



^{*}Significance at error level of Alpha 5% Figure 3 The histogram of the average

Figure 3. The histogram of the average changes before and after calcium and phosphor serum test in research groups

Table 1. The average changes in calcium plasma levels in experiment and the control groups before and after the test

After test & before test	After test & before test	Exercise Group	Control Group	Groups	Variables	Difference Mean*
After test & before test	After test & before test	0.117	0.108	9.54	10.08	0.04
After test & before test	After test & before test	0.001	0.005	10.02	9.99	0.11

Paired t test *

Table 2. The average changes in phosphor plasma levels in experiment and the control groups before and after the test

After test & before test	After test & before test	Exercise Group	Control Group	Groups	Variables	Difference Mean*
After test & before test	After test & before test	-0.117	0.108	3.45	3.18	0.09
After test & before test	After test & before test	-0.001	0.005	3.45	3.6	0.5317

Paired t test *



Significance at error level of Alpha 5% Figure 4. The histogram of the average changes before and after serum 25-OHD3 test in research groups



*Significance at error level of Alpha 5% Figure 5. The histogram of differences in average changes of measured variables in research groups

From the other side, results of correlated t test to compare the values before and after exercise period indicate that performing exercise protocol had no significant effect on back spine bone mineral density in either groups(p<0.05) (Fig. 6).



Figure 6. The histogram of the average changes of back bone mineral density in research groups

Discussion

Results of the study show that performing a 12week aerobic exercise period in water had significant effect on thigh bone mineral density and increased its density in the exercise groupthan the control group. Although not much research is done to study the effects of exercises in water on bone mineral density, results of present study are in accordance with the findings of Tanya et al (2006)[13]. These researchers, in their study of the effects of a 12week aerobic exercises in shallow water on bone mineral density in menopause women, reported that these exercises keep and improve bone density in thigh bones. Results of present study are in accordance with researches that show the positive effect of weight-bearing [14] and resistance exercises [15] on land on thigh bone mineral density. For example, George and et al, reported that doing aerobic exercises continuously increases thigh bone mineral density [16]. Rhodes and et al, also reported that doing aerobic exercises for a year increases thigh bone mineral density [17]. From the other side, results of present study are not in accordance with findings of Bravo and et al [28].

These researchers studied the effects of a 12week weight-bearing exercise in water on thigh and back spine bone mineral density in women after menopause and reported that back spine bone density decreased but thigh bone density didn't change. This difference seems to be due toduration and intensity of exercises in the two studies [18]. Bravo did his study with threesessions a week and no control on intensity of exercises, while we did our study in an increasing period starting from three sessions a week in first month to 5 sessions in third month. Intensity in the whole period was 65 to 75 percent of heart beat. It should be noted that the number ofsessions in a week, time-period and intensity of exercises are key factors that affect bones' response to mechanical and dynamic strains [15] [19]. For example, Snow and et al, reported that resistance exercises with low frequency and more weight improves thigh bone mineral density better than exercises with high frequency and less weight [15].Krall and et al, using an evaluative questionnaire for different levels of physical activities in women after menopause reported thatbone mineral density in women who walk more than 7.5 miles a week is significantly more than women that walk less than a mile in week [20]. Duration and intensity of exercises should be such that induce bone modeling factors [21]. The least intensity and duration that can cause this are called Minimum effective exercise intensity and Minimum effective exercise duration respectively [22]. Frost in his theory suggests that bone structure is maintained through a feedback system in a way that increase in mechanical and dynamic strain induces bones and causes modeling of bones. This theory is known as Mechanostate Theory. According to this theory,

mechanical strain should be as much to cause bone formation or modeling to precede bone reabsorption process. This mechanical strain is called minimum effective strain threshold [23].

So in Bravo's study, intensity and load of exercises were probably not in minimum effective strain threshold to improve thigh bone mineral density. From the other side, the present study showed that aerobic exercises in water for 12 weeks didn't have significant effects on back spine bone mineral density and just slightly increased bone mineral density in back spine in the exercise group than the control group (p>0.05). Few researches have been done to study effects of exercise in water on bone mineral density especially in back spine. Harush and et al, and Ay and et al, reported that doing aerobic exercises in water maintains and even improves bone mineral density in women after menopause [24] [25]. Yamazaki and et al. also studied the effect of walking on bone metabolism in menopause women and reported that doing these exercises for 12 months increases back spine bone mineral density insignificantly [26]. Sinaki and et al, also reported the insignificant difference in back spine bone mineral density after doing resistance exercises for three years [27]. From the other side, results of the present study were not in accordance with findings of Tskahara and et al [28]. These researchers studied the effect of 32 months aerobic exercise in water and reported a significant increase in back spine bone mineral density in the exercise group than the control group. This difference may probably be because of differences in duration and kind of activities [9]. Results of previous studies show site-specific effects of exercise on bones of different parts of the body[29]. Exercise affects bone mineral density of different parts of the body when it increases mechanical load or dynamic strain of that site of the body. It should be noted, however, that different bones reflect different bone modeling responses to mechanical and dynamic strains [27]. In a way that the level of bone formation in cortical bones like thigh bones is greater than cancellous bones like back spine bones. Results of different researches show that responses of cortical bones like thigh bone to mechanical or dynamic strains are greater than cancellous bones like back spinebones[30]. So these bones need more time to have positive responses to mechanical or dynamic strains of exercises [31].

Rockwell and et al, reported that resistance exercises for 9 months decrease bone mineral density in back spine bones [32]. While Frindlander and et al. showed that doing resistance exercises for 2 years with the same protocol has significant effects on back spine bone mineral density [31].

Results of present study indicate that doing aerobic exercises in water for 12 months had no significant effect on plasma phosphor level in the exercise group and there was no significant difference between the exercise group and the control group for this index (p>0.05). Alice and et al. also reported no significant change in phosphor level after doing aerobic exercises in women after menopause [33].

However, calcium and 25 hydroxy vitamin D3plasma levelsat the end of exercise period in present study increased in the exercise group compared with the control group. There was also a significant difference in calcium level between the exercise group and the control group (p<0.05).Researchers believe that these changes are related to hormone factors that regulate calcium levels [33] [34]. For example, parathyroid hormone (Parathormone) is an important factor in bone metabolism [35]. One of the most important roles of this hormone is maintaining compatibility of calcium ion / nonorganic Phosphate through PTH / PTH recipient related to protein in kidney, bone and intestine [36]. Parathormoneincreases calcium plasma level through provoking reabsorption of calcium in kidneys and intestine and increases reabsorption of calcium in kidneys by increasing formation of 25 hydroxyvitamine D3. [16][34] The process of modeling and temporal increase in bone transformation is reported after a period of enduring and aerobic exercises. According to this process, doing systematized exercises increases 25 hydroxy vitamin D3 calcium plasma levels and, in the long run, increases bone mineral density and bone formation in competitive bones [16].

These changes were also observed in present study; according to our results, doing aerobic exercises in water significantly increases parathormone, calcium and 25 hydroxy vitamin D3 plasma levels in the exercise group in comparison with the control group (p<0.05). It seems that doing aerobic exercises for 12 weeks in present study changes calcium homeostasis and parathormonesecretion in a way that increasesbone mineral density and bone formation [31].

Conclusion

Results of the study indicate that aerobic exercises in water as one of the most suitable and lessrisky exercises can be performed to stop Osteoporosis or maintain / adjust bone mineral density in old people especially women after menopause.

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Retrospectively evaluate prognosis and treatment results of patients with non small cell lung cancer

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Abstract

Purpose: The purpose of this study is to review the prognostic factors and treatment results of patients with non-small cell lung cancer (NSCLC) treated in our center.

Methods: The data of 238 patients with NSCLC who registered at the Radiation Oncology Department of Cumhuriyet University Medical Research and Application Hospital between at 2006-2010 were obtained from patients files.

Results: This study analysed data of 238 patients. The most observed histological type was squamous cell carcinoma at 97 (41%). The 2-year survival were 84% at stage I, 76% at stage II, 34% at stage III and 9% at stage IV. The prognostic factors were age, weight loss, ECOG, thrombocytosis and high level of lactate dehydrogenase, histopathology, and stage, the use of platinum and taxan and radiation dose .

Conclusion: Results of this study were that the most important prognosis factors were stage, ECOG performance status and the use of cisplatin.

Key words: Non-small cell carcinoma, stage, survival, prognosis, cisplatin.

Introduction

Worldwide, lung cancer is the most common (1.35 million of 10.9 million new cases) and deadliest (1.18 million of 6.7 million cancer-related deaths) form of cancer (1). Non small cell lung cancer (NSCLC) accounts for approximately 80% of all cases of lung cancer (2). Depending on tumor stage and patients characteristics, standard treatment options are surgery, chemotherapy, radiotherapy or combination of these modalities.

Surgery is the most effective treatment for patients with technically resectable NSCLC of stage 1A through 2B. In spite of a variety of efforts concerning staging procedures, selective surgical approaches and attempts of adjuvant treatment, the survival rate of stage IA has remained with ranging between 58 and 76% (3,4). There is a recession in prognosis with 5-year survival rates of about 52% in stage 2 (3,4). Definitive radiotherapy can perform for patients with stage 1 and 2 who refuse surgery or medically inoperable due to existing co-morbidities. Data accumulated over the last 5 decades showed that radiotherapy alone can produce median survival of >30 months and 5-year survival of up to 30% (5).

Approximately 25% to 40% of patients with NSCLC have stage 3 disease and also approximately one-third of these present with potentially resectable disease. Chemoradiotherapy has been accepted as the standard treatment modality at inoperable stage 3A and 3B NSCLC patients and the median survival time is approximately 20 months (6, 7). A meta-analysis based on individual data from 1205 patients examined the results of randomized trial comparing concurrent chemotherapy and radiation with sequential chemotherapy and radiation. Improved survival was seen in patients in the concurrent group. Although, survival rate was 10.6% at 5 years in the sequential group, the survival rate of 15.1% at 5 years in the concurrent group represented an absolute increase of 4.5% (8).

Despite of several new chemotherapy agents with activity in NSCLC, the survival for stage 4 remains poor. A median survival was 7.4 months at the National Cancer Institute of Canada trial and it was 7.9 month at ECOG 1594 trial (9, 10).

Stanley evaluated 77 prognostic factors in approximately 5,000 patients with inoperable carcinoma of lung cancer. Three most important prognostic factors affecting survival were patients specific variables including performance status (Karnofsky score), stage and weight loss (11).

The purpose of this study is retrospectively evaluate survival of patients with NSCLC, which registered at our clinic after being diagnosed with lung cancer, together with relevant references from literature.

Patients and Methods

A total of 238 patients diagnosed with NSCLC in the Radiation Oncology Department of Cumhuriyet University Medical Faculty Research and Application Hospital, between 2006 and 2010 were included in this study. All of patients with NSCLC were accepted as eligible. The patient's performance status was evaluated according to the ECOG performance status (Eastern Cooperative Oncology Group) scoring system at the time of their registration. A weight loss 10% in the 3 months before diagnosis were included. The stage of patients was determined in accordance with the 2002 UICC/AJCC TNM classification.

Toxicities were assessed by means of radiotherapy oncology group (RTOG) criteria and national cancer institute common toxicity crteria version 2.0 Toxicity was assessed at the start of radiotherapy and weekly. Post-treatment follow-up consisted of outpatients visits including thorax computed tomography every 3 months until 2 years and every 6 months after that.

The current state of patients that had not come for a check-up in the last three months was obtained by calling them in order to conduct their survival analysis. Permission was obtained from the Provincial Civil Registry to run identity checks on patients that could not be contacted by phone in order to identify whether they were dead or alive; results were recorded accordingly.

Statistical analyses were performed using SPSS 15.0 software. The descriptive analysis was expressed in term of frequency, mean and standard deviation. Frequencies were compared with the Chi-Square test for categorical variables. The Student-T test were performed when comparing continuous variables. Survival analysis was performed according to the Kaplan-Meier method. Survival curves were compared with the log-rank test. Multivariate analysis with Cox regression models was

used to assess the independent factors that have an effect on survival. P values ≤ 0.05 were considered statistically significance throughout.

The Departmental Ethical Committee of University of Cumhuriyet Faculty of Medicine approved this study in accordance with the declaration of Helsinki.

Results

This study analysed 238 patients; 214 (90%) men and 24 (10%) women. The median age of patients at diagnosis was 61 years (range 31-82 years) and 60 years (range 31-82 years) in men patients and 66 years (range 40-81 years) in women patients. There were no statistical differences in men and women patients accoding to age (p=0,092). In conclusion of patients answers regarding their family history and their own background, 50 (21%) patients had a history of cancer in family, 193 (81%) had a history of smoking, and 102 (43%) had a disease caused co-morbidity as diabetes mellitus, hypertension. Weight loss was diagnosed in 99 (42%) patients. According to histopathology diagnosis, the most common histology was squamous cell carcinoma; seen in 97 (41%) patients. Squamous cell carcinoma was the most frequent histology in men (93 (43%) patients), although adenocarcinoma was in women (14 (58%) patients).

The performance status of patients was assessed that 96 (40%) patients were identified as ECOG-0 and 88 (37%) were identified as ECOG-1 and 54 (23%) patients were identified as ECOG-2 and above. Stage I was diagnosed in 20 patients (8%) and stage II in 18 patients (8%), stage III in 107 patients (45%), stage IV in 93 patients (39%). Patients characteristics are showed in *Table 1*.

There was statistically a significant relation with stages between weigh loss (p:0,015), and ECOG performance status (<0,001).

Stage I disease had been treated with surgery alone in 11 (55%) patients, with surgery followed by chemotherapy in 8 (40%) patients and with induction chemotherapy followed by concurrent chemoradiotherapy in 1 (5%) patients. Stage II disease administered surgery followed by chemotherapy in 14 (78%) patients, surgery followed sequential chemoradioterapy in 3 (17%) patients

who had a residual disease after surgery, sequential chemoradioterapy in 1 (5%) patients. Stage III disease were treated with surgery followed by chemotherapy in 3 (3%) patients, surgery followed by sequential chemoradioterapy in 3 (3%) patients who had a N2 disease, sequential chemoradioterapy in 19 (18%) patients, induction chemotherapy followed by concurrent chemoradiotherapy in 35 (33%) patients, chemotherapy alone in 41 (38%) patients, radiotherapy alone in 4 (3%) patients, and in consequence of high ECOG performance status 2 (2%) patients received palliative treatment. Stage IV disease received chemotherapy alone in 66 (71%) patients and palliative treatment in 27 (29%) patients. Palliative radiotherapy was performed in 99 (42%) patients and most commonly radiotherapy sites were brain in 51 (52%) patients, bone in 31 (31%) patients and lung in 22 (22%) patients. Otherwise, the use of biphosphanate was in 48 (20%) patients.

At the present analysis after an overall median follow-up of 16 months (0-121 months), 60 (25%) patients were still alive with median follow-up 25 months. Overall median survival was 14 months and overall progression-free survival 9 months. While 99 (39%) patients had distant metastases at diagnosis, 64 (27%) patients have developed distant failure during follow-up. Distant failure was diagnosed after a median 13 months (7-56 months). Distance metastases was seen in the brain of 58 (24%) patients, the bone of 50 (21%) patients, the liver of 27 (11%) patients, the opposite lung of 27 (11%), the pleura of 22 (9%) patients and the adrenal glands of 19 (8%) patients. Locoregional progression was detected in 130 (68%) patients after a median 7 months (1-89 months).

For all stage, the survival rates of 2 years was 33% and the progression-free survival was 28%. The 2-year survival were 84% at stage I, 76% at stage II, 34% at stage III and 9% at stage IV respectively. In additional the progression-free survival rate of 2 years were 78% at stage I, 69% at stage II, 30% stage III and 8% stage IV. The 5-year survival rates were 28% for stage I, 48% for stage II and %18 for stage III respectively.

According to univariate analysis, host-related factors of affecting on survival were age (<70 years and \geq 70 years p=0,001), weight loss (p=0,002), ECOG performance status (p<0,001) at diagnosis,

thrombosytosis (p=0,047), and high level of lactate dehydrogenase (p<0,001).

Table 1. Patients characteristics

	No. of patients	(%)
Sex		
Female	24	10
Male	214	90
Smoking	193	81
Alcohol	18	8
Family history	50	21
Comorbidities	102	43
Common comorbidities		
COPD	38	16
Hypertension	59	25
Diabetes	29	12
Kidney failure	3	1
Weight loss	99	42
Histopathology		
Squamous cell carcinoma	97	41
Adenocarsinom	54	23
Large cell carcinoma	3	1
Neuroendocrin tumor	4	2
Adenoid cystic carcinoma	1	0,4
Unclassified subtype as reported	79	33
NSCLC*		
ECOG ^{**} performance status		
ECOG-0	96	40
ECOG-1	88	37
ECOG-2 and >ECOG-2	54	23
Stage	• •	
Stage I	20	8
Stage II	18	8
Stage III	107	45
Stage IV	93	39
Treatment		
Surgery alone	11	5
Surgery+chemotherapy	25	10
Surgery+sequential CRT***	6	3
Induction	36	15
chemoterapy+concurrent CRT***		
Sequential CRT***	20	8
Chemotherapy alone	107	45
Radiotherapy alone	4	2
Palliative treatment	29	12

* COPD; chronic obstructive pulmonary disease,

** ECOG: Eastern Cooperative Oncology Group

*** CRT; chemoradiotherapy

Table 2 shows host-related factors of affecting on survival. Tumor-related predictive factors in

univariate analysis were histopatology (p=0,009), stage (p<0,001), tumor size (tumor size <5cm and \geq 5cm p=0,001), N stage (p=0,001). Tumor-related predictive factors are illustrated at *table 3*. Besides, the use of platinum (p<0,001) and taxane (p=0,004)were treatment-related predictive factors in univariate analysis. There was no significant difference with radiation dose (p=0,172) when it was separation <60 Gy, ≥ 60 and ≤ 66 Gy and >66Gy in stage I-III but the median survival was effected by radiation dose in stage III (p=0,044) at these radiaiton dose. Otherwise there was almost significant difference by means of the delivered of <60 Gy and >60 Gy radiation dose in stage I-III (p=0,051). However, radiation dose of ≥ 60 Gy resulted in significant improvement of the median survival of patients with stage III (p=0,004). The median survival of stage III patients undergoing concurrent chemoradiotherapy was not influenced stastistically significant (p=0,333). These patients had an overall median survival of 17 months. On the other hand, the median survival of patients using sequential chemoradiotherapy and chemotherapy alone were at 18 months and 11 months respectively. There were no stastistical difference at chemotherapy regimens as platinum+etoposid, platinum+docetaxel, platinum+gemcitabine, platinum+paclitaxel and platinum+vinoralbine for patients of stage III (p=0,885). The median survival of stage IV patients was at 10 months in patients of received chemotherapy and at 2 months in patients undergoing palliative treatment (p<0,001). Table 4 illustrates treatment-related factors of effect on survival.

Variable	No. of patients	Median survival (month)	p value
Sex			
Female	214	15	0,872
Male	24	14	
Age			
< 70 years	195	17	0,001
\geq 70 years	43	9	
Co-morbidity			
No	136	16	0,719
Yes	102	13	
Weight loss			
No	139	17	0,002
Yes	99	10	
ECOG			
ECOG-0	96	23	<0,001
ECOG-1	88	17	
ECOG-2	54	4	
Hematologic and biochemical	factors		
Anemia			
Hemoglobin $> 12 \text{ g/dl}$	81	14	0,130
Hemoglobin \leq 12 g/dl	157	14	
Thrombocytosis			
\leq 400,000/mm ³	136	19	0,047
$>400,000/mm^3$	40	14	
White blood count			
$\leq 11,000/mm^{3}$	122	19	0,07
$> 11,000/mm^3$	32	9	
Lactate dehydrogenase			
\leq 240 IU/L	102	20	<0,001
> 240 IU/L	44	10	

Table 2. Univariate analysis: Host-related factors

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Table 3. Univariate analysis: Tumor-related factors

Variable	No. of patients	Median survival (month)	p value
Histopatology			
Squamous cell carcinoma	97	16	
Adenocarcinoma	54	17	0,009
Unclassified subtype as reported NSCLC*	79	10	
Tumor size			
< 2 cm	24	26	0,156
$\geq 2 \text{ cm}$	140	14	
< 5 cm	71	23	0,001
\geq 5 cm	93	12	
< 7 cm	119	17	0,153
\geq 7 cm	45	11	
N stage			
NO	53	27	
N1	43	17	
N2	94	13	<0,001
N3	13	8	
Nx	35	8	
Stage			
	20	51	
Stage I	18	39	<0.001
Stage II	107	15	-0,001
Stage III	93	8	
Stage IV		0	

* NSCLC: Non-small cell carcinoma

Multivariate Cox regression identified that stage, performance status (ECOG performance status) at diagnosis and the use of platinum were independently predictive factors. *Table 5* shows independent prognostic factors.

Acute radiation esophagitis grade I-II occurred in 50 (25%) patients but never seen stenosis of the esophagus. Esophagitis generally resolved after completion of radiation therapy. Grade III radiation pneumonitis occurred in 9 (5%) patients, all of whom were hospitalized and treated with prednisolone. The most common adverse effect was vomiting/nausea grade I-III in seen 158 (78%) patients. Hematological toxic effects consisted of anemia in 141 (70%) patients, leucytopenia in 74 (37%), neutropenic fever in 25 (12%), and thrombocytopenia in 40 (20%) occurred in 154 (76%) of 202 patients received chemotherapy, radiotherapy and concurrent chemoradiotherapy. There was no death because of neutropenic fever. All toxicies were statistical significant undergoing concurrent chemoradiotherapy of patients when compared with undergoing sequential chemoradiotherapy and chemotherapy of patients. Toxicities of treatment with p value are demonstrated at *Table 6*.

Discussion

The patients of lung cancer present a various clinical symptoms and biochemical values because of different manifestations of the primary tumor, distinct distribution of metastatic sites involved and the varied extent of paraneoplastic syndromes and comorbidities. In spite of the remarkable predictability of population survival outcomes, the knowledge is limited value to clinicians for treatment decisions in a single patients, due to the marked heterogeneity of the clinical course in the individual patient (12). In this situation, prognostic factors may play a critical role in explaining

Variable	No. of patients	Median survival (month)	p value
Total radiation dose delivered, Gy, at stage I-III			
< 60	16	17	0,172
$\geq 60 \text{ and } \leq 66$	45	28	
> 66	11	22	
Total radiation dose delivered, Gy, at stage I-III			
< 60	16	17	0,051
≥ 60	56	28	
The use of platinum, at all stage			
No	43	12	<0,001
Yes	195	17	
The use of taxane, at all stage			
No	103	12	0,004
Yes	135	17	
Treatment modalities, at stageIII			
Concurrent CRT*	35	17	0,002
Sequential CRT*	18	18	
Chemotherapy alone	40	11	
Radiation dose delivered Gy, at stage III			
< 60 Gy	12	13	0,044
\geq 60 and \leq 66 Gy	41	24	
> 66 Gy	9	22	
Radiation dose delivered Gy, at tage III			
< 60 Gy	12	13	0,004
\geq 60 Gy	50	22	
Chemotherapy regimes, at stage III			
Cisplatin+etoposid	16	17	0,425
Platin+docetaxel	41	13	
Platin+gemcitabine	11	15	
Platin+paclitaxel	23	13	
Platine+vinoralbine	10	71	
*CRT: Chemoradiotherapy			

Table 4. Univariate analysis: Treatment-related factors

Table 5. Multivariate analysis

Variable	p value	Exp(B)	95% Confidence interval
Stage	<0,001		
Stage (I-II)	0,715	1.196	0.457-3.130
Stage (I-III)	0,002	3.416	1.350-7.530
Stage (I-VI)	<0,001	5.300	2.332-12.049
Performance status	0,001		
ECOG (0-1)	0,412	1.170	0.804-1.702
ECOG (1-2)	0,001	2.350	1.451-3.806
The use of Cisplatin	<0,001	0.477	0.342-0.665

the different outcomes of the patients and might support treatment decisions, research design and analysis, and health policy development (13).

The literature is quite varied in the conclusions drawn about the prognostic value of gender and age

and the strength of the association with survival outcomes. Albain et al. (14) identified good performance status, female sex and age below 70 years as the most important prognostic factors. Quejada and Albain (15) suggested that younger age migth have

Toxicity	Chemotherapy alone n (%)	Sequential CRT* n (%)	Concurrent CRT* n(%)	p value
Acute Radiation Esophagitis	-	19 (53)	22 (61)	<0,001
Radiation pneumonitis (grade III)	-	3 (8)	6 (17)	<0,001
Neutropenic fever	13 (10)	3 (8)	9 (25)	0,039
Leucocytopenia	38 (29)	11 (31)	25 (69)	<0,001
Thrombocytopenia	19 (15)	5 (14)	16 (44)	<0,001
Anemia	90 (64)	24 (67)	27 (75)	0,723
Vomiting/nausea	104 (80)	27 (75)	27 (75)	0,712

Table 6. Treatment toxicities

* CRT: Chemorafiotherapy

a better prognosis but results of age in multivariate analysis have been inconsistent on the literature. A gender balanced sample of 152 cases was randomly selected for review from a tumor registry population of 368 NSCLC patients (16). Overall median survival was significantly shorter for men than women with NSCLC (40 weeks versus 78 weeks). In multivariate analysis, the strongest independent predictors of NSCLC patients survival were stage of disease, initial weight loss rate, and gender. In our study, survival rate of age above 70 years was negatively influenced than survival rate of age below 70 years but sex was not affected survival in univariate analysis. Actually, our female patients were very small groups than our male patients.

Numerous studies showed that performance status of patients with NSCLC was a significant predictive factor for survival. The Karnofsky Performance Status (KPS) and Eastern Cooperative Oncology Group (ECOG) Performance Status scales have been examined in large trials. Buccheri et al. (17) studied that 536 patients with NSCLC were assigned KPS and ECOG performance status scores before, during and after treatment. It was found that KPS and ECOG assignments were strongly related to each other. However the KPS showed less ability than the ECOG performance status to discriminate patients with different prognosis. They concluded that the ECOG performance status is the more reliable and useful (18). We usually noted ECOG performance status of patients and ECOG performance satus was an independent predictive factor by multivariate analysis. By the way ECOG performance status associated with advanced stage. Patients with NSCLC were usually elderly patients, so, this patients generally suffer a disease caused co-morbidity as diabetes mellitus, hypertension and etc. But comorbidity was not statistically importance on survival by univariate analysis in our study.

Body weight loss before diagnosis has a clear and important impact on prognosis. Several differrent weight loss definitions were prospectively compared in 388 patients with NSCLC (19). In univariate analysis, all weight loss variables were prognostically significant. In same study, stage of disease classification, performance status, and total weight loss were importance factors in the cox model for prediction. We were using for weight loss that 10% in the 3 month before diagnosis. Weight loss was a prognostic factor by univariate analysis similar other studies.

Wisnivesky et al. (20) analysed 5254 patients with stage II NSCLC from the Surveillance, Epidemiology and End Results (SEER) registry. They found that younger age, female gender and squamous histology were independently associated with improved prognosis by multivariate analysis. Quejada et al. (21) stated that the histologic subtype was not provided additional independent factors information in resectable NSCLC. According to WHO criteria, stage for stage survival rate is significantly better for squamous cell carcinoma than for adenocarcinoma. Approximately 80% of patients with resected stage I squamous cell carcinoma are alive 5 years after diagnosis compared to approximately 70% of similary staged adenocarcinoma (22). In our study, the median survival of patients with NSCLC was affected by histologic subtype. The median survival of squamous cell carcinoma and adenocarcinoma were approximately similar. But the median survival of unclassified subtype as reported NSCLC was worse than other subtypes.

In a specifically designed study, the prevalence of thrombocytosis was analyzed in a large cohort of patients with lung cancer (1115 patients) (23). The overall prevalence of thrombocytosis (>400,000/mm³) in patients with lung cancer was 32%. Platelet counts were significantly higher in advanced stage of disease (stage I and II: 23% versus stage III and IV: 37%). Patients with thrombocytosis had a significantly poorer survival than patients with normal platelet counts. Indeed, thrombocytosis was a significantly prognostic factor by univariate analysis in this study.

LDH is certainly the strongest prognostic determinant of NSCLC. In 10 NSCLC studies, LDH was found to significantly associated with survival (24). A study of 1052 patients with advanced NSCLC conducted by the European Lung Cancer Working Party (25) that analyzed 21 variables. In Cox regression model, the selected explanatory variables were extent of disease, KPS, white blood cell and neutrophil counts, metastatic involvement of skin, serum calcium level, age and sex. Equally important factor is plasmatic level of hemoglobin (24). We identified that the median survival of patients with NSCLC who have a high level of LDH was negatively affected, however, plasmatic level of hemoglobin and white blood count were not influenced on survival in univariate analysis.

Patients survival in NSCLC is directly related to stage as the majority of cancers. Japan's authors (26) compiled the data for 6644 patients with resected NSCLC from 303 instutions and published in 2005. According to this article, pathological stage influenced at patients's survival by multivariate analysis. The 5-year survival were 72% at stage IA, 49,9% at stage IB, 48,7% at stage IIA, 40,6% at stage IIB, 35,9% at stage IIIA, 28% at stage IIIB and, 20,8% at stage IV. Besides, tumor size is an important prognostic factor for NSCLC (27). The 5 year survival rates of our patients were 28% for stage I, 48% for stage II and %18 for stage III. Because, our patients usually were diagnosed at advanced stage and we determined very low survival rates. In terms of multivariate analysis, stage was an independent prognostic factor. In addition, tumor size also negatively affected at the median survival only for patients who have ≥ 5 cm tumor in univariate analysis.

A meta-analysis with inoperable stage III NSCLC by Rolland et al. (28) showed that sequenti-

al chemoradiotherapy results in significantly improvement of survival rates. Sequential chemoradiotherapy was compared to radiotherapy alone in same study. The investigators found that sequential chemoradiotherapy results in significant improvement of prognosis. Concurrent chemoradiotherapy and sequential chemoradiotherapy have been compared by a meta-analysis by Auperin et al. (8) at unresected stage III NSCLC. Their meta-analysis of seven randomized clinical trials showed a survival benefit of concurrent chemoradiotherapy over sequential chemoradiotherapy. In particular, concurrent chemoradiotherapy was superior in tems of local control. But there was no significant difference in the incidence of distant metastases in the two treatment arms. In our study, the median survival of patients with stage III NSCLC was influenced by treatment regimens. Results of concurrent and sequential concurrent chemoradiotherapy were similar, however, the median survival of stage III patients undergoing chemotherapy alone was worse than other treatment modalities. In fact, number of our patients who received curative radiotherapy was not enough in this study. Because, we may obtain this results.

Some investigators set out to reduce local failure with radiotherapy regimens. The RTOG (29) conducted a trial that five arms were tested; 60 Gy, 64,8 Gy, 69,6 Gy, 74,4 Gy and 79 Gy. The best results were seen in a cohort of patients with good performance (KPS \geq 70 and weight loss \leq 50%) who received 69,6 Gy. University of Michigan investigators performed a dose-escalation trial that included 106 patients with stage I-III NSCLC treated with 63 to 103 Gy in 2.1 Gy fractions using 3DCRT (3 dimensional conformal radiotherapy). Multivariate analysis revealed that weight loss and radiation dose were significant predictors for overall survival (30). We stratified at escalating radiation dose level that received 60 Gy, \geq 60 Gy and \leq 66 Gy and \geq 66 Gy. The median survival was not effected by these radiation dose in our stage I-III patients with NSCLC. But, there was significantly difference by univariate analysis for stage III. The median survival of delivered interval of ≥ 60 Gy and ≤ 66 Gy was higher than other two groups that <60 Gy and >66 Gy.

The CALGB phase II randomized clinical trial (CALGB: Cancer and Leukemia Group B 9431) (31) compared to efficacy and toxicity of the drug combinations cisplatin/vinorelbine, cisplatin/gem-

citabine, cisplatin/paclitaxel, but these regimens were administered in the scope of induction chemotherapy followed by concurrent chemoradiotherapy. The investigators found no significant differences between the groups in term of efficacy of treatment, as determined based on the rates of remission, median survival and 1-year survival. Correspondingly, chemoterapy regimens that platinum/etoposid, platinum/docetaxel, platinum/gemcitabine, platinum/ paclitaxel and platinum/vinoralbine were no difference each other for the median survival of stage III patients with NSCLC in our study. For all stage, we found that the use of platinum and taxane were influenced positively at the median survival of patients with NSCLC by univariate analysis. Furthermore, The use of cisplatin was an independently prognostic factor by multivariate analysis.

Many studies indicated that concurrent chemoradiotherapy results in higher rates of acute toxicity than sequential chemoradiotherapy (32-34). This was particularly true acute esophagitis (grade III/IV). The rate of hematologic toxicity was also higher in the concurrent arm of most studies. Similarly, in our study, acute esophagitis, radiation pneumonitis, leucocytopenia and thrombocytopenia were seen higher in treated concurrent chemoradiotherapy than received sequential chemoradiotherapy and chemotherapy alone.

Conclusion

The most importance prognostic factors were stage, ECOG performance status and use of cisplatin in this study similar studies on literature.

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Evaluation of choleseatoma microbiologic findings in patients with chronic supporative otitis media

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Abstract

Aim: this study was designed with the aim to investigate the most common microorganisms involved in cholesteatoma in patients with chronic otitis media and to determine their antimicrobial susceptibilities to in use antibiotics.

Methods: Thirty individuals with the diagnosis of cholesteatoma were enrolled into this study. The microbial samples of middle ear were gotten during the surgery and studied by the microbiologist for the culture and antimicrobial susceptibility tests.

Results: In total 26 out of 30 tested samples were culture positive (80%), of which 34 bacterial species were recovered. Two cultures (6.6%) were positive for fungi and 4 (13.4%) cultures were negative. The most prevalent gram-negative aerobic pathogens were *P.aeroginosa* (23.5%), Proteus mirabilis (14.7%) and E. coli (11.7) and the most common gram-positive organisms were S.epidermidis (8.8%), S.aureus (5.8%) and diphtheroides (5.8%). Based on the antibiotic susceptibility testing, ciprofloxacin and ceftazidime were the most effective antibiotics against gram positive and gram negative isolated bacteria respectively, except for P. aeroginosa. Among gram positive aerobic bacteria, the most resistant bacterium was S. epidermidis.

Conclusion: The results of this study showed that a wide variety of pathogens including aerobic and anaerobic bacteria are involving in cholesteatoma. For eradication of these bacteria we need to use broadspectrum antibiotics in addition to the surgery to control the infection in cholesteatoma.

Key words: cholesteatoma; microbiologic findings; supporative; otitis media

Introduction

Cholesteatoma is a type of chronic otitis media which occurs due to abnormal accumulation of squamos epithelium in the middle ear. The mean annually onset of cholesteatoma is 9.2 % in 100000 individuals [1]. Although it can be without any sign or symptom, most patients complain of otorrhea and hearing loss [2]. The infected epithelium and bacterial growth can involve the bones of middle and inner ear and cause hearing loss and vertigo meningitis [3], 7th nerve palsy and epidural abscess can occur due to nerves and meningeal involvement [4 5].

The most prevalent aerobic bacteria in chronic otitis media are *Staphylococcus aureus*, *Escheric-hia coli (E. coli)*, *Klebsiella pneumonia*, and *Pse-udomonas aeroginosa* [6, 7]. The main treatment for cholesteatoma is surgery, but use of appropriate antibiotic therapy before and after the procedure is essential to control the infection [8].

Since cholesteatoma is a disease which can cause significant morbidity and mortality, a reliable knowledge about pathogens and medication can assist in the selection of most appropriate antibiotic regimens and minimize the complications [1]. The aim of this study was to determine the aerobic and anaerobic organisms and their susceptibility to our antimicrobial drugs in the patients with cholesteatoma.

Materials and methods

In this cross sectional study, all the patients with chronic otitis media referred to Emam Khomeini Teaching Hospital of Ahvaz, during the years 2009-2010 were screened. Among them, 30 patients with the diagnosis of cholesteatoma (which was defined during the surgery) were enrolled in the study. All the patients received antibiotics before the surgery. During the surgery, samples were collected from the secretion of middle ear using a sterile swab and were put into thioglycollate broth and transferred to the microbiology laboratory of School of Medicine, for aerobic and anaerobic cultivation.

The Thioglycollate containing samples were incubated at 37°C for 24 hours and subcultured on duplicate blood agars, chocolate agar, McConkey agar and mannitol salt agar (Hi-media, India) for aerobic and anaerobic bacteria. One of blood agar plates were placed in anaerobic jar and the cultures were kept up to 24-48h at 37°C. The grown colonies on the plates were then examined by Gram staining and the organisms were then identified by culture characters, morphology and standard biochemical tests [9]. The antibiotic susceptibility testing were performed on the isolates in the next step, using disk diffusion method as per CLSI guideline [10]. The tested antibiotics were: ceftazidime, cefixime, cephalothin, nalidixic acid, imipenem, ciprofloxacin and trimethoprim-sulphamethaxazole (Mast Co., UK). The proposal of this work was approved by the Research Ethics Committee of the Ahvaz Jundishapur University of Medical Sciences.

Results

Based on the results, 26 out of 30 tested samples were microbiologically positive. Of these, 24 were positive for bacteria (80%) and 2 for fungi (6.6%). The rest 4 (13.4%) samples were negative for microorganisms. In culture, we isolated 34 bacterial species, which 27 (79.4%) were aerobic bacteria. Pseudomonas aeroginosa followed by Proteus mirabilis were the most common aerobic gram negative and S. epidermidis was the most prevalent gram positive bacteria isolated in this study. The isolated aerobic organisms are presented in Table 1. According to the results of anaerobic cultivation, 7 (20.5%) cultures were positive for anerobes, comprising gram positive cocci 4 (11.7%) and bacteroides 3 (8.8%). Figure 1 represents the total aerobic and anaerobic bacteria isolated in this study.

Table 1. Isolated gram positive and gram negati-ve bacteria in present study

Bacteria	No. (%)
P.aeroginosa	8 (23.5%)
Proteus.mirabilis	5 (14.7%)
E. coli	4(11.7%)
Klebsiella spp.	2 (5.8%)
S. epidermidis	3(8.8%)
S. aureus	2 (5.8%)
Diphtheroid	2 (5.8%)
S. spoitier	1(2.9)



Figure 1. Isolated aerobic and anaerobic bacteria isolated from middle ear pus (%)

The antibiotic susceptibility testing revealed that ciprofloxacin and ceftazidime were the most effective antibiotics against gram positive and gram negative isolated bacteria respectively. It is necessary to mention that all isolated organisms were susceptible to 3rd generation tested antibiotics except for *P. aeroginosa* which was resistant to these antibiotics. Among gram positive aerobic bacteria, the most resistant bacterium was *S. epidermidis*. Figures 2 and 3 represent the profile of antibiotic resistance pattern among isolated bacteria.



Figure 2. Antibiotic resistance of gram-negative aerobic species (%) in cholesteatoma



Figure 3. Antibiotic resistance (%) of middle ear aerobic gram-positive organisms in cholesteatoma

Discussion

Since now, various studies were conducted by some authors to assess the aerobic and anaerobic bacteriology of cholesteatoma. Although their studies could simply show the species and prevalence of pathogens which are responsible for cholesteatoma, new studies which can show bacterial resistance to antibiotics are still lacking. Due to widespread use of antibiotics, the response of pathogenic organisms to antibiotic therapy have changed dramatically [11]. So, knowledge of the species and resistance rate of current pathogens can help us find appropriate antibiotics for the patients with cholesteatoma.

We found in our study, that the most prevalent aerobic pathogens involve in cholesteatoma were *P. aeroginosa*, *Proteus mirabilis* and *E.coli* and the most common anaerobic organisms were gram-positive cocci and bacteroides. Our findings were in agreement with similar studies of Smith and Danner [5], Yeo et al. [11], Attallah et al. [12], and Maji et al.[13], which they reported *P.aeroginosa* , and *Proteus mirabilis* as the most prevalent isolated gram negative bacteria. Besides, in the latter mentioned study, the most common anaerobic bacteria recovered from samples were reported as peptostreptococcus and bacteroides, which was similar to our findings.

On the other hand another study, *S. aureus* was reported as the second most common isolated aerobic bacteria which was discordant to our findings. We recovered only 5.8% *S. aureus* from our samples [2]. In the study of Saini et al. there was a concordance for isolated anaerobic bacteria with our results [14].

Our study showed that the most effective antibiotic against aerobic gram negative bacteria causing cholesteatoma could be Ceftazidime which can eradicate most of them. However this antibiotic was less effective against P.aeroginosa and aerobic gram positive pathogens such as S. epidermidis. In such cases a combination of the drug with ciprofloxacin, could be a solution. Other investigators showed that the most effective antibiotics were amikacin followed by gentamycin and cefotaxime [13], and a combination of ofloxacin and erythromycin based on another survey [15]. Although our study and the study of Saini et al. [14], showed that *P.aeroginosa* was fully resistant to 3rd generation cephalosporins. In spite of the similar findings of causative organisms in most of similar studies, the result of antibacterial susceptibility tests, shows that the organisms isolate in different centers may show various response to antibiotics and this is related to the factors that facilitates the spread of resistance among bacteria such as widespread use of antibiotics and genetic mutations make especially gram negative bacteria resistant to a wide variety of antibiotics. So, due to these and other unknown reasons, the rate of antibiotic resistance was more predominant in the area of study. This study wasn't without limitation. Due to the laboratory difficulties, we could not define antibacterial resistance for anaerobic organisms and fungi, since it could be more helpful for choosing an appropriate antibiotic regimens for destroying the causative organisms.

In conclusion, according to the result of this study, many different pathogens comprising aerobic and anaerobic bacteria, both gram negative and positive, were responsible for infection in cholesteatoma. The most common aerobic pathogens were *P. aeroginosa* followed by *P. mirabilis* and *E. coli* which were the most susceptible to Ceftazidime except for *P. aeroginosa*. So, due to this, and resistance of *S. epidermidis* as the most prevalent gram positive cocci to ceftazidime, use of combination therapy according to susceptibility testing could be a guide to manage the infection and reduce the intracranial and extracranial complication of cholesteatoma.

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Evaluation of forensic deaths occurred in Sivas, Turkey

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Abstract

Backgrounds: Despite rapid developments in the science of medicine, increased number of innovative laboratory and imaging technologies; autopsies have a crucial role in gathering and transferring valuable information.

Methods: In this study; medical records and autopsy reports of forensic cases resulting in death between 2006 and 2009 in Sivas were examined, and evaluated as for medical and socio-demographic aspects.

Results: Total of 540 cases assessed consisted of 393 (72.8 %) males mostly (n=159; 29.4 %) over 60 years of age. Deaths were mostly seen during summer (n=154; 28.5%), and suspected deaths lead the way (n=144; 26.7%), followed by traffic accidents (n=138; 25.6 %). Death certificates were arranged for 425 (78.7 %) cases following postmortem examinations.

Conclusions: Findings in this study have shown some similarities with those of the literature. Since highest mortality rates are seen secondary to accidents, relatively simple preventive measures have vital importance. Traffic accidents, and falls from height which are among preventable causes of mortality still remain to be a challenging problem in our country and implementation of necessary safety measures, and training on this subject are of paramount importance.

Key words: Forensic autopsy, Cause of death, Type of the incident, Accident, Suspected death.

1. Introduction

In deaths subject to medicolegal investigation, causes of death, its mechanism, origin, potential factors involving in the case of death, and findings which might enlighten the causes of death have been scrutinized. Righteous implementation of justice will be ensured as a consequence of proper postmortem examinations performed by physicians having knowledge, and experience in forensic autopsies (1-3). The studies indicate that the physicians (medical examiners and coroners) have a high rate of error in determining cause of death in apparently natural deaths if autopsies are not performed (4). Autopsy may be valuable in uncovering the most frequent diagnostic pitfalls, and helping clinicians to learn and develop the medical science. Moreover, it is an essential element of medical auditing and teaching, as well as for the study of the cause, natural history and course of diseases (5).

Autopsies of forensic cases, and postmortem examinations analyzed in this study were performed in the morgue of Cumhuriyet University Hospitals in the city of Sivas, in Turkey. In this study postmortem examinations of forensic deaths, and autopsy and postmortem procedures performed between 2006 and 2009 were analyzed. In this evaluation, our aim was to examine causes of deaths, and sociodemographic characteristics, and also compare our outcomes with those of the literature.

2. Methods

In this study, a total of 540 forensic cases of death sent to the morgue of Cumhuriyet University Hospitals from city center and counties of Sivas, its environment, and abroad between 1996 and 1999 for their postmortem examinations and autopsies were retrospectively analyzed as for parameters such as gender, age, type, date, and scene of the incident, place of referral, history of previous autopsy and postmortem examinations. For statistical analysis data were evaluated using SPSS statistical package program version 16.0. For this study approval of The Ethics Committee of Clinical Investigations of Cumhuriyet University dated 29/09/2010 (protocol numbered 2010/198) was obtained.

3. Results

This study enrolled a total of 540 participants (females n=147; 27.2 %) (Figure 1).



Figure 1. Distribution of cases between males and females

Participants older than 60 years of age were in the majority (n=159; 29.4) (Figure 2).



Figure 2. Distribution of cases according to age groups

Mortality was at its peak during summer months (n=154; 28.5 %) (Table 1).

Table 1.	Distribution	of cases	according to	seasons
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Season	n	%
Winter	100	18.5
Spring	137	25.4
Summer	154	28.5
Autumn	149	27.6
Total	540	100.0

Among types of death incidents, 26.4 % (n=144) of them were in the suspected-pathologic

death group (Table 2). Most of the deaths took place at home (n=171; 31.7 %) (Figure 3).

Table 2. Distribution of cases according to the types of the incidents

Types of the incident	n	%
Suspected/Pathologic death	144	26.7
Traffic accident	138	25.7
Firearm injury	53	9.9
Falls	52	9.7
Hanging	36	6.7
Poisoning	29	5.3
Stab wounds /penetrating wounds	15	2.7
Drowning	14	2.6
Sudden infant death	9	1.7
Workplace accidents	9	1.6
Stillbirth	8	1.5
Exhumation	7	1.3
Freezing	5	1
Malpractice	4	0.7
Assault	4	0.7
Electrocution	4	0.7
Burns	3	0.5
Wild animal assault	3	0.5
Strangling-suffocation	2	0.3
Lightning strike	1	0.2
TOTAL	540	100



Figure 3. Distribution of cases according to scenes of incidents

Autopsies were performed on 78.7 % (n=425) of the cases and for the remaining cases postmortem examinations were done, and death certificate was arranged after inspecting medical documents

Most of the forensic cases of death (67.8 %; n=366) were referred from the city center (Figure 4). Whole body traumas were the most frequently (n=162; 30.0 %) seen causes of mortality (Table 3). Vital functions of 218 cases with bone fractures were severely (n=186; 85.3%), moderately

(n=25: 11.5 %) or slightly (n=7; 3.2 %) affected. Besides, they were mostly (n=93; 17.2 %) treated in the Emergency Clinic (Table 4).



Figure 4. Distribution of cases according to places of referral

Table 3.	Distribution	of injury	sites	based	on	<i>bo-</i>
dily regio	ons					

Site of the injury	n	%
Whole body	162	30
Head	54	10
Neck	35	6.5
Chest and abdomen	28	5.2
Head, neck and chest	11	2
Head and extremities	11	2
Abdomen	9	1.7
Head and neck	9	1.7
Chest	6	1.1
Chest and extremity	5	0.9
Extremities	4	0.7
Abdomen and extremities	2	0.4
Decayed corpse	2	0.4
Absence of any signs of trauma	202	37.4
TOTAL	540	100.0

Table 4. Distribution of the cases according to the departments they were treated

Departments	n	%
Emergency Service	93	17.2
Cebtral ICU	40	7.4
Neurosurgery	26	4.8
Gynecology and Obstetrics	6	1.1
Orthopedics	5	0.9
Pediatrics	4	0.7
Neurology	3	0.6
Infectious Diseases	3	0.6
Pediatric Surgery	2	0.4
General Surgery	1	0.2
Not available	11	2
Untreated	346	64.1
TOTAL	540	100

4. Discussion

Most of our study subjects were male cases (72.8 %). Similar investigations performed in Istanbul (6) (76.5 %), Eskişehir (7). (71.4 %), Kayseri (1). (76.3 %), Aydin (8). (70.0 %), and Elazig (9) (74.1 %) had analyzed comparable proportions of male cases, as indicated. Home was the scene of incidents for 46.9 % of the female and 25.9 % the male cases (Table 5). Besides, females had more frequently exposed to these incidents at home, while males were more often affected by these incidents outside home which was conceivably attributed to men's larger scale participation in social life activities.

Table 5. Distribution of male and female casesaccording to the place of the incident

Place of the incident	Female	Male	Total
Home	69	102	171
Hospital	12	12	24
Street	12	39	51
Open space	13	75	88
Prison	-	3	3
Motor road	24	43	67
School	-	2	2
Roof-construction	1	24	25
Lake-river-pool	-	13	13
Cemetery (exhumation)	3	2	5
Workplace	-	11	11
Unknown	13	67	80
TOTAL	147	393	540

Analysis of age groups revealed that relatively higher proportion (29.4 %) of the cases were aged 60 years or over. Since in some places death certificates especially for deaths caused by traumatic incidents are submitted by physicians apart from forensic medicine specialists without performing any autopsy, higher proportion of cases aged ≥ 60 years in our study can be interpreted as an expected outcome. However in Sivas, forensic medicine specialists are participating in virtually all investigations forensic deaths.

Seasonal distribution of incidents disclosed that most of them happened in summer (n=154; 28.5 %) months which was in accordance with outcomes of relevant investigations. (1,8,10). This higher incidence of forensic cases of death during summer months can be explained by revival of business, and social life, decrease in resistibility and tolerability of the individuals because of the adverse effects of higher environmental temperature leading to increase in the number of forensic cases.

Apart from types of incidents to be investigated, traffic accidents took the first place (25.7 %). Besides in a similar study conducted in Diyarbakir (11) traffic accidents ranked first with an incidence of 39.1 percent. In a comparable study conducted by Inanici et al. (6) in Istanbul, traffic accidents led the way (35.2 %) among causes of mortality In our country where transportation, and shipping are in a large scale realized via highways, number of vehicles increases in proportion with modern technologic advancements. In addition, all vehicles are using mainly the same highways, and thus defective infrastructure of continuously ruined highways results in continual increase in traffic accidents. Because of increasing number of domestic journeys, and foreign travelers coming from abroad, heavier traffic load constitutes a risk for safe travelling, and escalates the potential occurrence of traffic accidents.

In this study, firearm injuries took the second place (9.9 %) even in Istanbul with an incidence of

18.6 percent. In these days where possession of more than one firearms are tried to be legalized, abolition of this act, prevention of easy accessibility to these weapons, and emphasizing humanitarian principles are obviously mandatory measures to be taken.

Distribution of types of incidents based on age groups, (Table 6) traumatic cases such as traffic accidents, stab wounds, firearm injuries, and workplace accidents were more frequently seen in young, and middle age groups, while interestingly, suspected deaths with a higher incidence among types of forensic cases (26.7 %) were more often noted in the middle and old age groups.

Majority (n=425; 78.7 %) of the cases were autopsied. The frequency of postmortem examinations estimated in this investigation was found to be higher than those of similar studies conducted in our country (1,11,12). Higher percentage of autopsies in this study can be associated with the fact that forensic death investigations were performed in one center in Sivas with the participation of forensic medicine specialists, and also for traffic accidents, and suspected-pathologic deaths, death certificates are prepared after autopsy investigations, inspection of medical files, and necropsic explorations.

	Table 6.	Distribution	of types	of incidents	according to	age groups
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	0-9	10 - 19	20-29	30-39	40-49	50-59	60-69	70+	Unknown	TOTAL
Suspected- Pathologic	15	3	5	13	26	19	31	31	1	144
Traffic accidents	18	10	18	12	18	20	22	20	-	138
Firearm wounds	2	4	11	16	10	3	3	4	-	53
Fall from height	6	3	5	5	7	1	14	11	-	52
Hanging	-	5	7	4	7	5	4	4	-	36
Poisoniing	5	5	5	3	2	2	3	4	-	29
Stab wounds/penet	-	2	3	5	2	3	-	-	-	15
rating wounds	7	5	_	1	1	_				1/
Drowning Sudden infent deeth	0	5	-	1	1	-	-	-	-	0
Sudden mant death	9	-	-	-	-	-	-	-	-	9
Workplace accidents	-	-	1	2	3	2	1	-	-	9
Stilbirth	8	-	-		-	-	-	-	-	8
Exhumation	5	-	-	1	-	-	-	1	-	7
Freezing	-	-	-	2	-	-	-	3	-	5
Malpractice	1	-	-	3	-	-	-	-	-	4
Stroke	0	1	1	0	2	-	-	-	-	4
Electrolution	-	-	2	1	1	-	-	-	-	4
Burns	1	-	-	-	1	-	-	1	-	3
Wild animal assault	-	-	-	-	-	2	-	1	-	3
Strangling-suffocation	-	1	-	-	-	-	1	-	-	2
Lightning strike	1	-	-	-	-	-	-	-	-	1
TOTAL	78	39	61	65	80	57	79	80	1	540

In conclusion, in this study aiming at investigation of the cases of death occurring in a four-year interval, it was determined that these cases consisted of mostly men (72.8 %), and individuals aged 60 years or over with fatal incidents predominantly (29.4 %) taking place in summer months When types of death incidents were analyzed, apart from suspected deaths, traffic accidents (25.7 %), and firearm injuries (9.9 %) ranked on top, while the fatal incidents happened mostly (31.7 %) at home. Besides in 85.3 % of the cases with bone fractures, vital functions were severely impaired.

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Evaluation of therapeutic effects of Adcortyl and Myrtus communis (Myrtle) in patients with recurrent aphthous stomatitis: a clinical trial study

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Abstract

Introduction: Recurrent aphthous stomatitis is one of the most common oral lesions with unknown etiology. It can cause disability in eating, swallowing, speaking and also negatively effects in quality of life.

Aim: the aim of this study was to compare the therapeutic effects of Adcortyl and Myrtle in patients with RAS.

Materials and methods: One hundred fifty patients participated in this randomized, single-blind, placebo-controlled clinical trial. Patients were divided into three subgroups (A, B and C). The intensity of pain and burning sensation measured using visual analog scale (VAS). In A, B and C groups Myrtle, Adcortyl and placebo were used, respectively. Pain was evaluated by investigators at the initial visit and at each evaluation thereafter (days 2, 4,6, and 10). Healing of ulcers was also checked clinically. In addition, patients were examined after one month for recurrent ulcers. ANO-VA, paired t test and Chi-square test were used for statistically analysis.

Results: There was no significant difference between A and B groups in the mean time of pain elimination. There was no significant difference in the mean time of ulcer healing between A and B groups. There was significant difference between A and B groups in the frequency of recurrent ulcers.

Conclusion: Myrtle can use as an affective medication in treatment of RAS.

Key word: Adcortyl, Myrtus communis, Recurent aphtous stomatitis, Pain

Introduction

Recurrent aphthous stomatitis (RAS) is one of the most common painful oral lesions with unknown etiology (1,2). In epidemiologic studies, the prevalence of RAS in different population has been estimated up to 25% (3). The first appearance of the lesion occurs in the second and third decades of life. Clinical features of RAS are recurrent, small, round, or ovoid ulcers, with discrete margins and erythematous halo covered by pseudo- membranous layer (4). Although the exact etiology of RAS is unclear but some of predisposing factors such as genetics background, hematologic deficiency, hormonal changes, stress, micro organisms and immunologic discrepancy were considered (5-11). Recently, because of higher rate of systemic diseases and consumption of immunosuppressant drugs, the rate of RAS in the population is increasing (12). It can cause disability in eating, swallowing, speaking and also negatively effects in quality of life (13).

In order to reducing the signs and symptoms of RAS, Topical and systemic agents such as antimicrobials, steroids and immune- modulators have been suggested. But, these medications have the serious side effects which can make many problems for patients (14).

In Iran, Adcortyl (triamcinolone in orabase) that is local corticosteroid ,widely used for symptomatic treatment of RAS. Nowadays, especial attention is drawn to herbal treatment and the use of medicinal plants have been preferred because of their widespread availability ,non toxicity, ease of administration, absence of unwanted side effects and patients tendency (15,16). Several herbal

extract were studied in field of dentistry (17,18).

Iran is a country with various climates and geographical condition that result to growing the several plant species. Myrtle (Myrtus communis) is one of the famous and ancient medicinal plant with distribution in north of Iran. For several years, Myrtle has been used over the counter in Persia as a mouth-rinse for oral ulcers.

Therefore, the aim of this study was to compare the therapeutic effects of Adcortyl and Myrtle in patients with RAS

Materials and method

One hundred fifty patients participated in this randomized, single-blind, placebo-controlled clinical trial. All subjects were selected from patients diagnosed with recurrent aphthous ulceration (RAS), attending the Department of Oral Medicine, Dental faculty, Shahid Beheshti Medical Sciences. The inclusion criteria were as follows: 1) had a history of RAS (occurring at least 3 times a year), 2) presenting with one to four aphthous ulcers (less than 72 hours duration), 3)measuring less than 10 mm in diameter (minor aphthous ulcers), 4) had an expectation that ulcers normally takes over than 5 days to heal without treatment, 5) had no history of systemic diseases for example Behçet syndrome, Reiter's syndrome, Crohn disease, hematologic and immunologic disorders, 6) had no history of medication at least one month before entering the study. Pregnant women, smokers and alcohol abusers were excluded. Patients were informed about the purpose of the investigation and written consent was obtained. All participants were equally divided into three sub groups: A (Myrtle group, 50 subjects), B (Adcortyl group, 50 subjects), and C (Placebo group, 50 subjects). The intensity of pain and burning sensation measured using visual analog scale (VAS) from 0 to 10. Drugs and placebo were given to subjects. Patients were advised to apply Myrtle mouthwash (Barijessence, Kashan, Iran), Adcortyl ointment (Bristol-Myers Squibb/ Astrazeneca EEIG) and placebo (normal saline) five times a day, preferably after oral hygiene for seven days. In A, B and C groups Myrtle, Adcortyl and placebo were used, respectively. Pain was evaluated by investigators at the initial visit and at each evaluation thereafter (days 2, 4,6, and 10). Healing of ulcers was checked clinically during the study. In addition, patients were examined after one month for recurrent ulcers. In this study ANOVA, paired t test and Chi-square test were used for the comparison of therapeutic effects of studied agents between A, B and C groups. All data were analyzed by SPSS software (version 13, SPP Inc, Chicago, USA). The level of significance was considered at P.value less than 0.05.

Results

A total 150 RAS patients (age 20-40, mean \pm SD, 25.75 \pm 9.62) fulfilled the selection criteria and were included in the statistical analysis.

There were no statistically differences in age and gender between A, B and C groups ($\chi^{2=}$ 0.0574, F= 0.0699).The distribution of ulcer locations was summarized in table 1.

After using therapeutic agents following results were obtained:

The intensity of pain in A,B and C groups were shown in table 2. The pain was completely reduced after 2 to 4 days, 2 to 4 days and 5 to 7 days in A, B and C groups during the period of study, respectively (table 3).

There were significant differences between A and B groups with C group in the mean time of pain elimination, respectively (t=18.6, P<0.01and t=20.34, P<0.01)

There was no significant difference between A and B groups in the mean time of pain elimination (P>0.05).

Ulcers were clinically healed after 3 to 5 days, 3 to 4 days and 5 to 7 days in A ,B and C groups during the period of study, respectively (table 3).

There were significant differences between A and B groups with C group in the mean tine of ulcer healing (completely clinical healing was considered), respectively (t=11.12, P<0.01 and t= 11.37, P<0.01).

There was no significant difference in the mean time of ulcer healing between A and B groups (P>0.05).

Pain management and ulcer healing occurred earlier in A and B groups than C group.

The frequency of recurrent ulcers in studied groups, one month after the end of this study, was summarized in table 4.

Location	A group (n:%)	B group (n:%)	C group (n:%)
Labial	4:8	6: 12	8:16
Lingual Mucosa	6:12	6: 12	5: 10
Vestibule	40:80	30: 60	35: 70
Lingual(Ventral)	2:4	7:14	5: 10
Lingual(Boarder)	17: 34	21:42	19: 38
Lingual(Dorsal)	4: 8	8:16	3:6
Floor of the mouth	3:6	10:20	8:16
Soft palate	1:2	7: 14	4: 8

Table 1. Distribution of ulcer locations in studied groups

Table 2. Intensity of pain in studied groups based on VAS

Group	Days	Min	Max	Mean± SD
	0	4	8	5.75± 1.04
	2	0	6	2.19± 1.18
A	4	0	0	0
	6	0	0	0
	10	0	0	0
	0	3	7	4.60± 1.11
В	2	0	7	3.20 ± 0.95
	4	0	0	0
	6	0	0	0
	10	0	0	0
	0	4	6	4.45± 1.40
С	2	4	6	4.45± 1.40
	4	0	3	1.25 ± 0.85
	6	0	0	0
	10	0	0	0

Table 3. Time of pain management and ulcer healing during the time of study

Group	*Time of Pain Management Range: Mean± SD	**Time of ulcer healing Range: Mean± SD
A	2-4: 2.71± 0.95(Days)	3-5: 3.4±1.03(Days)
В	2-4: 2.64± 0.76(Days)	3-4: 3.5± 0.87(Days)
С	5-7: 5.90± 1.21(Days)	5-8: 6.8± 1.23(Days)

F*= 284.31, *F*= 91.56

Table 4.	Frequency of	recurrent	ulcers one	month after	end of study
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Group	Recurrent ulcer positive n:%	Recurrent ulcer negative n:%
A	39:78	11:22
В	19:38	31:62
С	43:86	7 :14

There were significant differences between B and A groups (χ^2 = 16.42, P=<0.001) and between B and C groups (χ^2 =24.44, P<.001) in the frequency of recurrent ulcers, respectively. There was no significant difference between A and C group in the frequency of recurrent ulcers (χ^2 = 1.08).

Discussion

Despite recurrent aphthous ulcerations are most common oral ulcers, the main etiology of this entity is still unknown. Cimen et al, demonstrated the increased oxidative stress levels and decreased antioxidant defense levels in oral mucosa of patients with RAS (19). Lehner et al and Hasan et al showed that local bacteria may have a key role in pathogenesis of RAS (20,21). It has been also pointed out that T cell-mediated response to antigens of streptococcus sanguis may be a cause of RAS in oral cavity (21).

Other factors such as local trauma, haematinic or zinc deficiency, hormonal changes and familial history may be associated with RAS (1,12). In order to reduce the pain of RAS a number of different medications were suggested: steroids (local or systemic agents), tetracycline and chlorhexidine mouthwashes, cholchicine, levamisole, thalidomide, dapsone and cimetidin (1, 4,5). But these medications have many side effects which can lade to serious problems for patients.

In the recent decades, the use of plants with therapeutic effects has increased dramatically (16,22). However, from 250.000 to 500.000 plants found on earth, only one percent of them have been evaluated for their pharmaceutical potential (23).

In this study, the clinical efficacy of Myrtle and Adcortyl (teriamcinolone in orabase) were assessed in treatment of RAS.

Efficacy of natural agents such as Rosa damascene, Licorice, Aloe vera and Propolis in treatment of RAS was considered by Hoseinpour et al, Moghadamnia et al, Ulbricht et al and Samet in previous studies (12,24-26). In this present study, the mean time of pain elimination and ulcer healing (complete healing) in patients who received Myrtle was lower than patients in C group (placebo). This finding is in agreement with Babaee et al., (27). The treatment effect of Myrtle in patients with RAS was also reported by Jafari et al., (28). Treatment potential of Myrtle may be related to some reasons which are listed as follows:

- 1) Anti-oxidant effect of Myrtle was showed by Romani et al(29).
- 2) Anti-inflammatory effect of Myrtle was pointed out by Feisst et al., (30).
- 3) Anti-bacterial effect of Myrtle was described by Bonjar et al., Al-saimary et al., and Rotstein et al. (31-33).
- 4) Anti-genotoxic and free radical scavenging activities of Myrtle were reported by Hayder et al., (34).
- 5) Analgesic effect of Myrtle was also reported by Levesqu and Lanfont (35).

Sumbul et al., evaluated the therapeutic effect of Myrtle in experimental ulcer models in rats and showed a significant reduction of ulcer index in all samples (36). On the other hand Babaee et al., demonstrated that Myrtle did not have any side effects in patients who used this drug for RAS (27).

In our study, there was no significant difference in the mean time of pain elimination between A and groups. The same results were also obtained for the mean time of ulcer healing between these groups.

Use of steroids in treatment of RAS was suggested in some previous studies.(37,38). Steroids hasten treatment of RAS (1).But these agents have serious side effects such as: hypertension, diabetes, lipid disorders, sleep apnea, osteoporosis, myopathy, and disorders of coagulation and fibrinolysis (39).

Our study also showed that the frequency of recurrent ulcers after the end of study period in patients who treated with Adcortyl was lower than patients who treated with Myrtle. It seems the preventive effect of Adcortyl is higher than Myrtle in subjects with RAS. This is a unique finding but additional studies with a larger sample size are recommended to clarify this result. In conclusion, Myrtle can use as an affective medication in treatment of RAS.

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Characteristics of Turkish marital properties of Turkish outpatient population

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Abstract

Objective: To dispose the marital properties, problems and resolution ways among Turkish people based on our trial.

Materials & methods: This was a population-based, cross-sectional study. Four hundred and ninety two people addressing to three different health centers have been contributed to study by a written informed consent during September, 2004 and November, 2004. Subjects completed a questionnaire assessing their marriages. Results analyzed in SPSS 11.0. T-test, covariance, linear regression and descriptive statistics used.

Results: Of subjects, 88 % were women and 12 % men. Mean age was 42.5 ± 10.34 (SD). Wedding age and marriage duration found higher in men than women. Youth prefers flirting more than elder people do. Violence found in 13.5 % of subjects: all women. Divorce thought by 22.6 % of the subjects in any time of marriage.

Conclusion: Turkish couples have different marital properties compared to other nations because of strictness to religion, morale and traditions.

Key words: Family, Marriage, Marital Problems

Introduction

Marriage is one of the major experiences of human life. The term marriage refers merely to the wedding process, by which the two persons united publicly as husband and wife. Marriage is adjustment between the individual's physical desire for mating and a social responsibility. It could not be cited as a biological necessity solely but as advantage of a permanent union. Marriage is a social institution related to the maternal function and assisted the mother in her biological contribution, but marriage itself was not an only physical necessity for the perpetuation of the human race. Marriage has three distinct centers of interest: economic, sex and potential parenthood¹.

Marriage demonstrates the transition of single roles to a couple roles. This new role affects the relationship with themselves, their parents, other couples and whole population. Marriage represents passage of old roles to future roles. A common life making two people happy, which provides discovering of a satisfied sexual interaction, common decision-making, family responsibility sharing, and conflicts resolving is important. First years of marriage are hard. Disappointments, reciprocal socialization failure are usually causes of divorce. Observing divorce peak in 2nd and 4th years of marriage, divorce ratio decreased as long as marriage time course increased. Problems in the first years of marriage are usually life conditions, economic, sex, general maladjustment problems and parental intervention. Koller cited that divorce could originate from unrealistic expectations of the couple. In contrast, Birdwithsell suggested the problem could not originate from the couple but from the society, which idealized matrimonial institution with presenting marriage as free of problems².

Contemporary social changes in the world affected to the concept of marriage³. Former marriages were "institution centered" by the social trust on marriage that it is an important social institution. Now marriages are "person centered" which is called also "developmental marriage".

Because few studies were performed in Turkey about marital problems, we aimed to expose the factors affecting the marriage among Turkish families. The study is performed by three different medical centers (one family medicine center, the Uludağ University Family Medicine Department's outpatient center, both in Bursa-Turkey, the other Prototype Research & Training Hospital's outpatient center in Ankara-Turkey) between January 2006 and May 2006.

Material & methods

Having had got written informed consent by the patients addressing to three different district outpatient clinics centers (Uludağ University Family Medicine Outpatient Clinic, Esentepe Family Health Center, and Outpatient Clinic of Prototype Research & Training Hospital of Ankara), a total of 492 patients (male or female) have been voluntarily contributed to our trial during September, 2004 and November, 2004. Thirty questions in questionnaire form (which was pretested in a sub-group) asked to patients assessing sociodemographic details (such as age, education, marital status, job, monthly income, etc) and internal dynamics of their marriages (premarital dating, thoughts of divorce, happiness, knowledge on marital counseling etc.). Monthly income is determined as low (<least wage=333\$), moderate (least wage-667\$), well (667-3333\$) and very well (>3333\$). Least wage (=333\$) is the amount determined by the Turkish government at the time the study is performed.

Data analysis

The data of the study were analyzed by using the Statistical Package for the Social Sciences (SPSS, Chicago, IL, version 11.0). Numerical data were expressed as arithmetical means \pm standard deviations (SD) and in numbers and percentages. A *p* value of less than 0.05 was considered statistically significant. Student's t test, covariance, linear regression and descriptive analyses are used to assess the data.

Results

Characteristics of subjects

A total of 492 patients have been participated to this trial in the three different outpatient clinics. Of subjects, 86.5 % were women and 13.5 % were men. Mean age was 42.49 ± 10.34 (SD). Marriage duration found significantly higher in women than in men (t-test, t=3.524, p < 0.01). Wedding age found highly significant among men (t-test, t=7.846, p < 0.01). Higher educated (Somer's d correlation coefficient, d=0.32, p < 0.01) and full time working spouses' wedding age is found highly (d=0.47, p<0.01). 43.7 % of patients stated that they did not meet with their spouses before marriage. Youth prefers premarital recognition (p<0.01). Dating duration found high in youngs (p<0.01). Higher educated persons prefer premarital dating (p<0.01).

Table 1. Sociodemographic characteristics of study population

	n	%
Age groups (years)		
20-29	77	15.7
30-39	138	28.0
40-49	162	32.9
50-59	98	19.9
60 and over	17	3.5
Have children		
Yes	468	95.1
No	24	4.9
Educational status		
Illiterate	21	4.3
Literate/primary	241	49.0
Secondary	126	25.6
College/Doctorate	104	21.1
Economical status	•	
Low (<least wage="333\$)</td"><td>75</td><td>15.2</td></least>	75	15.2
Moderate (least wage-667\$)	239	48.6
Well (667\$-3333\$)	176	35.8
Very well (>3333\$)	2	0.4
Have a job		
Yes, full time	138	28.0
Yes, part-time	11	2.2
Never	236	50.0
I had had but not now	97	19.7
Smoking		
Yes	137	27.8
No	355	72.2
Alcohol		
Yes	20	4.1
No	472	95.9

Women worked less than men did (t test, t=3.543, p < 0.01). Forty-eight percent of subjects had never worked or stopped working recently. Causes were childrearing in 18 %, disapproval of husband for work in 15 %.

Marital characteristics of subjects

92.1 % of subjects declared that they were happy in their marriage. Twenty two point six percent stated that they thought the divorce in any time in their marriage. As much as wedding age increased, knowledge on family counseling increased (p < 0.01).

According to ANCOVA analysis, divorce is found related with the income, number of children, way of acquaintance (by families, friends, relative e.g.), causes of discussion (housekeeping, child training, parental intervention, economical, jealousy, sexual, other e.g.) and the age (all p=0.000). According to way of acquaintance, divorce is found the highest among who are get acquaintance by courtesy of the family. Divorce is less seen among the moderate incomers. Consequently, the divorce is highest among lower incomers. Divorce is seen at the lowest degree among people who got acquaintance by friend. Divorce is the least in the 6^{th} decade regarding with other decades. According to ANCOVA analysis, the marital course-ling is found related with way of acquaintance (p=0.042), number of children (p=0.030), violence (p=0.028) (r²=0.731).

According to linear regression test, the divorce could be predicted by this equation: divorce =2.206 + 0.024*cause of discussion + 0.068*source of information for counseling - 0.096*dating duration - 0.122*thinking divorce period of marriage

Table 2. Marital characteristics of study population

Marital status	n	%	Did you ever think to divorce	n	%
Married	250	50.8	Yes	121	24.6
Married than one more time	242	49.2	No	371	75.4
Wedding age			In which period of marriage did you think to divorce		divorce
Under 20	250	50.8	During the first years	344	69.9
20-39	217	44.1	After birth of children	18	3.7
40-49	20	4.1	Sometimes	52	10.6
> 50	5	1.0	Other	78	15.9
Duration of marriage			Cause of problem		
< 1 year	76	15.4	Housekeeping	111	22.6
1-9 years	161	32.7	Child training	95	19.3
10-19 years	141	28.7	Parental intervention	60	12.2
20-29 years	93	18.9	Economical	83	16.9
30-50 years	21	4.3	Jealousy	31	6.3
Pre-marital recognition(dating)			Sexual 10 2.0		2.0
Yes	276	56.1	Other	102	20.7
No	216	43.9	Problem resolution		
Dating duration			Dispute	88	17.9
<6 months	206	41.9	Put out with	30	6.1
6 months-1 year	106	21.5	Intervention (parental, child)	29	5.9
> 1 year	180	36.6	Leaving for time	233	47.4
Recognition brokers			Other	112	22.8
Schoolship friend	37	7.5	Violence		
Families	151	30.7	Yes	65	13.2
Friends	71	14.4	No	427	86.8
Relative, neighbour, well-known	165	33.5	Marriage Counseling		
Other	68	13.8	Yes	169	34.3
Happiness			No	323	65.7
Yes	457	92.9			
No	35	7.1			

Discussion

The Turkish people are a tightly connected population with their culture and tradition. The Turkish Family is generally a patriarchal family. Whether educated or uneducated, father has a dominant character over the members of the family and brings income to them. Although traditional gender role for women were as wives and mothers staying at home during the day, after the Turkish Educational Revolution realized almost eighty years ago, Turkish women that have been taking education and had been working in order to obtain their economical independence, have changed their status in their family⁴.

Exogenous structural changes and social reforms led women to invest more in education⁵. Wedding age of both gender augmented, especially in full-time workers and well-educated persons. Our data were similar to literature.

Environmental (neighborhood) oppressions, sanctions of Islamic rules and the traditions of the Turkish culture, prohibit the approach of man to woman. However, nowadays, by courtesy of globalization, these rules seem to be underestimated. Although elder people are complying with those rules, youth prefers premarital recognition in our society. Indeed, therapists propose premarital counseling to reduce the odds ratio of a future marital dysfunction. This program helps the couple to recognize each other, differences and expectations in various content-focus areas. A preparation time is useful before marrying in order to know the partner. As much as education level increased, persons tend to dating and believe into the power of marital counseling^{6,7}.

As much as women's education augmented, marital bargaining increased. Because of empowering status of women in family contract and equity of responsibility, women participate more efficiently in familial issues besides their work problems. Especially, we found in our study that higher educated women contributed in everything regarding with the family. Therefore, life stressors could have more impact on working women causing more quarrels with spouse. Social transition and financial problems led women to have fewer children because of time problem spent mostly to education and work^{3,5,8}. Our data support this claim. By the evolution toward nuclear family, family became distant to parents. So any parental intervention is seen as a problem in point of view especially of well-educated persons.

The age is negatively correlated with rates of marital violence⁹. We found the same in our study. Therefore, young couples are at great risk of relationship violence. However, like in our study, in some periods such as birth of children or separation of children from house, violence could be increased and divorce could be thought. Young and well-educated persons prefer fewer fertility and much social involvements such as increased leisure activity and high consumption. Great number of children brings along a longer marriage duration, violence and ignorance¹⁰. In our study, we found also that the divorce rate is directly proportional with violence but inversely proportional with the number of children. In poor countries, knowledge on marital counseling is poor too. Well-educated persons are more skilled to use multimedia sources than few educated persons giving benefit to get more sophisticated knowledge than others sources do. We also observed this situation.

Lower socioeconomic status has greater risk for violence as underlined in our study⁹. Lack of money and/or the necessity to work long hour, lead to increased problems for couples. Family conflict researchers argue that physical aggression between partners involves both sexes to an approximately equal extent and arises from conflicts caused by the many everyday frustrations, hassles and stresses of living together. Despite mostly social class and the age of person is negatively related to violence, in fact, marital violence occurs in couples of all classes¹¹⁻¹³. Men are more likely to inflict an injury than women are, a result correlating with our study¹⁴.

Violence is a cause of the divorce according to our study^{7, 9, 15-17}. Moreover, alcohol addiction causes the divorce too^{4, 18-20}.

Conclusion

Turkey, while its population with traditional life style and rules demonstrated an Islamic country, has a modernizing community where effects of changes were seen in the family structure. This study was interesting to assess these changes. Therefore, according to our study; young, well-educated and high-income people prefer dating before marriage, having fewer children and in such families, violence has been shown rarely. Another interesting point is that divorce is most seen in those couples. This could be due to difficulty to adapt to changes in the community.

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Efficacy and safety of perioperative application of anaesthetics and steriods in tonsillar fossa on intensity of pain in first 24 hours after tonsillectomy in adults

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Abstract

Introduction: Tonsillectomy is the most common surgical procedure in otorhinolaryngology and one of the most common surgical procedures in children at all. While apparently surgicaly undemanding, it becomes problematic due to the postoperative morbidity, including postoperative pain, early (<24 h) or late (>24 h) postoperative hemorrhage and postoperative infection. The aim of the study was to examine the impact of perioperative application of local anaesthetics and corticosteroids in the surgical field on postoperative pain severity in first 24 hours after tonsillectomy.

Methods: This prospective, randomized, and single-blind study included 46 patients scheduled for a tonsillectomy according to National ISKRA Guidelines, at ENT Dept University Hospital Split from December 2009 till June 2010.

The patients were randomly assigned into one of three groups: the first group who received lidocaine in tonsilar fossa immediately after the operation, the second received dexamethasone, and the third with no additional local therapy, which served as a control group. All patients were operated on so – called "classic tonsillectomy" (blunt dissection with diatermic coagulation, with a surgical kit for repeated use in endotracheal anaesthesia).

We investigated the severity of postoperative pain in first postoperative 24 hours: 2, 12 and 24 hours after surgery. It was a subjective assessment of pain intensity using Visual Analog Scale - VAS (0 for no pain and 10 for maximal pain). The use of analgesics "on demand" during first 24 hours after surgery was also assessed as well as incidence of postoperative primary and secondary hemorrhage. **Results:** Seventeen patients (37%) were male and 29 (63%) women. The average age was 25 years (18-53). There was statistically significant pain reduction 2 hours after surgery in treated groups (P=0.017), while there was no statistically significant differences between groups in the later postoperative period (12 and 24 hours after surgery). There was no statistically significant difference in intensity of pain after first 2 hours between treated groups (P=0.315). Analgesics consumption "on demand" did not show statistically significant difference between treated and control group (P=0.821). There were no postoperative hemorrhage in any group.

Conclusion: Perioperative application of local anaesthetic or corticosteroid reduces immediate postoperative pain (2 hours after surgery), while the same medications have no therapeutic effect in later postoperative period. Local application of anaesthetics and corticosteroids does not increase the incidence of postoperative hemorrhage.

Key words: tonsillectomy – methods, postoperative pain, dexamethasone, lidocaine

Introduction

Tonsillectomy is one of the most common surgical procedures in otorhinolaryngology. This surgically undemanding procedure becomes problematic due to the distinctive postoperative morbidity, including severe postoperative pain and postoperative hemorrhage (1). In contrast to the majority of operative procedures associated with primary wound closure, tonsillectomy leaves an open wound that undergoes healing by second intention, thus opening the possibility of postoperative complications. Pain is the result of lesions of the mucosa, muscle and nerve endings of the 9th and 10th cranial nerves, leading to inflammation and spasm of the pharyngeal musculature, which in turn entails ischemia and intensifies the sense of pain. Pain completely resolves only after 14-21 days, when full re-epithelization has occurred (3). Tonsillectomy is a radical procedure that removes tissue of exceptional immune importance, which has positive and negative consequences, and is indicated when conservative treatment is not effective. Indications for tonsillectomy are still not the same in all parts of the world. Therefore, the Working Group of the Ministry of Health and Social Welfare of the Republic of Croatia published so-called ISKRA (Interdisciplinary Section for Antibiotic Resistance Control) guidelines for the treatment of sore throat with indications for tonsillectomy (2). Before making the decision for tonsillectomy it is recommended a six-month period of monitoring the patients. Once the indication is established, it is necessary to perform the procedure as soon as possible in order to achieve success (4).

Research conducted under the auspices of the American Academy of Otolaryngology and Head and Neck Surgery (AAO-HNS), showed that for more than 90% of parents whose children have been tonsilectomized, the pain was their biggest problem and concern (5). Faster post-tonsillectomy recovery with reduced postoperative morbidity is a challenge to every ENT specialist (3, 6, 7). A number of operative methods and conservative treatments have been investigated in terms of these issues, however, none yielding satisfactory results in all respects (3, 6, 7).

Obligatory oral forced fluid intake, perioperative and postoperative antibiotics administration or systemic or local corticosteroid or anaesthetic application were suggested in number of papers for reducing postoperative pain.

We investigated efficacy and safety of perioperative administration of local anaesthetics and corticosteroids in tonsillar fossa after tonsillectomy in adult patients.

The objectives

The objectives of the research were:

Assess postoperative pain severity in adult patients after tonsillectomy due to perioperative local anaesthetic or corticosteroid application in tonsillar fossa.

Assess the risk of primary and secondary postoperative hemorrhage after perioperative local anaesthetic or corticosteroid application in tonsillar fossa.

Patients and methods

The study was conducted at ENT Dept University Hospital Split from December 2009 till June 2010. It included 46 patients scheduled for a tonsillectomy according to National ISKRA Guidelines. Inclusion criteria were: age over 18 years and indications for tonsillectomy according to National ISKRA Guidelines. Exlusion criteria were absolute and relative contraindications to surgery.

Patients were randomly assigned into three groups: first received 5 mL of 2% lidocaine, 2.5 mL into each tonsillar fossa immediately after surgery, second received 8 mg of dexamethasone, 4 mg into each tonsillar fossa, and third with no additional local therapy, which served as a control group. The application was performed with a spinal needle (\emptyset = 0.53 mm – 25 G – L= 90 mm) VYGON, Ecouen, France, to avoid additional trauma of the operated area.

Patients were randomized using sealed opaque envelopes.

All patients were operated on so-called "classic tonsillectomy" (blunt dissection with diatermic coagulation with reusable surgical kit in endotracheal anaesthesia). All received same introduction to anaesthesia (midazolam 2 mg/kg, fentanyl 15 mg/kg, propofol 1-2 mg/kg, vecuronium 0.1 mg/ kg or rocuronium 0.6 mg/kg). For maintenance of anaesthesia inhaled sevorane 0.8 percent by volume was used or continuous infusion of propofol. Reversion of the neuromuscular block was achieved by the combination of prostigmin 2.5 mg and atropine 1 mg.

The pain severity was assessed by subjective pain assessment scale (Visual Analog Scale - VAS) as a numerical value on the pain scale from 0 to 10

(0 no pain, 10 maximum pain) 2, 12 and 24 hours after tonsillectomy. In addition, records were maintained on the number of requested ("on demand") oral analgesia after surgery for 24 hours. Books of operative protocols were reviewed for possible early and late postoperative hemorrhage.

The collected data were entered in Microsoft Office Excel program for Windows. The results were analyzed in Statistica 7.0, a software package for Windows. The Kruskal-Wallis test, Mann-Whitney test and the χ^2 test were used. The results were interpreted at a significance level P \leq 0.05.

Results

Our study enrolled 46 adult patients: 17 men (37%) and 29 women (63%). The average age was 25 years (18-53). Median for men was 25 years (20-48), and for women 27 (18-53) (z=0.35, P=0.723). After randomisation in control group were 26 patients (9 men with average age of 27 (20-48) and 17 women with average age 23 (18-53)). In the first intervention group who received dexamethasone there were 10 patients (3 men with an average age of 25 (24-26) and 7 women with an average age of 28 (22-38)). In second intervention group who received lidocaine there were 10 patients (5 men with average age of 23 (21 -28) and 5 women with average age of 22 (20-39)) (P=0.737) (Table 1).

We analyzed the charts of the subjective assessment of pain (VAS) which the respondents filled out on three occasions (2, 12 and 24 h) after tonsillectomy. There was a statistically significant reduction of pain 2 hours after surgery in treated groups (χ 2=8.1, P=0.017), no reduction 12 hours after surgery (χ 2=4.6, P=0.10), nor the next morning before discharge, 24 hours after surgery (χ 2=4.7, P=0.095) (Table 2).

There is no statistically significant difference in the intensity of pain after the first 2 hours between the intervention groups (z=1, P=0.315).

Consumption of analgesics "on demand" did not show statistically significant difference between treated and control group (P=0.821). Within 24 hours, patients asked for 0-3 analgesics. In the control group, 10 patients (38%) asked for one analgesic or less, and 16 patients (62%) asked for two or more. In treated groups, one analgesic or less was requested by 8 patients (40%), and 2 or more by 12 patients (60%).

Postoperative hemorrhage did not occur in any patient.

Discussion

In order to reduce postoperative morbidity, particularly pain, a number of studies were made where different surgical techniques or different conserva-

Parametar	control group (n=26)		dexamethasone (n=10)		lidocaine (n=10)		P*
gender	male	female	male	female	male	female	
no. of repondents	9	17	3	7	5	5	
age	27 (20-48)	23 (18-53)	25 (24-26)	28 (22-38)	23 (21-28)	22 (20-39)	0,737

 Table 1. Anthropometric characteristics of the repondents

* Kruskal-Wallis test.

Table 2. Median (range) of pain severity (VAS) in treated groups and control group, 2 hours, 12 hours and 24 hours after surgery

Parametar	lidocaine	dexamethasone	control group	P*
VAS I [‡]	4 (1-8)	4,5 (3-7)	6 (2-8)	0,017†
VAS II§	5 (1-9)	5 (3-8)	7 (4-10)	0,10
VAS III∥	5 (0-6)	5 (2-8)	6 (3-8)	0,095

 $*\chi^2$ test

† P <0,05

[‡] VAS I, median VAS after 2 hours.

§ VAS II, median VAS after 12 hours.

VAS III, median VAS after 24 hours.

tive treatments were used for that purpose. Since other studies have measured levels of pain for several days, and the positive results obtained only in the first postoperative day, we based our study exclusively on measuring the level of pain in the first 24 hours while patients were hospitalized.

Our results showed that the use of local anaesthetics or corticosteroids into tonsillar fossa immediately after surgery reduces early postoperative pain (2 hours after surgery), while the same therapy has no therapeutic effect in the later postoperative period (12 and 24 hours after surgery). There was no statistically significant difference in the intensity of pain 2 hours after surgery among the groups that received dexamethasone and lidocaine. The positive effect of corticosteroids can be associated with the research of Schinkela et al. which determined the level of systemic inflammatory response to surgery or minor trauma by specifying neurogenic and inflammatory mediators who would be responsible for the increase of the sensation of pain after tonsillectomy (8). The research of Giovannini et al. was conducted in the same direction which determined the plasma concentration of fibrinogen after surgery, assuming that the increased systemic inflammatory response is responsable for the increased pain in the postoperative period (9).

On same route are the results of Cardwell et al. (10), Takwoingi et al. (11) who tried to reduce postoperative morbidity using the anti-inflamatory drugs (corticosteroids and antirheumatic drugs).

Similar results were demonstrated in metaanalysis by Diakos et al. that included 580 patients older than 16 years who received corticosteroids systemically, not locally. There was statistically significant reduction in postoperative pain on the first day after surgery, especially after the common intraoperative and postoperative administration of high doses of dexamethasone (>10 mg). In addition to pain, perioperative use of corticosteroids has led to a reduction in nausea, vomiting, hemorrhage and other postoperative complications (12).

In other studies dexamethasone was applied intravenously, rather than locally in the tonsillar fossa, and the level of pain was measured longer. Research by Carr et al. included 29 patients older than 16 years, of which 15 received 20 mg of dexamethasone intravenously, and 14 served as a control group. The results showed that within 10 days after surgery there was no statistically significant pain reduction in treated group compared to the control, although the group that received dexamethasone showed a lower level of pain the first few days after surgery (13). The same results were presented by Lachance et al. (14).

Research by Naja et al. (15) that included 88 children showed that use of local anaesthetic in tonsillar fossa 5-10 minutes prior to surgery reduces postoperative pain in children which allows faster recovery and return to daily activities. Statistically significant lower consumption of analgesics "on demand" in the treated group compared to the control (P<0.05) was demonstrated, which was opposite to our (P=0.821). Simillar results were presented by Hollis et al. (16).

Combination of continuous remifentanil and single dose of midazolam were suggested by Draskovic et al. in order to provide better analgesia and sedation and better hemodynamic stability in critically ill newborns (17).

Iver et al., in meta-analysis suggests that perioperative use of antibiotics accelerates the return to normal physical activity for one day, but it has no effect on postoperative pain and hemorrhage (18). Overview of the latest literature, submits conclusions that antibiotics reduce postoperative fever, unpleasant breath, but have no significant effect on reducing postoperative pain and incidence of postoperative hemorrhage (19). According to research by Stephens et al., in patients in whom pathogenic bacteria were isolated from tonsil swabs prior surgery, there is an increased risk of postoperative hemorrhage, and therefore it makes sense to use postoperative beta-lactam antibiotics to decrease the frequency of postoperative hemorrhage (20).

Obligatory oral forced fluid intake during the postoperative period was considered to be protective from infection and hemorrhage. However, Tabaee et al. showed that forced drinking of fluids does not effect the reduction of pain, but increases the tendency of vomiting (21).

Conclusion

Based on the results of this study we can conclude the following:

- Perioperative application of local anaesthetic or corticosteroid in tonsillar fossa reduces immediate postoperative pain (2 hours after surgery), while this therapy has no therapeutic effect in later postoperative period.

- There is no difference in the intensity of pain after the first 2 hours between the groups that received dexamethasone or lidocaine.
- Consumption of analgesics "on demand" in the first 24 hours after surgery does not differ between treated and control groups.
- Local application of anaesthetics or corticosteroids does not increase the incidence of early and late postoperative hemorrhage.

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Knowledge and attitude towards caring for HIV/AIDS patients among nurses at Golestan hospital, Iran

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Abstract

Increasing number of people suffering from HIV/AIDS and it affects healthcare sectors. Nurses play a critical role in caring the HIV positive patients. People living with HIV/AIDS usually experienced excessive negative attitudes from health care workers in Iran. The aim of this study was to assess the knowledge and attitude of nurses related to care of patients with HIV/AIDS. This was a cross-sectional survey of 331 nurses from Golestan Hospital in Ahvaz, Iran. Self-administered questionnaire was used to determine the knowledge and attitude of nurses. The study showed a moderate level of knowledge among nurses (55.6% have good knowledge) which is significantly associated with nurses education background, nurses departments and having experience of caring for HIV/AIDS patients. Fear of contagion was great among nurses (76%). Slightly more than half of the nurses had unfavourable attitude towards caring for HIV/AIDS patients (53%). There were several areas of deficiency in knowledge and attitude towards caring for HIV/AIDS patients among nurses. Implementing specific and focused educational programme on HIV/AIDS for nurses is necessary in the health care system in Iran.

Key words: Knowledge, Attitude, Nurses, Care, HIV/AIDS, Iran.

Introduction

The Human Immunodeficiency Virus (HIV) and Acquired Immunodeficiency Syndrome (AIDS) epidemic have become one of the most important public health problems in recent years. One of the devastating hazards for countries all over the world is HIV/AIDS not merely economically but also because of its negative impacts within societies (Ahmed et al. 2011). HIV infection and AIDS are complicated diseases. They are one of the important causes of morbidity and mortality all over the world. HIV/AIDS influence all aspects of human life such as physical, social, emotional and spiritual. HIV/AIDS decrease life expectancy for infected individuals, creating confusion in health systems, and helping to monetary insecurity (Sowell 2004).

A total of 4.7 million individuals were living with HIV/AIDS in Asia in 2008, the number of new infections were about 350,000 individuals. In this year, 330,000 AIDS-related deaths occurred in Asia (WHO 2009). In Asia, the main modes of HIV transmission are unprotected sex (sex worker) and injection drug (UNAIDS 2008). The first case of HIV in Iran was reported in 1987. According to the recent report from Iran, there were 6,532 Iranians who suffered from HIV/AIDS in 2004. The number of infected was raised to 20,130 HIV positive people (92.9% males) in 2007. The estimated HIV infected patients are about 86,000 individuals. A total of 66.7 percent of HIV patients are injecting drug users, sexual contact is about nine percent of infected people. About 17% of HIV/AIDS patients were grouped in "unspecified" mode of transmission. There is concern that HIV/ AIDS condition in Iran can possibly be more severe than these official data. The main worry is the dissemination of HIV infection (Iran CDC 2009).

Increasing number of people suffering from HIV/AIDS and it affects healthcare sectors. Nurses play critical role in caring the HIV positive patients. Health professionals refused to face the HIV/AIDS patient because they have fear of contagion at workplaces. Irrational and discriminatory treatment of HIV/AIDS patient is the result of health professionals fear (Eisenberg 1986; Adebajo et al. 2003). Unfortunately, most of health professionals have this kind of perspective and practice related

to people living with HIV/AIDS. Healthcare providers especially nurses, general physicians and laboratory technicians are concerned about the care of HIV-positive patients (Aghamoalemi et al. 2009). Nurses must be aware of the fact and reality about HIV/AIDS. Lack of knowledge about ways of transmission can affect nurse's behaviour in caring for HIV/AIDS patients. Nurses reactions are varied about HIV/AIDS patients, from positive appropriate care to inadequate isolation techniques, minimum contact with such patients, and even avoidance to care of HIV/AIDS patients (Walusimbi & Okonsky 2004).

Educational and occupational training programmes have led to decrease fear and inadequate knowledge regarding HIV/AIDS transmission. For planning and evaluating nursing care, it is necessary that the truth about disease be identified. Inadequate knowledge is probably dangerous in nursing interventions and causing to both excessive positive events and loss resources (Unwakwe 2000). Proper knowledge base regarding HIV/ AIDS with sufficient understanding of patients needs may help relieve fear and anxiety associated with caring of patients who suffer from HIV/ AIDS. Appropriate knowledge and perception can promote quality care for these patients (Lohrmann et al. 2000). Lack of knowledge can affect outcome of care for HIV/AIDS patients.

Most studies about knowledge and attitude of healthcare workers regarding HIV/AIDS have shown the lack of knowledge about HIV transmission and risk of prevention with fear of contagion (Kohi & Horrocks 1994; Adelekan et al. 1995; Lohrmann et al. 2000; Mbanya et al. 2001; Oyeyemi et al. 2006). One factor that causes the negative attitude is fear of being affected by occupational exposure in contact with HIV/AIDS individuals. Social stigma is the second factor affected nurses attitude in contact with HIV/AIDS patients. Thus, negative attitude cause to poor management of PLWHAs who need support, treatment and care (Baylor & McDaniel 1996). Considering the global pandemic of HIV infection, the increasing number of people who are suffering of HIV/AIDS and the possibility of people with HIV living a longer life, we can conclude that it is very important to ensure the quality of life and care of people living with HIV, which are in Iran today, unfortunately, most of HIV/AIDS patients faced with societal stigma and discrimination (Brkic et al. 2011). The purpose of this study was to assess the knowledge and attitude of nurses related to care of patients with HIV/AIDS.

Materials and Methods

This was a cross-sectional study carried out at Golestan University Hospital in Ahvaz, Iran. Convenience sampling method was used in which all nurses who worked at this hospital were involved. A self-administered questionnaire was used in this study. The questionnaire was based on existing instrument developed for use in nursing (Eckstein 1987; Froman & Owen 1997). For the current study, all questions were reviewed for applicabilityy in Iranian nursing population and culture. The questionnaire comprised of the following sections: part 1 consists of socio-demographic factors, work characteristics of respondents, experience for caring HIV/ AIDS patients and also training programme about HIV/AIDS. Part 2 consists of 32 true/false questions that addressed knowledge related to care of HIV/ AIDS patients. It includes agent and immunology, course and manifestation, transmission and incidence, risk group and precaution and prevention. The total score was 32 and each statement was answered with "true", "false", or "I don't know". Each correct answer was scored 1 and each incorrect answer was scored 0 ("I don't know" responses were treated as false) and scores above the mean indicates good knowledge. Part 3 consists of questions that addressed attitude towards care of HIV/AIDS patients. Section (c) consists of 20 five-point Likert scale items. These items include five subscales as emotions toward people with HIV (6 items); caring of patients with HIV (5 items); effectiveness of care (3 items); fear of contagion (3 items); and readiness to care (3 items). Each item has a five-point Likert scale ranging from 1 (strongly disagree) to 5 (strongly agree) and negative attitude was scored reversely. Scores more than mean indicates favourable attitude. The original English version of HIV Knowledge Questionnaire was translated into Persian Language (Persian-Draft 1) by Persian individual who were bilingual in English and Persian. Other bilingual Persian individual performed backtranslation of the Persian-Draft-1. The researcher compared these two questionnaires to ensure equivalence of items. The

Persian version of HIV Attitude Questionnaire was used by Aghamoalemi et al. (2009) among nurses in Iran. Pre-test of questionnaires were done among 30 nurses to ensure that the questions are easily understandable and to assess the comprehension of the questionnaire. These results were not included in the study analysis. The questionnaire on knowledge had the Cronbach's alpha coefficient of 0.71. The questionnaire on attitude, for each part had the Cronbach's alpha coefficient of 0.68, 0.69, 0.73, 0.88 and 0.87, respectively. Data analysis was done using "Statistical Package for Social Sciences (SPSS)" Version 17. Descriptive analysis was used to show the frequency and percentage, the mean, range and standard deviation of data from all three parts of the instrument and the subcategories. Chi-square test was used for qualitative data. Pearson correlation test was used to find the association between continuous variables and Students t-test was used to find association between continuous and categorical data. Multiple logistic regression analysis was done to find the predictors of good knowledge and positive attitude among nurses, as well as to control the confounders. Written informed consent was given to all the participants under study.

Results

Of 385 questionnaires distributed, 86 percent were returned completely. The mean age of nurses was 34.82 (7.10 SD) years old, and ranged from 22 to 56. A total of 25.9 percent of the respondents were between 20-29 years, around half of them (47%) were in 30-39 years and 27.1 percent were 40 years and above. Majority of the respondents were married (n=209, 64%). The education background of respondents differ in which majority of the respondents (around 90 percent) had bachelor degree while the others had diploma (n=27, 8.3%) and master (n=4, 1.2%). Two hundred and forty six out of 331 respondents (74.8%) are working in non-surgical departments while eighty three of respondents (25.3%) are working in surgical departments. The mean working experience was 10.22±6.83 (SD) years in the hospital (Table 1). One hundred and seventy eight of the respondents (54.3%) did not attend any training programme such as workshop or seminar and only 45.7 percent of nurses have had training programme about HIV/AIDS. Source of information for 30.9

percent of respondents was mass media, 24 percent from Medical Journals and posters and 45 percent through seminar and workshop. More than half of respondents (n=181, 55%) had provided care for HIV/AIDS patients. A total of 55.6 percent of respondents scored above the mean (Table 2).

Table 1. Socio-demographic factors & work characteristics of respondents

Factors	Frequency	Percentage (%)	Mean ± SD
Age(year)	317		34.82±7.10
20 – 29 years	82	25.9	
30-39 years	149	47.0	
\geq 40 years	86	27.1	
Marital status			
Single	117	35.9	
Married	209	64.1	
Education Background			
Diploma	27	8.3	
Bachelor	296	90.5	
Master	4	1.2	
Work			
experience	322		10.22±6.83
(year)			
0-5 years	99	30.7	
6-10 years	79	24.5	
11-20 years	113	35.1	
> 20 years	31	9.6	
Nurses			
department			
Surgical	83	25.2	
Non surgical	246	74.8	
Working hour			
(per week)			
Below 44	102	21.5	
hours	105	51.5	
44 hours and	224	68.5	
above			

Table 2.	Total score	on knowl	ledge	among	nurses
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Total scores	Frequency (n=331)	Percentage (%)			
Less than 10	1	0.3			
10-15	49	14.8			
16-20	128	38.7			
21-25	136	41.1			
More than 25	17	5.1			

Note: Mean = 19.95, *SD*=3.79, *Median* =20, *Mode*=22 and *Full score*=32.

Item	Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly Agree
1)Emotions towards people with AIDS/HIV					
Patients with HIV/AIDS are responsible for their illness	61(18.4)	147(44.4)	39(11.8)	71(21.5)	11(3.3)
Patients with HIV/AIDS deserve the punishment for their risk behaviours.	91(27.5)	115(34.7)	59(17.8)	50(15.2)	15(4.5)
Patients with HIV/AIDS should be isolated from society	93(28.4)	157(48.0)	43(13.1)	30(9.2)	4(1.2)
Patients with HIV/AIDS should not be admitted to hospitals	135(40.9)	153(46.2)	22(6.6)	19(5.8)	1(0.3)
Most of the patients with HIV/AIDS have immoral and high- risk behaviours.	66(19.9)	133(40.2)	36(10.9)	77(23.3)	10(3.0)
Not admitting patients with HIV/AIDS in hospitals makes them to have a feeling of hate.	12(3.7)	17(5.1)	31(9.5)	190(58.1)	77(23.3)
2) Working with AIDS/HIV patient					
People with HIV/AIDS should be on a separate ward in a hospital.	14(4.2)	51(15.4)	21(6.3)	149(45.4)	93(28.4)
Staff and healthcare professionals should be notified when a patient has HIV/AIDS	9(2.8)	2(0.6)	2(0.6)	97(29.7)	217(66.4)
The beds of patients with HIV/AIDS should be marked.	12(3.6)	38(11.5)	20(6.1)	113(34.1)	145(44.2)
Caring of HIV/AIDS patients should be done with total security and precaution.	2(0.6)	5(1.5)	8(2.4)	113(38.7)	203(61.3)
Relatives/sexual partner of patients with HIV/AIDS should be notified of the patient's status even without his/her consent	5(1.5)	10(3.0)	7(2.1)	95(29.0)	211(64.3)
3) Effectiveness of care					
The quality of life of patients with HIV/ AIDS can be improved with counselling.	4(1.2)	9(2.7)	19(5.7)	172(52.0)	124(37.5)
Treating someone with HIV/AIDS is a waste of resources	99(30.0)	148(44.7)	46(13.9)	21(6.3)	16(4.8)
Medications to treat opportunistic infections may prolong the life of patient with HIV	9(2.7)	14(4.3)	58(17.5)	172(52.3)	76(23.1)
4) Fear of contagion					
I am scared to have contact with patients with HIV/AIDS in hospital.	36(10.9)	94(28.4)	42(12.7)	99(30.1)	58(17.6)
Thinking about caring of HIV/AIDS patients worry me	38(11.5)	88(26.6)	34(10.3)	114(34.4)	57(17.2)
I am concerned about becoming infected with HIV through patient care	30(9.1)	76(23)	23(6.9)	137(41.4)	63(19.1)
5) Readiness to care					
I am willing to take care of patients with HIV/AIDS	51(15.4)	84(25.4)	112(33.8)	70(21.3)	12(3.6)
I accept caring of patients with HIV/AIDS	44(13.3)	85(25.7)	108(32.7)	83(25.2)	10(3.0)
I satisfy with caring patients with HIV/AIDS	55(16.6)	101(30.5)	107(32.3)	53(16.2)	12(3.7)

Table 3. Frequency of responses about attitude towards care of HIV/AIDS patients

The strength of knowledge among respondents was in areas related to "transmission and incidence" and "prevention and precaution", while weak areas were related to "agent and immunology", "course and manifestation" and "risk group". In this study, the total attitude score was 100 and the attitude mean score was 72.04 ± 8.84 (SD) among 331 nurses. A total of 46.8 percent of nurses had favourable attitude towards caring of HIV/AIDS patients. The mean scores of attitudes by dimensions including emotions towards patients with HIV, caring of patients with HIV, effectiveness of care, fear of contagion, and readiness for care were 22.55 ± 3.94 (SD), 21.27 ± 3.23 (SD), 11.93 ± 2.08 (SD), 8.23 ± 3.54 (SD) and 8.05 ± 2.88 (SD), respectively.

There was a significantly higher HIV/AIDS knowledge among those who had bachelor degree (χ^2 =5.943, p<0.05). There was a significant association between nurses department where they work and knowledge level (χ^2 =8.525, p<0.05) in which 60.6% respondents in non-surgical departments had good knowledge as compared to 42.2% in surgical departments. A total of 61.3 percent of those who had experience for caring HIV/AIDS patients have significantly good HIV/AIDS knowledge (χ^2 =4.758, p<0.05). There is a significant different in knowledge mean score between respondent with and without training programme (t=2.148, p<0.05).

Most of nurses (53%) had unfavourable attitude towards caring for HIV/AIDS patients. Table 3 shows the frequency of responses in each category. Attitude towards care of HIV/AIDS patients was statistically significantly correlated with work experience of respondents (r=0.134, p<0.05). There was also a significant association between nurses departments where they work and attitude (χ^2 =7.973, p<0.05), A total of 51.6% of nurses who were in nonsurgical departments had favourable attitude towards caring of HIV/AIDS patients. In addition, a significant positive relationship was found between knowledge score and attitude score (r=0.253, p<0.001), indicating that more knowledgeable nurses had favourable attitudes toward patients with HIV/AIDS.

As can be seen in Table 4, multiple logistic regression found that there were significant associations between two variables and knowledge, namely department where the nurses work and experience of caring HIV/AIDS patients (p<0.05). Nurses in nonsurgical departments on average have 2.5 times (95% CI 1.222-3.475) better knowledge as compared to respondents who were in surgical department. It was also found that nurses with longer work experience of caring HIV/ AIDS patients have 1.5 times (95% CI 1.0-2.541) better knowledge as compared to those who had shorter work experience. Multiple logistic regression also found that, there was a significant association between department where the nurses work and attitude (p<0.05). Nurses in nonsurgical department had 2.12 (95% CI 1.256-3.575) times more favourable attitude as compared to respondents who were in surgical department.

Discussion

This study results showed that, in general, nurses in Golestan Hospital had relatively moderate knowledge level related to issues of HIV/AIDS. The significant association between knowledge towards HIV/AIDS and education background has been reported in previous studies (Horsman & Sheeran 1995; Tierney 1995). This study found that there was an association between nurses academic grade and knowledge level (p<0.05).

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Variable	B-value	Wald	p-value	95% confidence interval
Constant value	-1.368	0.255	0.003***	
Education background	0.784	2.191	0.072	0.933-5.145
Departments	0.723	2.061	0.007**	1.222-3.475
Training programme	0.166	1.181	0.480	0.744-1.874
Having experience of caring HIV/AIDS patients	0.467	1.594	0.049*	1.000-2.541

* significant at p < 0.05. **significant at p < 0.01, ***significant at p < 0.001.

Knowledge (Good:1,Poor:0), Education background (Diploma:0,Bachelor:1), Department (Surgery:0,NonSurgery:1), Training programme (Not- Trained:0,Trained:1), experience of caring HIV/AIDS patients (No:0, Yes:1).

Nurses who had bachelor degree had higher level of knowledge as compared to those who had diploma (p<0.05). Further analysis found that education background of nurses was not significantly associated with knowledge level (OR=2.191, 95%CI=0.933-5.145, p>0.05). This was similar to the finding of Dellobele et al. (2009) among nurses in South Africa (p < 0 .001), the result showed that senior and well-trained nurses had more satisfactory level of knowledge. Also, Walusimbi & Okonsky (2004), Suominen et al. (2010) and Mbanya et al. (2001) reported similar finding among nurses.

In this study, there is no significant association between nurses age and marital status with knowledge level towards care of HIV/AIDS patients. Some other studies showed similar results (Suominen et al. 2010; Dellobele et al. 2009; Oyeyemi et al. 2006; Kermode et al. 2005; Walusimbi & Okonsky 2004).

This study also found that there is no significant association between nurses duration of employment and working hours per week with knowledge level towards care of HIV/AIDS patients. Other studies reported similar findings (Dellobele et al. 2009; Oyeyemi et al. 2006; Kermode et al. 2005; Walusimbi & Okonsky 2004; Lohrmann et al. 2000). However, Suominen et al. 2010 found that working experience of nurses correlated negatively with knowledge score (r =-0.127, p=0.004). This study found that there is a significant association between nurses who had experience caring of HIV/AIDS patients and their knowledge level (p<0.05). In the study by Suominen et al. (2010) among nurses in European countries, it was found that previous experience of caring HIV/AIDS patients had positive impact on knowledge level. Williams et al. (2006) also found that nurses who had cared more HIV/AIDS patients, their knowledge were better and they scored higher on knowledge scale. Some other studies reported similar results (Oyeyemi et al. 2006; Kermode et al. 2005; Walusimbi & Okonsky 2004; Lohrmann et al. 2000). Meanwhile, knowledge towards care of HIV/AIDS patients was moderately adequate but there is some gap and misconception due to occupational HIV transmission, disease presentation and HIV risk prevention. Some previous studies also reported the same gap and

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misconception among healthcare workers (Kohi & Horrocks 1994; Adelekan et al. 1995; Mbanya et al. 2001; Walusimbi & Okonsky 2004; Oyeyemi et al. 2006; Dijkstra et al. 2007; Delobelle et al. 2009). More than sixty eight percent agreed with the statement "*HIV/AIDS is highly contagious*". However this statement is not true. According to CDC report (2001), the average risk of HIV transmission has been estimated to be about 0.3% (95% CI = 0.2%-0.5%). Study by Delobelle et al. (2009) reported similar finding in which more than 72.1 percent of respondents agreed with this statement. However, in the study by Walusimbi & Okonsky (2004) among nurses in Uganda, more nurses (56.2%) did not agree with this statement.

Our findings showed that attitudes towards HIV/AIDS patients are in line with those found in other studies, where around half of nurses (47%) had a favourable attitude towards care of HIV/ AIDS patients (Mbanya et al. 2001; Nobandegani et al. 2005). This study found that there were no significant associations between socio-demographic variables and nurses attitude (p>0.05). This result was similar to the finding of other studies (Walusimbi & Okonsky 2004; Gulifeiya & Rahmah 2008; Baylor & McDaniel 1996). This study also showed that there was a significant association between the departments where the nurses work and attitude (p<0.05). Nurses who were in nonsurgical departments had more favourable attitude compared to those who were in surgical departments (p=0.005). Delobelle et al. (2009) found that there was a significant positive association between nurses attitude and ward allocation (p<0.05). This study found that nurses attitude was positively correlated with the length of work experience (r=0.134, p<0.05). This result showed that more experienced nurses had more positive attitude. The rationale is that more experienced nurses had provided care for more HIV/AIDS patients. Aghamoalemi et al. (2009) in the study among Iranian healthcare workers showed similar results. However, Suominen et al. (2010) in their study among European nurses reported negative correlation (r=-0.171, p<0.001). In this study, "Direct care" had the lowest score compared to other subcategories of attitude (mean=8.05±2.88 SD), It means that participants had less favourable attitude to provide care to patients with HIV/AIDS.

The study by Aghamoalemi et al. (2009) among Iranian healthcare workers in Bandar Abbas supported the finding of this study. The main reason was fear of being infected when providing care for HIV/AIDS patients. A total of 36 percent of Swedish nurses in the study by Rondhal et al. (2003) want to refrain from caring HIV/AIDS patients if it is possible. The wish to avoid caring HIV/AIDS patients cannot be described with the fear of contagion alone. Some factors such as moral and social values could also be a possible description. Nurses who wished to refrain from caring HIV/ AIDS patients might provide basic care to these patients, however, there is a risk that it would be given without compassion. In this study, fear of contagion and occupational exposure were major concerns of the nurses, as indicated by responses to "I am concerned about becoming infected with HIV through patient care" (60.5% agreement, n=331). In this study fear of contagion was positively correlated with knowledge (r=0.144, p<0.01). Nurses who are more knowledgeable had less fear of being infected. Educational and occupational training programmes have led to decreased fear and inadequate knowledge regarding HIV/AIDS transmission. In the study by Armstrong-Esther & Hewitt (1990) among Canadian student nurses, it was shown that after four months of education on AIDS and care of the patients, there was a significant decline (from 83% to 57%) in fear and concern about treating HIV/AIDS patients. Knowledge score was significantly positively correlated with attitude (r=0.0253, p<0.05). Some other previous studies showed significant positive correlation between knowledge and attitude of nurses and healthcare workers towards HIV/AIDS patients (Suominen et al. 2010; Delobelle et al. 2009; Umeh et al. 2008; Walusimbi & Okonsky 2004; Lohrman et al. 2000; McCann & Sharkey 1998; Uwakwe 2000). It is suggested that empowering nurses with better knowledge would promote their attitude towards patient care as has been found by several studies.

There are some limitations to this cross-sectional study. The researchers have some restriction in asking questions about sexual beliefs concerning sexual behaviours of respondents in the religious country like Iran. This study was carried out in only one university hospital, therefore, generalization of findings should be carefully done. In the cross-sectional studies, always the nonresponder bias is a major concern. Identifying the nurses characteristics who failed to return the questionnaire was not possible. Therefore, the differences between responders and non-responders could not be recognized. However, in this study the response rate (86%) was high, and there was no reason to assume that non-responders were substantially different from responders.

Conclusion

While most of nurses in this study had satisfactory level of essential knowledge towards HIV/ AIDS, more than half of them had negative attitude. Health provider must plan to change nurses behavior in communication with HIV/AIDS patients. The findings of the study highlighted the requirement to plan programmes to improve the occupational safety of nurses at teaching hospitals and to minimize the fear and concern of nurses in caring of HIV/AIDS patients. The results of this study recommend that such programmes would be of benefit. Eventually, a well-educated nurse with more positive attitude and fewer concern will be more beneficial for HIV/AIDS patients.

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The role of Xanthine Oxidase in oxidative stress induced by exercise to exhaustion

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Abstract

Background. Although the sources of oxidative production during exercise continue to be debated it is undoubtedly that intense and prolonged exercise can result in oxidative damage of proteins and lipids. Xanthine oxidase catalized reactions are known as major source of free radical generation in the ischemia-reperfusion processes.

Objectives. The aim of our study was to examine the role of prooxidative enzyme xanthine oxidase on oxidative stress generation induced by exercise (swimming) to exhaustion.

Material and Methods. Experiments were conducted to ten male guinea pigs (Dunkin Hartly). From peripheral blood samples taken at rest, immediately after and 24 hours after exercise following parameters were estimated: total plasma peroxides (TPPC), total plasma thiols (TPT), plasma xanthine oxidase activity (XOD) and total plasma proteins.

Results. TPPC didn't show significant difference between concentration measured at rest and immediately after swimming test (p=0,138), while value measured 24 hours after test was significantly lower (p=0,007). TPT value significantly decreased (p=0,022), while XOD activity significantly increased immediately after performed test (p=0,039). Value obtained 24 hours after test for TPT was also significantly lower comparing to basal value (p=0,005), while XOD activity decrease was right behind the limit indicating statistical significance (p=0,059).

Conclusions. Significantly increase in XOD activity immediately after exercise pointed the role of this enzyme and ischemic-reperfusion process in the pathogenesis of exercise induced oxidative stress.

Key words: exercise, free radicals, oxidative stress, xanthine oxidase

Introduction

The well documented benefits of regular physical exercise include reduced risk of cardiovascular diseases, cancer, osteoporosis and diabetes. The complex mechanisms that contribute to those effects include decreased adipose tissue, altered lipid and hormonal profiles, receptor and transport-protein adaptation, improved mitochondrial coupling and alteration of antioxidant defenses [1]. Exercise induces a multitude of physiological and biochemical changes in blood that may affect its redox status. Some of the well described events that arise during exercise are increases in blood temperature and blood lactate concentration and decreases in blood pH and blood oxygen partial pressure. All these exercise associated homeostasis disruptions are able to modify blood redox status [2]. The term oxidative stress was at first defined as a 'disturbance in the prooxidant-antioxidant balance in the favor of the former'. In an effort to refine the meaning of oxidative stress Jones has proposed that this term should be redefined as a 'disruption of redox signaling and control' [3]. Regardless of whether this new definition gains widespread acceptance, it can be anticipated that the description of oxidative stress will undergo further modification as a field of redox biology advances [4].

Since the initial findings of increased lipid peroxidation following acute aerobic exercise, the topic of exercise induced oxidative stress has received a considerably attention. This increased interest can be explained by both the enhanced awareness of the role of RONS in the pathogenesis of different human diseases on the one side, as well as urge to promote exercise as a mean for the improvement of health on the other side, accompanied by widespread development and availability of various antioxidant agents [5]. Exercise related

oxidant production is based on number of potential pathways. These include mitochondrial respiration (electron leakage from electron transport chain and subsequent production of the superoxide radical), prostanoid metabolism, the autooxidation of catecholamines, and oxidase enzymatic activity (NADPH oxidase, xanthine oxidase). Additional secondary generation of prooxidants include phagocytic respiratory burst, a loose of calcium homeostasis and/or the destruction of iron containing proteins. Free radical generation also depends on the mode (aerobic/anaerobic), intensity and duration of exercise [5].

Xanthine oxidase is widely distributed among species and within the various tissues of mammals. This enzyme is most recognized for its role in nuclear acid degradation, through which all purines are channeled for terminal oxidation. Xanthine oxidase exists in vivo predominantly as a NADH dependent dehydrogenase, which can be transformed to an oxygen dependent oxidase by a variety of conditions. Interest for the enzyme as a source of oxidizing agents has increased since it has been implicated in the pathogenesis of ischemia-reperfusion injury of tissues [6]. During strenuous exercise blood flow through the working skeletal muscle is increased significantly (up to 40 fold), whereas other organs such as liver, kidney or gastrointestinal tract receive less oxygen (less of 20% or resting values). After exercise the reperfusion of those organs is elevated, known as the ischemia-reperfusion phenomenon which leads to an accumulation of oxygen free radicals in the reperfused organs [7]. During ischemia ATP is degraded to ADP and AMP for the energy demand of contracting muscle. Due to the insufficient oxygen supply, AMP is continuously degraded to hypoxanthine, which may be converted to xanthine and uric acid by xanthine oxidase coupled with one electron reduction of oxygen and giving rise to superoxide [8]. Ischemia-reperfusion process can lead to tissue injury and cause serious complication in organ transplantation, myocardial infarction and stroke [9].

The aim of our study was to examine the role of prooxidative enzyme xanthine oxidase on oxidative stress generation induced by exercise (swimming) to exhaustion.

Material and methods

Experimental animals

Experiments were conducted on 10 male guinea pigs (Dunkin Hartly) initially weight between 500-550 g. The animals were housed in the temperature controlled ($22\pm2^{\circ}$ C) and ventilated room, under natural lightening condition, and they had free access to standard food and water.

Handling of animals was performed in accordance with the European Community Guidelines (86/609/EEC) and the American Physiological Society's "Guiding Principles for Research Involving Animals and Human Beings" [10]. All procedures were previously approved by the Ethical Committee of Medical School Pristina (situated in K.Mitrovica).

Experimental protocol

The swimming program used in the study (swimming to exhaustion) was defined by Dawson and Horwat [11, 12]. Swimming was performed in the cylindrical tank with 100 cm diameter and 50 cm depth, containing water at 30 - 32 °C. The animals were manually supported below their thorax, placed in to water tank and allowed to swim. The time point at which the guinea pig remained below the water surface for 10 seconds was recorded as exercise endurance capacity. The average endurance capacity in this study was 45 ± 5 min.

Biochemical Analysis

Peripheral blood samples were taken by lateral saphenous venipuncture at rest, immediately after finishing maximal exercise test and 24 hours after finishing maximal exercise test. The following parameters were estimated in our study: total plasma peroxides as a marker of lipid peroxidation process, total plasma thiols, plasma xanthine oxidase activity and total plasma proteins.

Determination of total peroxides

Total plasma peroxides were assessed by the ferrous-oxidation xylenol orange method (FOX2), based on ability of various types of peroxides to oxidize ferrous ion in acidic medium containing the dye xylenol orange [13]. The resulting ferric-xylenol orange complex can be measured at 560 nm. In brief, 90 μ L of plasma was mixed with 10 μ L of HPLC-grade methanol, or 10 μ L of triphenylphosp-

hine (TPP) solution (20mM in methanol), in 1.5 mL microcentrifuge vials, and left at room temperature in the dark for 30 min before adding 900 µL of FOX solution (250 µM ammonium ferrous sulfate, 100 µM xylenol orange, 25 mM sulfuric acid, and 4 mM butylated hydroxytoluene in 90% (v/v) methanol in a final volume of 100 mL). Samples were further incubated at room temperature for 30 min, being vortex mixed every 10 min, and spoon (10 min; 10 000 g). Absorbance readings were taken at 560 nm on UV/VIS spectrophotometer (SAFAS 2, Monaco) against appropriate blank probe prepared with FOX-blank reagent in which the xylenol orange was omitted. Concentration of total peroxides (TPPC) was calculated as the difference between untreated and TPP treated samples, and calibrated with H₂O₂ standard curve in the concentration range of $0-20 \,\mu$ mol/L. The results were expressed as nmol/g protein.

Total plasma thiols assay

Concentration of total plasma thiols (**TPT**) was determined by Ellman's reagent [14]. An aliquot of 20 μ L of plasma was mixed with 800 μ L of sodium phosphate buffer (Na₂HPO₄; 0.3 M) and 200 μ L of Ellman's reagent (40 mg of 5, 5'-dithiobis-(2-nitrobenzoic acid) in 100 mL of 1% (w/v) sodium citrate). After 10 min the absorbance was measured at 412 nm against reagent blank. The amount of TPT was calculated using the molar absorbance of 1.36×10^4 L × M⁻¹ × cm⁻¹. The results were expressed as μ mol/g protein.

Measurement of plasma xanthine oxidase activity

Plasma xanthine oxidase (**XOD**) activity measurement was carried out at 25° C in a quartz-glass spectrophotometric cuvette, by the rate of oxidation of xanthine to uric acid [15]. All reagents were prewarmed at 25° C. In brief, 0.3 mL of TRIS-HCl buffer (50mM; pH 7.4), 0.3 mL cooper (II) sulfate (10 mM) and 50 μ L of freshly prepared substrate (14 mg xanthine, sodium salt, in 3 mL of 0.1 M NaOH) were added to a cuvette followed by 100 μ L of plasma sample, mixed and diluted with water to make up the volume of 3 mL. After 15 sec lag-phase, the formation of uric acid was continuously measured at 293 nm for 120 sec and corrected for pre-existing uric acid. One unit of XOD activity was defined as 1 μ mol/min uric acid formed at 25° C, calculated using the molar absorbance of $1.26 \times 10^4 \text{ L} \times \text{M}^{-1} \times \text{cm}^{-1}$. The results were expressed as milli units per gram protein (mU/g protein).

Determination of total plasma proteins

Concentration of total plasma proteins was determined by biuret method, using bovine serum albumin as a standard (50 g/ L).

Statistical Analysis

Statistical analysis was performed using a commercial software package (SPSS version 12.0 for Windows, SPSS Inc., Illinois, USA). The data are reported as means \pm SE. The statistical procedures included paired samples Student *t*-test. Differences were considered significant at value p < 0,05.

Results

All measured parameters are shown in Table 1 and Figure 1, 2 and 3.

TPPC as a marker of lipid peroxidation didn't show significant difference between concentration measured at rest and immediately after exercise swimming test (p=0,138). In contrast value measured 24 hours after performing the test was significantly lower comparing to basal value (value at rest) with p=0,007 (Figure 1).

Two other parameters TPT (as marker of oxidative protein modification) and XOD activity (as

Table 1. Oxidative stress parameters (TPPC, TPT, XOD) in plasma before, immediately after and 24 hours after swimming exercise test

	At rest	After exhaustive exercise	24 hours after exhaustive exercise
TPPC – nmol/g protein	256,35±25,44	200,90±24,39	154.06±17.48*
TPT – μ mol/g protein	25,35±3,58	15,31±2,10*	10.71±2.30*
XOD – mU/g protein	160,61±19,59	244,42±29,30*	100,14±21,71

TPPC – Total Plasma Peroxide Concentration,

TPT – **T**otal **P**lasma Thiols concentration,

XOD - Plasma xanthine oxidase activity, p < 0.05 statistical significance

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marker of ischemia-reperfusion injury) showed significant difference before and after swimming exercise test. Namely, TPT value significantly decreased (p=0,022), while XOD activity significantly increased immediately after performed test (p=0,039). Value obtained 24 hours after performing test for TPT was also significantly lower comparing to basal value (p=0,005) as shown in Figure 2, while XOD activity decrease was right behind the limit indicating statistical significance (p=0,059). On the other hand where was statistically significant decrease (p=0,002) of XOD activity comparing values immediately after and 24 hours after performing test (Figure 3).



Figure 1. Effects of swimming to exhaustion on blood lipid hydroperoxide concentration (nmol/g protein). A-Basal value, B- Immediately after test, C-24 hours after performed test (* statistical significance obtained with t-test (p<0.05))



Figure 2. Effects of swimming to exhaustion on total plasma thiol concentration (μ mol/g protein). A-Basal value, B- Immediately after test, C-24 hours after performed test (* statistical significance obtained with t-test (p<0.05))



Figure 3. Effects of swimming to exhaustion on catalytic activity of xanthine oxidase (mU/g protein). A-Basal value, B- Immediately after test, C-24 hours after performed test (* statistical significance obtained with t-test (p<0.05))

Discussion

During the past 4 decades our knowledge about the biological implications of exercise induced oxidative stress has expanded rapidly. Now, we can say that while high levels of free radicals can damage cellular components, low to moderate levels of oxidants play regulatory rolls in cells such as the control of gene expression, regulation of signaling pathways and modulation of skeletal muscle force production [4]. Physical exercises, especially under curtain circumstances such as unaccustomed intensity or duration, increase the production of free radicals and leads to oxidative stress even in trained individuals. During intense exercise skeletal muscles are exposed to levels of mechanical and metabolic insult that would seriously injury most other cells in the body. No other body tissue undergoes such drastic change in oxygen metabolism during the state considered as 'normal activity' [16]. Exercise also strongly increases the physical forces acting on blood vessels, such as transmural pressure and cyclic stretch, which increase the vascular generation of reactive species and activate NADPH oxidase [2]. All these changes became an interesting topic not only for medical scientists but for other specialists of sport and exercise s well [17, 18].

Studies involving physical exercise have been conducted on both, human and animal models. It is believed that the ones conducted on animal models have limitation in relation to the determination of the animal effort intensity during exercises which have to simulate adequately situation that human beings are exposed to. But it is also believed that studies using animal models are more controlled because of homogeneity of experimental group and possibility of measuring oxidative stress biomarkers in different biological tissues. In experiments involving animals the most popular type of exercise are treadmill running and swimming [19].

Polyunsaturated fatty acids of membrane are attacked repeatedly by free radicals to form highly destructive polyunsaturated fatty acid (PUFA) radicals like lipid hydroperoxy radicals and lipid hypoperoxides. This is termed as lipid peroxidation. To examine acute oxidative stress in response to exercise most researchers have assessed various stress markers in blood and urine. Lipid hydroperoxides are considered as biomarkers of early damage of lipids and proteins induced by RONS. In our experiment the value of plasma lipid peroxide concentration immediately after exercise test didn't show significant difference compared to value at rest. Similar results were reported by other researchers [20, 21]. On the other hand, value measured 24 hours after performing the test was significantly lower comparing to basal value (154.06±17.48 compared to 256.35±25,44; p=0,007) as shown in Figure 1. One of the explanations for these results can be that duration and intensity of the proposed exercise were not enough to promote reactive oxygen species production able to induce lipid peroxidation process. The other explanation is that oxidative stress occurred but it did so preceding or following the sample collection, or in a different tissue other than that utilized (blood) or resulted in oxidative damage to cellular constituents other than those measured [5].

High overall abundance of proteins in different biological systems makes them major targets of RONS. Proteins modification induced by RONS is a rapid and linear one though representing a more sensitive biomarker of oxidative modification of biomembrans compared to lipid peroxidation [22]. Thiols (sulfhydryl groups) are known to scavenge aqueous peroxyl radicals, which make them important in the regulation of both cellular redox status and antioxidant capacity. In our work concentration of total plasma thiols in exercising animals significantly decrease both immediately after exercise test (25,35±3,58 vs. 15,31±2,10 μ mol/g protein, p = 0,022) and 24 hours after exercise (25,35±3,58 vs. 10.71±2.3010 µmol/g protein, p = 0.005). According to these results the observed decrease of plasma thiols concentration could reflect their oxidation by exercise induced oxidative modification of protein molecules caused by RONS. Our results are consistent with reported findings of increased protein oxidation in [20, 23, 24]. Oxidative damage to proteins can occur directly by interaction of the protein with RONS or indirectly by interaction of the protein with a secondary products resulting from interaction of radical with lipid or sugar molecule. Modification of protein under condition of oxidative stress can occur via peptide backbone cleavage, cross-linking and/or modification of the side chain of virtually every amino acid. Most protein damage is irreparable and oxidative modification of the protein structure can lead to loose of enzymatic, contractile or structural function in the affected proteins, thus making them increasingly susceptible to proteolitic degradation [5].

It is believed that the acute ischemia and rapid reperfusion observed during and following prolonged exercise increase free radical production via the radical generating enzyme xanthine oxidase. Interest in this enzyme as a source of oxidizing agents has increased markedly since it has been implicated in the pathogenesis of ischemia-reperfusion injury of tissues such as the intestine, kidney and heart. Ischemia is a considerable different stimulus from hypoxia because it is characterized by acidosis, accumulation of adenosine and other energy metabolites, and accumulation of oxidants and oxidant products. During reperfusion tissue is suddenly capable to generate large level of reactive oxygen species as well as metabolites are transiently changed prior to the ability of the tissue to reestablish equilibrium [16]. In his work Vina et al. [25] explained that exercise caused an increase in blood xanthine oxidase activity in rats and that inhibiting the xanthine oxidase activity with allopurinol prevented exercise induced glutathione oxidation both in rats and in humans. He also pointed that inhibiting xanthine oxidase prevented the increase in plasma activities of cytosolic enzymes-lactate dehydrogenase (LDH), aspartate amino-transferase (AST) and creatine kinase

(CK) that occurs after exhaustive exercise. Hellsten et al. [26] concluded that eccentric exercise lead to an increased level of xanthine oxidase in human muscle and that this increase is followed with secondary inflammatory processes. Elevated expression occurred mainly in the endothelial cells of micro vessels but also in the leukocytes present in the muscle. This restricted localization suggests that during exercise induced inflammatory process in the muscle xanthine oxidase could cause injury of micro vessels and the surrounding tissues.

Animal studies investigating the effect of ischemia and reperfusion on tissue damage and the level of xanthine oxidase have demonstrated an increase in tissue xanthine oxidase activity in ischemic tissue as determining from measurements whole-tissue homogenates [26]. Studies conducted on rats also suggested that a large part of the source of oxidative damage came from xanthine oxidase activity [16]. Hypoxanthine was reported to accumulate after intense muscle contraction and uric acid concentration was shown to increase in both contracting arm muscle and in plasma suggesting that xanthine oxidase was activated [8]. In the present study xanthine oxidase activity also were significantly higher immediately after exercise swimming test. (160,61 vs. 244,42 mU/g protein, p=0,039). The observed increase in xanthine oxidase activity could reflect the role of ischemia-reperfusion injury in oxidative stress generation. The value obtained 24 hours after swimming test didn't show significant difference compared to basal level (160,61 vs. 100,14 mU/g protein, p=0,059) which can be explained by the reestablishing of normal circulation at that time. In healthy tissue xanthine oxidase mainly exists in a dehydrogenase form, not capable of producing superoxide radicals but enzyme can be modulated to its prooxidant form via oxidation of critical sulfhydryle groups or via limited proteolysis [26]. It is also recognized that adhesion of leukocytes to micro vascular endothelium is a critical initial step in the pathogenesis of ischemia-reperfusion injury. Reperfusion of ischemic tissues leads to dramatic increase in the number of leukocytes that adhere to the endothelial cells of post/capillary venules [27]. Exercise to exhaustion leads to a depletion of the cellular pool of adenosine-triphosphate. Consequently the function of the adenosine-triphosphate-dependent calcium ionic pump is impaired. The increased intracellular calcium concentration activates the calcium-dependent proteases (calmodulin or calpain). The proteases cut a peptide group from xanthine dehydrogenase which converts the enzyme to the oxidase form. The formed oxidase uses oxygen as an electron acceptor and thereby generates superoxide radicals and hydrogen peroxide as byproducts [7]. Due to the propensity of xanthine oxidase to generate reactive oxygen species this enzyme has been considered to be a potential cause of muscle damage during exercise.

Conclusion

As a conclusion we can say that results of this study provide evidence that exercise to exhaustion induced oxidative stress generation, predominantly by oxidative modification of protein molecules. Significantly increase in XOD activity immediately after exercise pointed the role of this enzyme and ischemic-reperfusion process in the pathogenesis of exercise induced oxidative stress.

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Pharmacy practice and concept of pharmaceutical care among Malaysian pharmacists

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Abstract

Objective: study aim to make an assessment and gather baseline information that necessary for the implementation of pharmaceutical care and identify needs and issues confronting pharmaceutical care practice in Malaysia. Our objective of the study is to evaluate the pharmacist perception in term of pharmaceutical care in pharmacy practice.

Methodology: A questionnaire was designed to explore the pharmacist's understanding, knowledge, and their perceptions on the philosophy of pharmaceutical care and barriers to its provision, and also the current pharmacy practice. The cross-sectional study was conducted, which involved exploring and collecting data from community and hospital pharmacists in the West and East Malaysia (Sabah and Sarawak), employing the self-administered mailed questionnaire approach. The community pharmacists participated in our study were selected according to pharmacies names, rather than pharmacists names. The mode of data collection chosen was a self-administered mailed questionnaire. The data was analyzed using the SPSS® (Statistical Package for the Social Sciences) software program for windows® Version (12.0), and Microsoft Office Excel 2003.

Results: Of the 927 questionnaires mailed to the hospital and community pharmacists, 269 were returned back. In terms of the responses from both the hospital and community pharmacists; provide a response rate of 45.8% and 18.5%, respectively. It was observed that most of the respondents from the both the hospital and community pharmacy settings tend to be in the younger age group (24-35 years) (77%) and (48.2%) respectively, (P< 0.001, Chi-square)

It was noted also that the majority of the hospital pharmacy respondents were engaged in more than one practice site (73.6%). Only a small per-

centage of them were involved in a specific pharmacy practice site such as in the satellite pharmacy (2 %) and drug information service (0.7%). In response to the question about the average number of prescriptions that they have received for each month, the answers given were varied and ranges from none (2.7%) to more than 300 prescriptions per month (0.9%). Nevertheless, most of them (69.6%) stated that they might receive prescriptions ranging from one to 30 for each month.

Conclusion: We concluded from the findings of this study that although there is a sizeable gap in the practice perception of both groups of pharmacist. Pharmaceutical care concept is devastating tool among pharmacists.

Key words: Pharmaceutical care, Pharmacy services, patient-oriented care, patient safety.

Introduction

Over the past few decades, with the health care environment worldwide especially in the United States witnessing the gradual and remarkable growth of the managed care system and pharmacy practice becoming more medically sophisticated, pharmacists are employing innovative patient care strategies such as pharmaceutical care practice. The philosophy of pharmaceutical care has been accepted worldwide as the primary mission of pharmacy. Pharmaceutical care mandates that practitioners not only to dispense medications, but also to assume responsibility for improving the quality of patients' outcomes (Helper and Strand, 1990). The traditional role of the pharmacist that involves in the preparation, dispensing and selling of medications is no longer adequate for the pharmacy profession to survive. Additionally, it has been argued that pharmacists have assumed a paternalistic role in discussions with patients about therapeutic options. Under this "pharmaceutical care" model, the patient delegates decision-making authority to the pharmacist. Implicit assumptions in delegating this authority include the perception that the "pharmacist knows best" and would be in the best position to make a therapeutic decision in the patient's best medical interests for the purpose of achieving definite results that improve a patient's quality of life (QoL) (Hepler and Strand, 1990). To achieve these results, pharmacists need to co-operate with patients and other healthcare providers in designing, implementing, and monitoring a care plan aimed at preventing and resolving drug therapy problems (DTPs) (Bell et al, 2006; Haugbølle and Sørensen, 2006; Blix et al., 2006; Soendergaard, 2006; Sturgess et al., 2003).

For the pharmaceutical care to achieve its goals it needs the traditional pharmacy to evolve and transform (Winslade, 1994; Winslade, 1993; Duncan-Hewitt, 1992). The perception and understanding towards pharmacy need to be changed, evolved, and transformed as well as to reorient the practising pharmacists to meet the challenges of the contemporary health care system. This is vital as the pharmacists are the main drive and main factor behind this transformation and application of pharmaceutical care practices. Hence, pharmacists' knowledge, perception, and attitude about the new emerging philosophy of pharmaceutical care are important.

Pharmacy practice has been aptly described as evolving in three distinct stages. These stages are namely; (1) the traditional or drug distribution stage; before 1960s, generally, pharmacists are known as apothecaries, their function was to procure, prepare, and compound medicinal products. However, this role was gradually waned and taken over by the pharmaceutical industry. (2) the transitional or clinical pharmacy stage; born in the mid-1960s, The notion of the pharmacy practice had shifted to place much less emphasis on compounding and considerably more emphasis on clinical service delivery (Higby, 2003). (3) The patient-focused or pharmaceutical care stage (Hepler and Strand, 1990; Hepler, 1987) began in 1990 and continues to the present time. It is the "patient care" era in which the pharmaceutical care reached maturation and became the mainstream function of pharmacists. Patients and their effective treatment with drugs are now central to the pharmacists' role. The pharmacist's role as a "therapeutic advisor" subsequently began to emerge.

The growth of clinical pharmacy in hospital has lead some people to incorrectly conclude; that clinical pharmacy is a variety of hospital practice and or limited to hospital only (Hassan, 1993). Community pharmacy shift to clinical practice coincided with hospital pharmacy transformation. Unlike hospital pharmacy, the burdens of business nature like of the practice and the distance from the clinical environment made the transition slower and more difficult (Higby, 2003; Posey, 1997; Carter and Barnette, 1996; Sisson and Israel, 1996).



Figure 1. Evolution/ transformation of pharmacy practice

The concept of clinical pharmacy practice in hospital settings comprises functions require pharmacists applying their scientific body of knowledge to improve and promote health by ensuring safety and efficacy of drug use and drug use- related therapy in seven major categories: prescribing drugs, dispensing and administrating drugs, documenting professional activities, direct patient involvement, reviewing drug use, education, and consultation (Hassan, 1993). Community pharmacy practice in Malaysia varies from one pharmacy to another. Chain-store pharmacies usually offer a significant proportion of non-professional services and activities alongside the traditional professional services. Smaller independent pharmacies normally focus on professional pharmacy services. Both types are representative of community pharmacy practice in Malaysia (Wong, 2001). In general, the application of clinical knowledge and skills although necessary, are not sufficient for effective pharmaceutical care (Todd et al., 1987). There must also be an appropriate philosophy of practice called pharmaceutical care and an appropriate organizational structure to facilitate providing that care called pharmaceutical care system (Hepler and Strand, 1990).

Since the landmark description of the concept of pharmaceutical care by Hepler and Strand (1990), there have been numerous definitions of the concept (Hepler, 1993) and suggestions and also evaluations of models for implementing pharmaceutical care practice. These include the Therapeutic Outcome Monitoring (TOM) model of Grainger-Rousseau et al., (1997); and the Pharmacists Implementation of Pharmaceutical Care (PIPC) model of Odedina et al., (1997) among others. Currently, pharmaceutical care is widely understood as "the direct, responsible provision of medication-related care to achieve definite outcomes intended to improve the patient's quality of life", The principal elements of pharmaceutical care are that it is medication related; it is care that is directly provided to the patient by pharmacist in collaboration with the patients and healthcare professionals. This role requires pharmacists to apply a higher level of drug knowledge, clinical skill, and independent judgment to their work which involves designing, implementing and monitoring a therapeutic plan. The care provided is to produce definite outcomes; these outcomes are intended to improve the patient's quality of life; and the pharmacists who practice PC have accepted personal responsibility for their patients' outcomes. These therapeutic outcomes are: cure of a disease, elimination or reduction of a patient's symptoms, arresting or slowing a disease process or symptoms, outcomes is the goal of pharmaceutical care. Pharmaceutical care involves identifying, resolving, and preventing drug-related problems (Strand et al., 1993; ASHP, 1993).

This study aim to make an assessment and gather baseline information that necessary for the implementation of pharmaceutical care and identify needs and issues confronting pharmaceutical care practice in Malaysia. Our objective of the study is to evaluate the pharmacist perception in term of pharmaceutical care in pharmacy practice.

Methodology

Constructions and development of the questionnaire

A questionnaire was designed to explore the pharmacist's understanding, knowledge, and their perceptions on the philosophy of pharmaceutical care and barriers to its provision, and also the current pharmacy practice. The initial pool of items was identified by previous studies, an extensive literature review on pharmaceutical care and pharmacy practice, and personal communication with researcher's supervisor.

The initial questionnaire consists of ninety items (Appendix 1). The main points in constructing the thirty items related to "the understanding of pharmaceutical care, as well as perceived important, competent, and practicality on pharmaceutical care process" were generated from the nine-steps pharmaceutical care process proposed by Strand, Cipolle, and Morley (1992), and also was drawn from concepts that inherent and representative of pharmaceutical care (Hepler and Strand, 1990; Hepler, 1987); five items of these thirty items were adapted from one New Zealand study (Dunlop and Shaw, 2002). Another twenty-two items related to current pharmacy practice was developed from numerous studies (Smith et. al, 1990; Rosenfeld et al., 1987; Smith, 1985). The main points used in constructing the seventeen items related to "barriers to implement pharmaceutical care" scale was drawn from several national and international articles (Rossing, 2001; AphA, 2001; Bell et al., 1998; Campbell and Saulie, 1998; Odedina et a.l, 1995; Sarriff, 1994; May, 1993; Swift, 1993; Louie and Robertson, 1993; Hassan, 1990a). The other twenty-one items related to pharmacists characteristics and practice background were not direct adaptation but were made up through review and designed based on the experiences of the researcher's supervisor, and feedback from our pretests as mentioned earlier.

The questionnaire consists of five sections as follows:

1 Section one: this section contains questions related to the samples of demographic characteristics and their practice profiles in the hospital and community pharmacy settings, respectively.

- 2 Section the questionnaire two: was understanding on pharmacists' and comprehension on pharmaceutical care. In this section, the instrument was designed according to the traditional Likert format (Likert, 1934) in which it was structured as statement of opinion and the response choice ranged from strongly disagree to strongly agree. The scores in each statement ranging from 1 to 5.
- Section three: this section was further divided 3 into two parts, part one was constructed to explore the pharmacists perception on the various activities related to their current pharmacy practice. The activities that were considered essential to both the hospital and community pharmacists include the management, dispensing, patient care, and public health activities. For each of the statements constructed in part 1; the respondents had to provide responses to the different scales, which is namely, the practice scale, the importance scale, and the competent scale. The practice scale measures whether the respondents are currently performing the activity or not. Then the respondents need to state the importance of such activity based on 5-point Likert scale. Lastly, the respondents were asked to rate their competency on the 5-point Likert scale same as importance scale. In the second part of section 3 of the instrument, the respondent was asked to state the percentage (%) of time spent in their current pharmacy practice. The respondent was also asked to state the percentage (%) of time that they would like to spend on the various activities of pharmacy practice.
- 4 Section four: this section comprises 15 items. It was constructed to explore the pharmacists' perception towards achieving and developing pharmaceutical care practice. For each of the statement constructed in this section, the respondents had to provide responses to three different scales; namely the importance, competence, and the practicality scales. Firstly, by rating a 5- point Likert scale, the respondents had to determine the importance of the stated activity, followed by stating their

level of competence to perform the activity. Lastly, the respondents had to determine the practicality of such activity with respect to the local scenario of the pharmacy practice in Malaysia.

5 Section five: this section explores the respondent's perception with regards to the barriers on the provision of pharmaceutical care practice. To ease the respondents' lists of perceived barriers to the provision of pharmaceutical care practice was tabulated along with a 5-point Likert scale. The respondents were asked to also specify any other perceived barriers, which were not in the list. Lastly, the respondents were requested to provide suggestion and recommendation to overcome such barriers.

Stages of construction and development of questionnaire

The process of instrument construction and development was carried out in four stages.

- Validity Phase: The opinions of the lecturers of the School of Pharmaceutical Sciences (USM).
- Phase of Criteria of item Mean and Standard Deviation with pharmacists at National Poisoning Center and postgraduate students.
- Reliability Phase: The Reliability Test with pharmacists at National Poisoning Center and postgraduate students.
- Pilot Phase: The Pilot Test with the pharmacists at Pulau Pinang

Validity Phase: The opinions of the lecturers of the School of Pharmaceutical Sciences, (USM)

Content validity is a subjective measure of how appropriate the items seem to a set of reviewers who have some knowledge of the subject matter (Wilkin *et al.*, 1992; McDowell and Newell, 1987).

After minor revisions of the English version of the questionnaire by the center of languages, the first draft of survey tool was reviewed by five faculty lecturers to establish content validity of the questionnaire. The purpose was to assess general acceptance of the survey instrument, comprehension, question organization and sequencing. It is also done to detect any flaws in the questionnaire and generate comments and suggestion. The researcher also hopes to seek their general opinions on the meaningfulness of the issue to the pharmacists as respondents.

All the five reviewers responded and returned the questionnaire with some reviewers giving positive comments through the direct discussion. The most common comments from two of the five lectures were on length of the questionnaire, which were considered as too long.

The questionnaire was then given to the researcher's supervisor for further comments and suggestions. The questionnaire was found to require some minor amendments particularly in section one where more of the variables were re-written as to be more specific such as question number (4), and number (5). In addition, two questions on the barriers to implement pharmaceutical care, which is about "lack of information technology" and "insufficient physical space" were added, and reworded the questionnaire's instructions and formatted to improve its clarity. The researcher then looked out for misunderstandings in terms of wordings, sentence constructions and ambiguity. At last, the first draft of the questionnaire was divided into five sections as discussed in section. The final draft of the questionnaire used in this stage is shown in (Appendix 2).

The items in the questionnaire were organized and sequenced based on the suggestion by Sproull (1988), Easy insensitive questions (sex, age, years of service) were asked at the introductory of the questionnaire to engage the respondents without taxing him/her. These will be followed by the main and more complicated questions. Sensitive or riskier questions came later in the survey so that if the respondent refuses to continue, less information will be lost. The sequencing of items of major interest was in logical order to facilitate smoother transitions from topic to topic.

Study design

The cross-sectional study was conducted, which involved exploring and collecting data from community and hospital pharmacists in the West and East Malaysia (Sabah and Sarawak), employing the self-administered mailed questionnaire approach.

Sample size calculation

The sample size was calculated based on a pilot test of our study and depended on two issues. Fir-

stly, the differences in mean scores between hospital and community groups. Whereas the sample size was calculated, using the software Power and precision in sample size calculation computer program (Borenstein et al., 2000). The detectable difference in mean scores of main outcome was set at 0.3 score, from 3.1 to 3.4 of score means of the two groups (Appendix A-20). We used the statistical (1- β) of 80% and the statistical significance level at $\alpha = 0.05$. The estimated sample size was 100 pharmacists for each group to detect these differences in mean scores.

Secondly, the sample size was calculated based on formula stated by Habbani *et al*, (2000) assuming 5% level of reliability (accuracy) with 95% confidence interval. The 60% of the target population (hospital and community pharmacists) estimated to have a particular characteristic (direct patient contact), since out of 3223 registered pharmacists in Malaysia, there are 1496 community, 413 hospital pharmacists (MOH, 2005). A sample size of 369 pharmacists was calculated as followed.

$$n = z \frac{p q}{d}$$
$$n = (1.96) \frac{(0.60)(0.40)}{0.05} = 369$$

Where:

n = The desired sample size

z = The standard normal deviate, set at 1.96 which corresponds to the level of the confidence interval

p = The proportion in the target population estimated to have a Particular characteristics

$$q = 1.0 -$$

d = The degree of accuracy desired, set at 0.05

According to the response rate of our pilot test (41% as mentioned earlier), 927 pharmacists were consider as a suitable target for our mail survey, so as to catch a number of respondents approximately equal to the calculated sample size.

Sampling technique

The community pharmacists participated in our study were selected according to pharmacies names, rather than pharmacists names. They recruited by systematic random sampling technique. Sampling frame was compiled from menus of "Pharmacy Directory Malaysian Pharmaceutical Society Kedah and Perlis", "website of Malaysian Pharmaceutical Society", and "Malaysian MIMS". Pharmacies names were arranged alphabetically and the last one of each three names were selected. One pharmacist represented each pharmacy.

Since we could not find any source to create such sampling frame for hospital pharmacists, subjects were recruited by stratified random sampling technique. Five and two sets of questionnaires were sent to 18 state hospital and 110 district hospitals, respectively. The chief pharmacists were asked to select and distribute the questionnaires to the required number of pharmacists working under their supervision. Cover letter addressed to the chief pharmacists, had specified that the pharmacists must be selected randomly from different pharmacy departments.

Data collection procedures

The mode of data collection chosen was a selfadministered mailed questionnaire. The method was chosen in relation to the big sample frame and the characteristics of the sample. Mail survey is an economical method of surveying large samples (American Statistical Association, 1997).

To reduce human error and survey's cost, all the tasks including those related to precision and accuracy in the data collection such as typing, printing, sorting and posting was done solely by the researcher. The steps taken had implications to the response rates and survey costs.

Several ways to increase the response rate of mails which have been suggested by Sproul, (1988) and Fowler, (1984) were done in this study: inclusion of a cover letter, providing clear directions; including all checked items rather than having to generate responses; structuring item responses for the entire questionnaire so that it could be answered quickly and easily. In addition, the addresses were typed on sticker paper rather than hand written to pledge the clarity of pharmacists' addresses. The questionnaire was professionally typed and printed so that its appearance gave the expression of credibility and professionalism.

In the final phase of the study, 323 and 604 questionnaires were mailed to the pharmacists in hospitals and community pharmacy settings on the 5 and 13 May 2005, respectively. In reducing the non-response rate of the mailed survey, verbal reminders regarding the survey were done by telephoning the subjects who had not responded by the first dateline (25th & 31st May 2005). The importance of the survey and a high response rate of the study were also emphasized. Reminders in the form of verbal conversation by Malay and Chinese trained data collectors were chosen because the researcher felt that this mechanism would be more friendly and thus more effective than written reminders. Receipt of the survey's feedback was recorded in a log sheet to monitor responses and minimize follow-up telephone calls. A second verbal reminder was not done due to financial constraints.

Data collection was finally terminated on the 30th June 2005, approximately two months after the initial mailing. The subjects' responses were then immediately entered into the chosen statistical computer software. All the ethical clearances was made with the concerning governing bodies.

Evaluation of non response bias

The failure to collect data from a high percentage of subjects in a sample was considered one of the main contributory factors to survey error (Fowler, 1984). The effect of non-response on survey estimates; depends on the percentage of these non-respondents and the extent to which those not responding are biased (i.e. systematically different from the whole population).

Data analysis

The data was analyzed using the SPSS® (Statistical Package for the Social Sciences) software program for windows® Version (12.0), and Microsoft Office Excel 2003. Both descriptive statistics and inferential statistics were used to analyze the data obtained from the research.

Descriptive statistics were used to organize the data (answers of the respondents to each structural indicators) obtained in the survey (i.e. frequency distribution, percentile, range, mean, and standard deviation). Thus was used to summarize the data in general and by different categories of each variable to describe the findings of the survey.

Inferential statistics that often rely on probability theory and statistical tests (i.e. One Sample t-test, Mann-Whitney U test, Student t-test, Chi Square test, Kruskal-Wallis test, ANOVA, Wilcoxon test, and 2-Proportion Sample test) were also used to enable the researcher to generalize the findings of the descriptive statistics to the population (all community and hospital pharmacists in Malaysia) that were being studied.

In addition, regression analysis was conducted to explore which of the respondents' variables that will be predictive of the likelihood to implement and develop pharmaceutical care practice in the studied population.

Result(s)

Of the 927 questionnaires mailed to the hospital and community pharmacists, 269 were returned back. Out of these, nine (9) were rejected as many of the sections were not filled or it was returned as a blank questionnaire. Thus, the final sample consisted of 260 usable questionnaires which represented a response rate of 28%. Further analysis of the usable questionnaires, in terms of the responses from both the hospital and community pharmacists; provide a response rate of 45.8% and 18.5%, respectively.

The respondents' demographic characteristics were collected in two institutions (Hospital and community pharmacies) and analyzed according to age, race, and gender of respondents.

The medians age of the hospital and community pharmacy respondents were found to be 29 and 36 years old, respectively (mean 31.8 ± 7.03 and 36.8 ± 8.78 respectively) (Table 1). It was observed that most of the respondents from the both the hospital and community pharmacy settings tend to be in the younger age group (24-35 years) (77%) and (48.2%) respectively, (P< 0.001, Chi-square) (Table 2).

Table 1. Descriptive statistics for age of hospital and community respondents

Pharmacy setting	Hospital (n= 148)	Community (n= 112)
Age (years)		
Mean \pm SD	31.8 ± 7.03	36.8 ± 8.78
Median	29.0	36.0
Minimum	25	24
Maximum	53	67

As for the ethnicity groups of the respondents, most of them were Malays (60%) with the remaining being Chinese (32.3%), and others (7.3%). An interesting observation was noted with regards to the preponderance of a particular ethnicity group with respect to the pharmacy practice setting. It was found that community pharmacy practice seems to be more favorable among Chinese respondents (57.1%) where as hospital pharmacy practice seems to be more favorable among Malay respondents (74.1%) (P <0.001, Chi-square) (Table 2). As expected, in relation to gender of respondents, more than two-thirds of them were female. It seems that majority of hospital (83.7%), and community (53.6%) respondents were females (P <0.001, Chi-square) (Table 2).

The socio-demographic characteristics of the respondents were summarized in Table 3.3. Most of the respondents (61.2 %) were graduates from USM, followed by other universities. Majority of respondents (77 %) were recent graduates (1990 -2005). The Chi-square analysis of the socio-demographic variables with the type of pharmacy practice settings were also shown in Table 2. Out of these variables listed in the table, only the respondent's pharmacy degree was noted not to be significantly different in regards to their practice setting (P= 0.49, Chi-square). Most of respondents in the study had earned a baccalaureate degree in pharmacy as their highest professional degree.

The medians length of practice of the hospital and community pharmacy respondents are 3 and 8 years respectively, (means 5.91 ± 6.02 and 8.33 ± 5.8 , for the hospital and community pharmacy respondents, respectively). Further analysis into the respondent's length of practice with the type of pharmacy practice settings revealed that the respondents from the hospital and community pharmacy settings tend to be new in practice (5 years and less in pharmacy practice). Chi-square analysis shows a significant association for the above observation (P< 0.001) (Table 3).

The majority of the respondents from the hospital pharmacy were mainly staff pharmacist (73%) with the remaining being the chief pharmacist (18.9%) or holding other positions in the pharmacy (6.8%). It was noted also that the majority of the hospital pharmacy respondents were

Table 2.	Socio-demogr	aphic backgroi	ind of respo	ondents in r	elation to	type of p	ractice sett	tings (I	hospital
and com	nmunity pharma	acy)							

Socio-demographic	Hospital †	Community †	Total ‡	P-value *	
Age category (years)					
24-35	114 (77)	54 (48.2)	168 (64.6)		
36-45	24 (16.2)	40 (35.7)	64 (24.6)	< 0.001	
46 and above	10 (6.8)	18 (16.1)	28 (10.8)		
Total	148 (100)	112 (100)	260 (100)		
Ethnicity					
Malay	109 (74.1)	47 (42)	156 (60.2)		
Chinese	20 (13.6)	64 (57.1)	84 (32.4)	< 0.001	
Other	18 (12.2)	1 (0.9)	19 (7.3)		
Total	147 (100)	112 (100)	259 (100)		
Gender					
Male	24 (16.3)	52 (46.4)	76 (29.3)	<0.001	
Female	123 (83.7)	60 (53.6)	183 (70.7)	<0.001	
Total	147 (100)	112 (100)	259 (100)		
Place of graduation					
USM	90 (61.6)	69 (61.6)	159 (61.6)		
UKM	23 (15.8)	4 (3.6)	27 (10.5)	0.002	
UM	9 (6.2)	6 (5.4)	15 (5.8)	0.003	
Other	24 (16.4)	33 (29.5)	57 (22.1)		
Total	146 (100)	112 (100)	258 (100)		
Year of graduation					
Less than 1990	22 (15)	36 (32.4)	58 (22.5)	<0.001	
1990 - 2005	125 (85)	75 (67.6)	200 (77.5)	<0.001	
Total	147 (100)	111 (100)	258 (100)		
Qualification					
Bpharm	97 (65.5)	71 (63.4)	168 (64.6)		
B.Sc pharmacy	33 (22.3)	32 (28.6)	65 (25)	0.40	
Mpharm	14 (9.5)	6 (5.4)	20 (7.7)	0.47	
Other	4 (2.7)	3 (2.7)	7 (2.7)		
Total	148 (100)	112 (100)	260 (100)]	

 \dagger Percentages of hospital and community pharmacy respondents are column %

‡ Percentages are total, * Chi- Square test

engaged in more than one practice site (73.6%). Only a small percentage of them were involved in a specific pharmacy practice site such as in the satellite pharmacy (2%) and drug information service (0.7%). While the practice profiles from the community pharmacy setting showed that the majority of the respondents in this study were owners (36%) or managers (30%), while 29% were staff pharmacists. More than two-thirds (78.6%) of the respondents practicing in independently owned pharmacies and mainly (76%) involved in retail business. Some (26.8%) of them considered their pharmacy to be large in size (> 800 square feet). In response to the question about the average number of prescriptions that they have received for each month, the answers given were varied and ranges from none (2.7%) to more than 300 prescriptions per month (0.9%). Nevertheless, most of them (69.6%) stated that they might receive prescriptions ranging from one to 30 for each month.

Table 3. Practice profile of respondents in relation to type of practice settings (hospital and community pharmacy)

Practice background	Hospital† n (%)	Community† n (%)	Total ‡	P-value*
Service duration (years)				
< 5	96 (65.8)	44 (39.6)	140 (54.5)	
6-10	25 (17.1)	30 (27.0)	55 (21.4)	<0.001
11-20	17 (11.6)	34 (30.6)	51 (19.8)	< 0.001
21-30	8 (5.5)	03 (2.7)	11 (4.3)	
Total	146 (100)	111 (100)	257 (100)	
No of pharmacists				
One	36 (29.3)	85 (76.6)	121 (51.7)	
Two	24 (19.5)	16 (14.4)	40 (17.1)	
Three	4 (3.3)	5 (4.5)	9 (3.8)	< 0.001
4-10	35 (28.5)	5 (4.5)	40 (17.1)	
11 30	24 (19.5)	0	24 (10.3)	
Total	123 (100)	111 (100)	234 (100)	
No of support staff				
None	1 (0.8)	3 (2.7)	4 (1.7)	
One	1 (0.8)	14 (12.6)	15 (6.5)	
Two	0 (0)	29 (26.1)	29 (12.5)	
Three	6 (5.0)	17 (15.3)	23 (9.9)	< 0.001
4-10	46 (38.0)	44 (39.6)	90 (38.8)	
11-40	37 (30.6)	4 (3.6)	41 (17.7)	
Above 40	30 (24.8)	0 (0)	30 (12.9)	
Total	121 (100)	111 (100)	232 (100)	
Geographical locations				
Rural	25 (20.0)	14 (12.6)	34 (14.4)	_
Urban	64 (51.2)	52 (46.9)	120 (50.8)	0.18
Suburban	36 (28.8)	45 (40.5)	82 (34.7)	
Total	125 (100)	111 (100)	236 (100)	
Consultation room				
Available	86 (68.8)	43 (38.7)	129 (54.7)	
Under-consideration	32 (25.6)	56 (50.5)	88 (37.3)	< 0.001
Not available	7 (5.6)	12 (10.8)	19 (8.1)	
Total	125 (100)	111(100)	236 (100)	

 \dagger Percentages of hospital and community pharmacy respondents are column %

‡ Percentages are total

Chi- Square test

		Hospital (n= 148)		Community (n= 112)					
No	Statement	Incorrect 1+2 n (%)	Unsure 3 n (%)	Correct ‡ 4+5 n (%)	Mean	Incorrect 1+2 n (%)	Unsure 3 n (%)	Correct ‡ 4+5 n (%)	Mean
1	A philosophy of pharmaceutical care	2 (1.4)	11 (7.4)	135 (91.2)	4.34	5 (4.5)	19 (17)	88 (78.6)	4.11
2	*PC is same as medication counseling service	60 (40.5)	33 (22.3)	55 (37.2)	2.89	63 (56.3)	23 (20.5)	26 (23.2)	2.45
3	Use drugs safely, effectively, and appropriately	0 (0)	2 (1.4)	146 (98.6)	4.47	1 (0.9)	2 (1.8)	109 (97.3)	4.46
4	Identifies the patient's drug related needs (DRNs)	2 (1.4)	3 (2)	143 (96.6)	4.41	1 (0.9)	6 (5.4)	105 (93.8)	4.38
5	*PC can be considered an extension of current pharmacy services	111 (75)	22 (14.9)	15 (10.1)	2.02	87 (77.7)	14 (12.5)	11 (9.8)	1.99
6	Assess patient's actual and potential drug related problems (DRPs)	0	7 (4.7)	141 (95.3)	4.41	2 (1.8)	8 (7.1)	102 (91.1)	4.32
7	Initiate a monitoring plan to check patient's progress	4 (2.7)	20 (13.5)	124 (83.8)	4.20	14 (12.5)	41 (36.6)	57 (50.9)	3.57
8	*PC is merely is a new name for clinical pharmacy	40 (27)	47 (31.8)	61 (41.2)	3.19	29 (25.9)	43 (38.4)	40 (35.7)	3.17
9	Empower patient's compliance, check patient's understanding, and provides counseling to patient	3 (2)	4 (2.7)	141 (95.3)	4.43	3 (2.7)	9 (8)	100 (89.3)	4.30
10	Documents his/her interventions to update the patient's record	3 (2)	15 (10.1)	130 (87.8)	4.26	7 (6.3)	19 (17)	86 (76.8)	4.05
11	*All patients taking medication require, pharmaceutical care (PC)	103(69.6)	25 (16.9)	20 (13.5)	2.17	66 (58.9)	23 (20.5)	23 (20.5)	2.38
12	The primary aim of PC is to improve the patient's quality of life	2 (1.4)	4 (2.7)	142 (95.9)	4.38	2 (1.8)	13 (11.6)	96 (85.7)	4.24
13	Prepare PC plan in collaboration with patient and other health care professionals	2 (1.4)	2 (1.4)	144 (97.3)	4.44	3 (2.7)	25 (22.3)	84 (75)	4.04
14	*A pharmacists require a post-graduate qualification to practice PC in Malaysia	48 (32.4)	20 (13.5)	80 (54.1)	3.33	28 (25)	42 (37.5)	42 (37.5)	3.16
15	Establishes therapeutic objectives based on the patient's desired outcomes	1 (0.7)	20 (13.5)	127 (85.8)	4.26	8 (7.1)	29 (25.9)	75 (67)	3.88
	Overall average	17.1	10.6	72.2	3.81	19	18.9	62.1	3.61

Table 4. Respondent's understanding of the fifteen statements of pharmaceutical care

‡ The scale used is as follows: 1 and 2- disagree and recoded as (incorrect answer), 3-Not sure, and 4 and 5-agree and recoded as (correct answer)

In this table, the incorrect answers as determined by the researchers and marked with an asterisk (*)

The overall average scores for the correct and incorrect responses for both the hospital and community pharmacy respondents were 72.2 % and 62.1 %, and 17.1 % and 19%, respectively. As noted in Table 3.8, the responses given by the respondents were varied in terms of the correct and incorrect answers. It was important to note that there were five statements (item number 2, 5, 8, 11, and 14) which were considered to be false statements. Thus, it was expected that the respondents gave a low score to those items, and means of respondents understanding of PC were ranged from 1.99 to 3.33. The result revealed that these five statements scored by less than 50% of the hospital and community pharmacy respondents as correct answers except for item 14 which was scored by 54% of the hospital and 37.5% community pharmacy respondents as correct answers. In contrast, the rest of the 10 statements were judged to be correct statements about the concept of pharmaceutical care. Out of these statements, seven of them (items number 1,3,4,6,9,12, and 13) scored by more than 90% of the hospital pharmacy respondents as compared to only three (3) statements (items number 3,4, and 6) scored by more than 90% of the community pharmacy respondents as correct answers, and the means were between 4.32 to 4.47. The remaining three statements (items number 7, 10, and 15) scored by less than 90% of the respondents and the means ranging of 3.57 to 4.26. However, the hospital pharmacy respondents showed a higher percentage to these items as compared to the responses given by the community pharmacy respondents.

Out of these variables listed in Table (5), only the respondents' year of graduation showed significant differences among cell means of their understanding of pharmaceutical care (p-value= 0.03). Hospital pharmacy respondents who graduated in the year 1990 to 2005 gave a higher rating of their perceptions (mean= 3.82) with regards to the pharmaceutical care process compared to those

Pharmacist characteristics		Understanding of	Average			
		Hospital (n= 148) Community (n= 112)		mean	P value ⁴	
	24-35	3.82	3.64	3.76		
Age group	36-45	3.77	3.66	3.70	0.564	
	45 and above	3.81	3.55	3.64		
	Malay	3.81	3.63	3.76		
Ethnic group	Chinese	3.77	3.62	3.66	0.105	
	Other	3.88	3.97	3.90		
Condon	Male	3.84	3.66	3.74	0.962	
Gender	Female	3.81	3.61	3.71	0.862	
	USM	3.82	3.63	3.74		
Diago of graduation	UKM	3.75	3.80	3.76	0.453	
race of graduation	UM	3.92	3.66	3.81		
	Other	3.78	3.61	3.68		
Voor of quaduation	Before 1990	3.72	3.63	3.66 ‡	0.02 *	
fear of graduation	1990-2005	3.98	3.61	3.75	0.05	
	B-pharm	3.82	3.64	3.74		
Qualification	B. Sc Pharmacy	3.78	3.68	3.73	0.110	
	M-pharm	3.80	3.33	3.66	0.119	
	Other	3.90	3.57	3.75		
Practice setting mean		3.81	3.63 ‡			

Table 5. The effect of respondent's characteristics and type of practice setting on mean understanding of pharmaceutical care

† Two factors interaction effects mode (Kruskal-Wallis Test)

 $\ddagger P < 0.05$ level Mann-Whitney U Test, * P < 0.05 level significant

who graduated prior 1990 (mean= 3.72). A similar observation was noted when compared to their counterparts in the community pharmacy setting who graduated prior 1990 (mean= 3.64) and after 1990 (mean= 3.63), respectively.

On the other end, there were no significant differences in the means of the respondents' perception of their understanding of pharmaceutical care among age groups, ethnic groups, gender, their place of graduation, and highest degree they achieved.

Similar analyses were conducted to determine whether the differences in mean of the respondents' perception of their understanding of pharmaceutical care were related their practice profile (that is, duration of service, geographical locations, and the presence and absence of a consultation room) and the type of practice settings (i.e., hospital and community pharmacy).

Discussion

The response rate of this study was 28%, in more detail; the hospital and community pharmacists provide a response rate of 45.8% and 18.5%, respectively. The result was not unusual for this type of research method. Several authorities in the survey research method had categorized the mail survey response rate into four categories: (i) weak, when the mail survey response rate was less than 40; (ii) common, when the return rate was between 40- 50%; (iii) good, when it more than 50%; (iv) excellent, when the response rate was 60% or more (Readex Learning Center, 2001; Richardson, 2000; Kelinger, 1986; Warwick, and Lininger, 1975). Evidence from other local studies had reported a response rate of 61.94% (Bahri, 2002), and a response rate of 51.1% (Othman, 2004). The possible explanation for the low response rate in this study may include the following reasons; (i) the concept and philosophy of pharmaceutical care was relatively new to most of the pharmacists; (ii) most of the pharmacists had no experience or had not implemented such a concept in their daily practice; (iii) the target population studied. The studies which were quoted obtained a reasonably high response rate which basically dealt with a specific population of pharmacists. Since one of the previous two local studies targeted a population of the managers pharmacists at the federal, state and district level in the Ministry of Health (MOH) (Bahri, 2002), and the second one targeted the hospital pharmacy settings only (Othman, 2004).

However the present study dealt with a diversity of pharmacists in both the hospital and community pharmacy settings. Although, one of the studies conducted locally produced a quite reasonable response rate (38.8%), which studied the population of the community pharmacists, sample was based on the MPS directory (Sarriff, 1994). However, based on the category of response rate mentioned above, it was considered a weak response rate. This phenomenon was not only confined to the local context but seems to be an international issue as one of the studies conducted in Canada targeted a population of the community pharmacists. The purpose of this study was to study the pharmacists' attitude and to determine whether community pharmacists are prepared to assume a more active role as members of the primary health care team. The study revealed that, the overall response rate was 35.2% (470/1337) with the highest response rate in the Prairie Provinces (40.6%) and the lowest in Quebec (24.4%) (Dobson et al., 2006).

The socio-demographic characteristics of respondents in relation to the types of practice settings

In terms of age groups, both the hospital (77%) and community (48%) pharmacy respondents tend to be in the younger age group (24-35 years). This was consistent with another local study conducted in 2004 with hospital pharmacists, which reported that this study population consists of quite young pharmacists, as majority of them (53.5%) have not exceeded 35 years old (Othman, 2004). However, comparisons across literatures were limited by the lack of studies particularly in the local community pharmacy setting.

In terms of ethnicity groups, significant findings were noted with regards to the preponderance of a particular ethnic group with respect to a particular pharmacy practice setting (P< 0.001, Chisquare). It was found that community pharmacy practice seems to be more favorable among the Chinese pharmacists where as the hospital pharmacy practice seems to be more favorable among the Malay pharmacists. This finding was similar

to another local study conducted by Ab Rahman et al., (2001). As expected, more than two-thirds (n= 183; 70.7%) of the respondents were female. It seems that a majority of the hospital and community pharmacy respondents were females (83.7%), and (53.6%), respectively. This might not necessarily reflect a response bias but merely the portrayed scenario of gender distribution in the government hospitals and community pharmacy settings. Slightly higher proportions of female pharmacists had been reported by other studies (Rossing et al., 2003; Kang et al., 2002; Dunlop and Shaw, 2002; Smith et al., 1990), and resemble a local study conducted by Othman, (2004). The "Feminization" of pharmacy was an aspect which had received much attention, with an increased number of studies in the developed and developing countries (Gidman et a.l, 2007; Carvajal and Hardigan, 2004; Hassell, 2003; Carvajal, 1999; Wolfgang, 1995; Muzzin et al., 1994).

The present study found that the majority of the respondents were USM graduates (n= 159; 61.2%), and most of the respondents (n= 200; 77%) were considered recent graduates (1990 - 2005). This was an expected finding as until 1995, there was only one pharmacy school in Malaysia, the Universiti Sains Malaysia (USM) which was established in 1972, to offer pharmaceutical education leading to a degree in pharmacy (B.Pharm.). Only in 1995, two more universities, the University of Malaya (UM) and the Universiti Kebangsaan Malaysia (UKM), started to offer pharmaceutical courses. Currently, there are eight pharmacy schools in the country (Ab Rahman and Bahari, 2004; Ab Rahman *et al.*, 2001; Yeoh, 1997).

The practice Profile of respondents in relation to the type of practice settings (hospital and community pharmacy)

With regards to the respondents' length of practice (or experience), the study found that the medians length of practice for hospital and community pharmacy respondents were 3 and 8 years, respectively. The mean lengths of practice were 5.91 ± 6.02 and 8.33 ± 5.8 , for the respondents in the hospital and community pharmacy settings, respectively. Also, the study revealed that most of the hospital and community pharmacy respondents were new in practice (i.e., 5 years and less).

Chi-square analysis showed a significant association for the above observation (P < 0.001). This observation was in agreement with a study conducted by Sarriff, (1994), which found that the mean length of practice for the community pharmacy respondents was 8.6 years. However, the mean and median length of practice for hospital pharmacy respondents in this study was less than what had been reported by Othman, (2004) which found that the mean and median duration of service were about 11 years. In response to questions asked about the number of pharmacists and their supporting staffs, the results found that only one or two pharmacists had been working in a pharmacy, however, the majority of pharmacies, particularly in the rural areas, employed only one pharmacist (MCPA, 2006b). Although the total number of registered pharmacists has increased over the years, there was still a marked shortage at an average of 40.9% of the pharmacists in the public sector (Bahri, 2002). The result also showed that the number of pharmacist was found to be less in the community pharmacy setting as compared to the hospital pharmacy setting. This finding was also observed in the study conducted by Sarriff, (1994) which reported that three-quarters of the community pharmacies had only one pharmacist. A similar observation was noted regarding the number of supporting staff in the pharmacy.

With regards to the geographical locations of the pharmacies, the study noted that there were less numbers (n= 14; 12.6%) of the community pharmacies in rural areas. This observation confirmed the annual report of the Malaysian Community Pharmacists Association (MCPA, 2006b) which stated that there were about 30 rural districts in Malaysia where there was no private community pharmacy. Most of these rural districts were presently served only by the government health facilities. The distribution of private (community) pharmacies varies widely across the states. A recent study found that there are 23,451 inhabitants per private pharmacy (Ab Rahman and Bahari, 2004; Soo *et al.*, 2002).

In response to the question asked about the availability of a consultation room, the response varied among the respondents. About two-thirds of the respondents from the hospital pharmacy setting (n= 86, 68.8%) stated that they had such

a consultation room, however, for the community pharmacy respondents (n= 56, 50.5%) responded that they would consider a consultation room. This scenario was alarming as patient counseling and education activities were part of the components of the pharmaceutical care (ASHP, 1999). As pointed out by the previous study (Othman, *et al.*, 2004) that counseling was introduced in most of the MOH hospitals as one of the components of the clinical pharmacy services.

The characteristics of the practice profile of the hospital and community pharmacy settings

The current study revealed that the majority of the community pharmacy respondents were owners (36%) or managers (30%), while 29% were staff pharmacists. Our finding was in contrast with a previous study by Sarriff, (1994), which found that most (50%) of the respondents were staff pharmacists with the remaining being managers (27%) and owners (7%). In addition the present study revealed that more than two-thirds (78.6%) of the community pharmacy respondents were practicing as independently owned pharmacies and a majority of them (76%) were involved in retail business. These observations were consistent as reported by Sarriff, (1994). With regards to the size of the pharmacy, only 26.8% of the respondents from the community pharmacy setting considered their pharmacies to be large in size (> 800 square feet). Several studies undertook the issues of the pharmacy design and the limitations of space. Space limitations of pharmacies are an obvious but potentially crippling obstacle to pharmaceutical care. These particular pharmacies did not make use of technical staff because the pharmacist felt that they overcrowded the dispensary and the time taken to actually dispense the medication was minimal. The small pharmacy size also lead to lack of privacy especially if there is no counseling booth, this made the patients come into the pharmacist office, if they have issue to discuss (Futter and Burton, 1998; May, 1993). Another study by Fortner et al., (2007) discussed such problems and tried to find some solutions. They mentioned that in the most pharmacies, this physical barrier is very difficult to overcome. Relocating to a large location is not practical in most cases. Each individual pharmacy must determine if a particular

section of their store can be made smaller in order to accommodate the practice of pharmaceutical care.

In response to the question about the average number of prescriptions that they received for each month, most of the community pharmacy respondents (69.6%) stated that they might have received prescriptions ranging from one to 30 per month, which indicates that they might have received one prescription or none per day. This phenomenon was not a usual finding in the local community pharmacy setting. However, the findings reflect the scenario of the general health care system in Malaysia. The medical doctor practitioners still hold the right for drug dispensing (Wong, 2001).

Respondents' understanding of the concept of pharmaceutical care

The study revealed that 72.2% of the hospital and 62.1% of the community pharmacy respondents had a correct understanding of the pharmaceutical care process and were generally well disposed towards it. However, in contrast to another study conducted locally, which showed a low ratio of the hospital pharmacists possessed knowledge about pharmaceutical care. Although pharmaceutical care was regarded as highly important; only 5% of the subjects were considered to have adequate knowledge about pharmaceutical care (Othman, 2004).

In this regards, there were five statements that were scored by less than 50% of both the hospital and community pharmacy respondents as correct answers. Those were, item number (2) "pharmaceutical care is the same as medication counseling service", items number (5) "pharmaceutical care can be considered as an extension of current pharmacy services", item number (8) "pharmaceutical care merely is a new name for clinical pharmacy", item number (11) "all patients taking medication require pharmaceutical care" and item number (14) "A pharmacist requires a post-graduate qualification to practice PC in Malaysia". These items were false statements about the concept of pharmaceutical care, thus, it was expected that the respondents may get a low scores. One of the reason attributed to this finding was probably the respondents may have some confusion about the several terms used. This was not an unusual phenomenon for those respondents who probably may not be familiar with the new concept of the pharmacy practice. A similar

observation was seen by Hassan, (1990a) who reported that, some of the study population believed that the phrase "patient-oriented" may essentially mean clinical pharmacy. Another study conducted locally showed that the respondents attempted to explain pharmaceutical care but most of them were misled into thinking that pharmaceutical care was only concerned with education and provision of information and carrying out some discrete services of clinical pharmacy such as therapeutic drug monitoring, drug information service, and in-patient services (Othman, 2004).

The confusion about the idea of the pharmaceutical care practice seems to be a global problem. As reported by May, (1993), that the majority of pharmacists lacked a true understanding of what pharmaceutical care was meant and how it differed from what they were currently practiced. In this regards, some pharmacists' commented that they were already practicing pharmaceutical care. They view that there clinical pharmacy activity, such as recommending pharmacokinetic dosing, rounding with physicians, provision of nutritional support, and drug information services, which were constituted by themselves as the provision of pharmaceutical care. Hepler, (1993) mentioned that the clarity of the pharmaceutical care definition may not have prevented pharmacists from inventing their own personal understanding and meanings attributed to it or from emphasizing some aspects at the expense of others. Further, he added that the response to the pharmaceutical care idea had been positive, not only in the United States but in other countries. Some practitioners, though, have responded "deceptively" by using the term "pharmaceutical care" to describe what after all are traditional pharmacy services.

Moreover, related to item number (14) "A pharmacist requires a post-graduate qualification to practice PC in Malaysia", was scored by 54% of the hospital and 37.5% of the community pharmacy respondents. In actuality, it was not necessary or mandatory for Malaysian pharmacists to require a post-graduate qualification to practice pharmaceutical care. The earlier pharmacy curriculum at the School of Pharmaceutical Sciences (USM) was based on courses offered by British universities, with put emphasis on chemistry, compounding, and pharmacognosy (Ab Rahman and Bahari, 2004). However, in a continuing effort to advance, expand, and promote the practice of clinical pharmacy in Malaysia, most of the Malaysian universities began to adapt its curriculum to focus on the patient care and on clinical practice (Hassan, 1993).

Many of these changes had been brought about by new faculty members returning from the United States with a Doctorate in Pharmacy (Pharma.D.) degree beginning in 1983. Curriculum changes were made based on courses in pathophysiology and therapeutics, clinical pharmacy practice, biostatistics, and pharmacokinetics. Therefore, the proportions of clinical components were increased to prepare students with specialized knowledge and skills to assume roles in the provision pharmaceutical care. The updated curriculum and activities were aimed at equipping students with the ability to prevent or correct drug therapy problems by participating in the initiation and monitoring of drug therapy. Daily clinical drug monitoring allows students to interact and communicate with patients, peers and other health practitioners.

The effect of socio-demographic characteristics of respondents and type of practice setting on their mean understanding of pharmaceutical care

Among the variables that were analyzed, only the year of the graduation was noted to have an influence on the respondents' perception of their understanding about the concept of pharmaceutical care. It was observed that those who graduated in the years 1990 - 2005 gave a higher score compared to those who graduated earlier. This was expected as the School of Pharmaceutical Sciences (USM) had undergone vigorous curriculum revisions (Ab Rahman and Bahari, 2004). Furthermore, the school had taken steps to impart clinical pharmacy in the country by offering a Master of pharmacy (M.Pharm) programme in 1992. As stated earlier, this observation was favorable for the hospital pharmacists compared to their counterparts in the community pharmacy setting. Although there was a trend to transform the community pharmacy to be more patient-oriented, but, the transformation was somewhat slow and the transition was not widely implemented, particularly in the local context (Higby, 2003; Sarrif, 1994). Although, the pharmacists in the hospital setting were in a more favorable environment as they are not to be a burdened by the business nature of their practice compared to their counterparts in the community pharmacy, however, the patient-oriented activities did not also widely exist (Higby, 2003; Sarrif, 1994).

Conclusion

We concluded from the findings of this study that although there is a sizeable gap in the practice perception of both groups of pharmacist. Pharmaceutical care concept is devastating tool among pharmacists. Regardless to practice site there are numerous unidentified barriers that reflects the practicability of pharmaceutical care in the practice setting.

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The Determinated On The Development Of Critical Thinking In Midwifery Students

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Abstract

Objectives: The aim of this study is to define and evaluate in faculty of health sciences midwifery students The California Critical Thinking Disposition Inventory (CCTDI) related factors.

Methodology: The population of the study consisted of 44, 4. class midwifery students studying in the faculty of health sciences a state university. The sample size was 41 students who volunteered to participate in the study. For data collection, a questionnaire inquiring about, age group, number of siblings, education level of parents and CCTDI were used.

Results: The research found that low levels of the midwifery students score on CCTDI. CCTDI sub-scale scores of students were found to be low and medium level. No statistically significant difference was determined between the socio demografic and the success grade average of the midwifery students in the CCTDI total score mean and the subscale score means (p>0.05).

Conclusions: To improve midwifery students' critical thinking disposition and skills presenting theoretical knowledge, scenario studies and making exercises, giving homework can be suggested, as implemented in this research. It can be developed tools for midwifery for scale the critical thinking disposition and skills in our country.

Key words: Critical Thinking, Critical Thinking in Midwifery, Midwifery Students

Introduction

Human presence, different from other creatures that make the mind, spirit and heart. It is necessary to add that thinking and talking. Thinking is function of the mind. Thinking is not enough. One thing you need to critical thinking¹. According to Yıldırım (2011), critical thinking is the process of searching, obtaining, evaluating, analyzing, synthesizing and conceptualizing information as a guide for developing one's thinking with self-awareness, and the ability to use this information by adding creativity and taking risks².

Methodology

The aim of this study is to define and evaluate in faculty of health sciences midwifery students The population of the study consisted of 44,4. class midwifery students studying in the faculty of health sciences a state university. The sample size was 41 students who volunteered to participate in the study. For data collection, a questionnaire inquiring about, age group, number of siblings, education level of parents and CCTDI were used. The data collected by the researchers created with the socio-demographic form and CCTDI. Delphi project conducted by the American Philosophical Society in 1990 developed CCTDI Turkish validity of the scale reliability study was conducted in 2003 by Kökdemir³.

Socio-demographic data of midwifery students, academic achievement scores year-end evaluation with CCDTI was performed. This inventory was developed based on the results of The Delphi Report in which critical thinking and disposition toward critical thinking were conceptualized by a group of critical thinking experts⁴. The original CCTDI includes 75 items loaded on seven constructs. These are inquisitiveness, open-mindedness, systematicity, analyticity, truth-seeking, critical thinking self-confidence, and maturity. Briefly, the inquisitiveness construct including 10 items that measures one's intellectual curiosity and one's desire for learning without considering any profit. The open-mindedness construct contains 12 items that measures being tolerant of divergent views and sensitive to the possibility of one's own bias. The systematicity construct comprised of 11 items,

and it measures how a person is organized, orderly, focused, and diligent in inquiry. The analyticity construct involving 11 items addresses the application of reasoning and the use of evidence to resolve problems. The truth-seeking construct including 12 items measures the disposition of being eager to seek the best knowledge in a given context, courageous about asking questions, and honest and objective about following inquiry. The critical thinking self-confidence construct consisting of 10 items measures the trust the soundness of one's own reasoning processes. Finally, the maturity construct involving 10 items measures cognitive maturity and the disposition to be judicious in one's decision-making³. Kökdemir (2003) carried out an adaptation study to transform this inventory into Turkish version because of cultural concerns. Finally, 51 items with six constructs were kept in the scale Reliability of the whole scale was found .88. Reliability coefficients of each subscale ranged from .61 to .78. In this study, 51 items with six constructs were kept in the scale reliability of the whole scale was found .80 Reliability coefficients of each subscale ranged from .61 to .73. Data were analyzed using numbers, percentage, mean and t test.

Results

Socio-demographic characteristics of the midwifery students were determined. Table 1 illustrates the distribution of data related to characteristics such as, age group, number of siblings, education level of parents.

Once total score means are examined, it is seen that the score mean obtained by the students was 207.14 ± 15.65 . CCTDI score means of the students taken into the scope of the study reveal that the score mean of the "truth-seeking" subscale was 24.73 ± 4.12 ; the score mean of the "Openmindedness" subscale was 39.41 ± 5.15 ; the score mean of the "Systematicity" subscale was 21.57 ± 3.16 ; the score mean of the "Self-confidence" subscale was 27.21 ± 4.52 ; the score mean of the "Inquisitiveness" subscale was 37.63 ± 6.29 (Table 2).

Table 1.	Distribution of Socio-Demographic Cha-
racteristi	cs of Midwifery Students

Characteristics	Number	%*			
Age Group					
17-19	23	56.1			
20-22	16	59.0			
23-25	2	4.9			
Number of Siblings					
A Sibling	9	22.0			
Two Siblings	9	22.0			
Three Siblings	18	43.9			
Four and more sinlings	5	12.1			
Mother Education Levels					
Illiterate	21	51.2			
Primary Education	16	39.0			
High School	4	9.8			
Father Education Levels	Father Education Levels				
Illiterate	3	7.3			
Primary Education	22	53.7			
High School	10	24.4			
University	6	14.6			
Total	41	100.0			

*Column Percentage

Table 2. Midwifery Students' Distribution of CC-TDI Scores

Sub Scales	X =	⊧ SD
Truth-seeking,	24.73	4.12
Openmindedness	39.41	5.15
Analyticity	50.10	6.08
Systematicity,	21.57	3.16
Self-confidence	27.21	4.52
İnquisitiveness,	37.63	6.29
Total	207.14	15.65

Discussion

Once total score means are examined, it is seen that the score mean obtained by the midwifery students was 207.14 \pm 15.65 (Table 1). They are determined to have had scores at low levels (239 points and below). In descriptive studies conducted using the CCTDI in schools of nursing in Turkey between 2005 and 2008 proved that the lowest score was 200.92 \pm 19 at low level, whereas the highest score was 277.0 \pm 19.7 at medium level^{5,6,7}. As for the descriptive studies carried out abroad, they determined that the lowest score was 264.70 ± 24.01 at low level, whereas the highest score was 312.3 ± 36.4 at medium level^{8,9}.

In the "truth-seeking" subscale, the midwifery students was determined 24.73±4.12 low level scores. In descriptive studies conducted on nursing students in Turkey, it was determined that the lowest score was 25.69±382 and the highest score was $44.0\pm7.0^{5,10}$. The studies conducted by Öztürk and Karayağız (2005), Sevil et al. (2005), Zaybak and Khorshid (2006), and Öztürk (2006) could not provide the possibility of experiment because they did not evaluate the subscales^{6,11,12}. Descriptive studies conducted on nursing students abroad observed that they had 30.12±4.06, the lowest, and 37.60 ± 6.90 , the highest, at low levels in this subscale^{8,13}. The results of Senturan's (2008) study and the results of other studies abroad related to this subscale revealed that nursing students had scores at low level, which is similar to the result of the study^{8,9,10,13,14,15}. The subscale of "truthseeking" reflects the disposition of evaluating alternatives or different ideas. It is recommended that both the course of "Critical Thinking" and the subjects in the education program should be rearranged in order to enhance the midwifery students' critical thinking dispositions and skills by taking these subscale characteristics into account.

In the "openmindness" subscale, the midwifery students was determined 39.41±5.15 close to medium level scores. It was observed that while nursing students had scores mostly at medium level in studies in which these subscales were investigated in Turkey, they had scores at low and medium levels in studies conducted abroad^{5,7,10,16,17}. The "openmindness" subscale expresses a person's tolerance towards different opinions and his sensitivity to his own mistakes. The basic logic in openmindness is a person's taking not only his own ideas but also the others' views and ideas into consideration while making a decision.

In the "analyticity" subscale, the midwifery students was determined 50.10±6.08 medium level scores. It was observed that nursing students had scores at medium and high levels in studies in which this subscale was investigated in Turkey, whereas they had scores at low and medium levels in studies conducted abroad^{5,8,9,11,12,13,14,16}. Moreover, the "analyticity" subscale expresses the disposition of paying attention to the situations that can potentially create problems and reasoning and using objective evidence even against difficult problems.

In the "systematicity" subscale, the midwifery students was determined 21.57 ± 3.16 . It was observed in studies conducted in Turkey and abroad that the nursing students had scores at low and medium levels in this subscale^{7,8,9,10,13}. It was also determined in the findings of the study that the students had scores at low level in this subscale. The "systematicity" subscale is the disposition of using a decision making strategy which is based on information and which follows a certain procedure instead of both an organized, planned and careful investigation and a behaviour of considering different views and a complex reasoning.

In the "self-confidence" subscale, the midwifery students was determined 27.21±4.52. It was also determined in the findings of the study that the students had scores at low level in this subscale. In descriptive studies conducted abroad, nursing students were seen to have had scores at medium level in this subscale. In studies conducted on nursing students in Turkey, they were found to have had 26.97±4.49 the lowest and 43.4±6.1 the highest^{7,10,17}. It was seen that the score obtained from this subscale in our study was parallel with the studies conducted in Turkey. The students' self confidence characteristics progressed, it is important to revise the conducted curriculum by paying attention to the characteristics of this subscale and examining the factors to be effective in its development. Although self confidence is personal, it is possible to tell to enhance self confidence of the individuals who have high critical thinking skills.

In the "inquisitiveness" subscale, the midwifery students was determined 37.63 ± 6.29 . It was also determined in the findings of the study that the students had scores at low level in this subscale. In studies conducted both in Turkey and abroad, Şenturan (2008) determined that nursing students scored 39.31 ± 6.81 at low level in this subscale, Topçu and Beşer (2005) determined that they had scores at medium level as 48.65 ± 5.8 , Ip et al. (2000) determined that they had scores at low level as 38.30 ± 6.48 , and Shin et al. (2006) determined that they had scores at medium level as $44.64\pm5.19^{9.10,13,17}$. The "inquisitiveness" subscale reflects the disposition of a person's obtaining information and learning new things without any expectations of profit or benefit. It is recommended that in the opening course of "Critical Thinking" and the subjects in the education system should be rearranged in order to enhance the students' critical thinking dispositions and skills by taking these subscale characteristics into account.

No statistically significant difference was determined between the success grade average of the midwifery students in the CCTDI total score mean and the subscale score means (p>0.05). According to the results of the studies conducted both in Turkey and abroad, no statistically significant difference was determined between the grade averages of the academic success and the CCTDI score means^{3,18}. They explained the fact that a statistically significant difference was not determined in the studies conducted abroad on nursing students was owing to the fact that the scale was not for nursing students.

Conclusions

The research found that low levels of the midwifery students score on CCTDI. CCTDI sub-scale scores of midwifery students were found to be low and medium level. To improve midwifery students' critical thinking disposition and skills presenting theoretical knowledge, scenario studies and making exercises, giving homework can be suggested, as implemented in this research. It can be developed tools for midwifery for scale the critical thinking disposition and skills in our country.

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The use of a total ossicular replacement prosthesis after radical trepanation of temporal bone (TORP after TROT) - a case report

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Abstract

This paper presents an original operative method of hearing recovery after radical trepanation of the temporal bone (lat. Trepanatio radicalis ossis temporalis, TROT) in a young girl who underwent an operation for a massive cholesteatotoma.

A 13-year old girl was admitted to our hospital after TROT. There were no signs of cholestearoma or infection. The girl's parents refused implantation or any hearing aids due to possible aesthetic problems.

The described operation was performed in two steps. The first step was performed in order to restore the destroyed cavum tympany with chondroperichondral novel membrane with pin-like "guide" as collumela. The second step was insertion of TORP (total ossicular replacement prosthesis) after guide excision.

Clinical and audiometry follow up showed hearing recovery with no aesthetic impairment and a closure of air bone gap (ABG) to the values of 5 to 15 dB.

Key words Radical trepanation of the temporal bone, total ossicular replacement prosthesis (TORP), hearing recovery

Introduction

By definition, radical trepanation of temporal bone (lat. Trepanatio radicalis ossis temporalis/ TROT) includes mastoidectomy, antrotomy, cleansing of the whole middle ear and closure of the Eustachian tube. [1] This procedure is often indicated in patients with huge cholesteatoma processes or tumors in the middle ear and the mastoid region. After TROT the hearing impairment frequency is high. [2]

There are many attempts to improve hearing after this procedure (BAHA, [3] Vibrant-Soun-

dbridge, [4] Cochear implants... [5]). In case of partial defects in ossicular chain, there are different types of tympano-ossiculoplasty with partial or total prosthesis in use. [6] If there isn't any bone left, a total prosthesis must be used.

The cost of these procedures are so high in the developing countries but there are also aesthetic problems in young individuals which prevent them from accepting the hearing aids. Therefore, here we represent the original two-step operative method for hearing reestablishment.

Case report

A 13-year old girl was admitted to the University hospital with poor hearing in the left ear.

She underwent her first operation when she was 8 years old, for suppurative chronical otitis with cholesteatoma. She experienced severe pain in her left ear with moderate mastoidismus, and otorrhea. Laboratory findings indicated inflammation (hs CRP elevation with moderate leucocythosis). At that time tympano-ossyculosplasty, antrotomy and partial mastoidectomy were performed. Intraoperative finding was positive for cholesteatoma spreading through attic subtegmentaly and across the upper part of mastoid. After one year, due to residual cholesteatoma and new onset of granulations over the ossicular chain, radical treapanation was performed.

Four years after radical operation clinical findings were very good. CT of the mastoid showed no signs of residual cholesteaoma. There were no recidives of cholesteatoma and no signs for infection. Pure tone audiometric examination showed insufficient air-conduction. At her age, the patient and her family refused any surgical procedure with the use of visible hearing aids.

At admission otoscopic finding revealed wide postoperative cavity after radical mastoidectomy with good epithelization. There were no signs of infection or residual cholesteatoma. Audiometrical findings were with satisfied bone-conduction (aprox. 25- 30 dB in whole frequencies) and poor air-conduction (aprox 55 dB) in the same range (see fig 1.)



Figure 1. Audiometry before stage one

After preoperative planning the operation was performed in two steps. Both operations were performed in general endotracheal anaesthesia with intubation.

After local infiltration, through retroauricular incision the whole epithelized cavity was performed. The first step of operation went through several phases.

At the beginning of the operation we performed deepithelization of the common cavity after radical trepanation of the temporal bone. Special attention was paid not to injure footplate of stapes, promontorium (first turn of cochlea) and facial nerve.



Figure 2. Deepithelization of common cavity after radical trepanation of temporal bone

Deepithelisation is very necessary, with special attention paid to the area of former tympanal space. Deepithelization in other parts should be performed only in case of suspicion of infected mastoid cells.



Figure 3. Identifying a closed Eustachian tube and its opening

It is very important to see the place of the tube's closure and to slightly release a tympanal orificium of the tube.



Figure 4. Aspiration or sondage of the auditory tube

This procedure is useful in identifying sticky, transparent secret which confirms the right and proper tube position.



Figure 5. Preparing of a neomembrane



Figure 6. Created neomembrane

Creating a neomembrane / Preparing a chondroperichondral flap from tragus

After skin incision on the external ridge of tragus and visible cartilage, a semilunar excision was performed. Excised cartilage was divided in the shape of butterfly wings for neomembraine. One half of cartilage was trimmed in order to reduce the volume and thickness. On another part an triangular semiexcision was performed where the base of the triangle was fixed to the cartilage. This triangular cartilage part will be used as a "guide" (see fig. 6)



Figure 7. Positioning of the neomembrane with cartilaginous ,,guide"

Two marks should be fallowed: anteriorly, above the tubal orifitium and posteriorly, on the bony part of the facial ridge. The "guide" must be positioned to touch the base of stapes. This "guide" enabled sound conduction and prevented collapsing of a neomembrane. The "guide" is useful in the second stage - to easely apply/ find a footplate of stapes.

The closure is very delicate. Peripheral part of chondroperichondral flap must be fixed under the planned excision during the deepithelisation and posterior part must lie on the facial ridge of the antral part (see fig.8). Good fixation of this kind of graft ensures a good aeration and good elasticity of neomembane.



Figure 8. Closure of neo- cavum tympany and tamponage of external auditory canal

At the end of this procedure the postoperative course was uneventful. The dressing was changed on the third postoperative day. The patient was dismissed from the hospital after 6 days.

One month postoperatively audiometry showed better air- and better bone- conduction.



Figure 9. Audiometry after stage one - closed "cavum parvum" and influence of the "guide" after stage one

Tree months after the first stage the **second stage** was performed. Using the transmeatal approach, the neomembrane was identified and opened like a tympanomeatal flap. The cavity below neomembrane was well epithelized with respiratory epithelium. This respiratory-epithelium invasion probably originates from the Eustachian tube. The "guide" was seen with epithelium on the footplate of stapes. A proximal part, fixed to the neomembrane, was cut with micro-scissors and totally removed. A small incision on the stapes footplate was made. Thereafter the TORP was placed in a standard way.

Stage two also went through several phases:

Prepairing a tympanomeatal flap A classical approach of preparing a tympanomeatal flap on five millimeters of fixed neomembrane border which was very slightly pushed up until the "guide" was exposed.

Removing a "guide" The trapezoid space, which remained after removing the "guide" was very suitable for the placement of the upper part of TORP.

Insertion of TORP in its place (see fig.10 and 11)



Figure 10. Prosthesis on the place (intraoperative)



Figure 11. Closure of tympanomeatal flap with a slight tamponage

The patient was dismissed from the hospital two days after the procedure without any complications. She did not experience dizziness, vomiting or severe pain.

One month after the second stage postoperatively otoscopic findings were very good. Audiometrical findings after one month were showed (see fig. 12)



Figure 12. Audiometry one month after stage two of the operation ABG in range of 5-15 dB

Discussion

The use of this operative method was based on the wish to recover hearing in patients with hearing impairment after radical trepanation of temporal bone. These patients did not want to have any visual impairments. It should not be forgotten thatfor a patient with childhood cholesteatoma this process has some special characteristics.[7] This patient was a girl in puberty ...

This patient had a few wishes. First, to have a better hearing, security after primary cause and no aesthetic changes (she did not want any hearing aids).

Considering different types of tympanoplasty and reported success with different ossicular prosthesis, [8,9,10,11] the right questions is: Who are the suitable candidates and why use this prosthesis? The patients had good bone-conduction but air-conduction was poor. The "Aerial-Vario" prosthesis is ideal for fast and adequate positioning depending on two important things. The first is the possibility of changing distances between stapes footplate and neomembane. The second is the accommodation of tissue elasticity (neomembrane) for better conduction. Do not forget that neomembrane's posterior ridge is on the bony facial canal up to the second knee, in lower part of antrum. For this reasons prosthesis must be adequate before implantation.

The first stage is delicate - how to find the tube's closure. In case of small tubal diameter in

tympanal part, it is preferable to make it larger using a diamond bur. Finding a "gluey" tubal secret is a proof that tubal lumen was formed. Curettage of a tympanal part of the tube should support the microvascular and epithelial invasion in "cavum parvum". In stage two only vascular net was formed. For this reason stage two should be performed after tree months.

Neomembrane creation differs from other cartilage and/or perichondral grafts. [8,12,14,15] For this neomembrane the tragal [17,18,19,20] cartilage-perichondral- "butterfly" graft [21] was used. This shape is large enough to cover the future neo-cavum [15]. One half of the cartilage had been removed to enable better elasticity depending on the weight and volume of the graft. Taking into consideration that this patient could have a tubal disfunction, cartilage "guide" (triangular pin-like cartilage part) was used for two reasons. First, to prevent collapsing the neomembrane and second, for sound conducting (collumela effect).

"Cavum parvum" is not the same as the one Wullstein reported on type IV of tympanoplasty[1]. In this case it is a space under the neomembrane bordered anteriorly, superiorly and inferiorly on the new ridges (made with 0,5 mm diamond bur), and which lies on facial ridge posteriorly.

The mastoid cavity was not filed or closed because of the ability to view a mastoid part. Of course, filing of mastoid cavity is possible with bone dust or commercial preparations [22,23,24] as in any "wall-down" tympanoplasty.

The second stage is simple – cut out the "guide", remove it and position a T.O.R.P. in its place. It is very useful to make [25] a small incision on the stapes footplate to prevent dislocation or migration of the prosthesis. For this reason, the upper part of prosthesis was placed in an empty triangular space inside of neomembrane.

Before the first stage, the audiometrical findings showed 25-39 dB of bone-conduction and 55 dB of air-conduction. Air-bone conduction gap was 30 dB. Two months after the first stage ABG was 10 to 20 dB (depending of frequencies). It showed better value in ranges between 250 Hz and 2 kHz. At this time, the bone conduction also showed increased values from 5 dB. It could have been a sign that the cochlear activity was getting better. After three months, the second stage was performed. Three months after the second stage, the audiometry showed BC of 20 - 25 dB and AC of 30 - 35 dB. Air-bone conductivity gap (ABG) was 5 - 15 dB.

With the use of TORP, a ABG closure was expected.[26,27] The surprising fact was that the bone conduction was improving. The reason for it may be found in a better and more permanent stimulation of cochlea.

Conclusion

It is a new, two-stage operative method with very good results (benefit of 20 dB for bone-conduction and 40 dB for air-conduction).

"Aerial-Vario" prosthesis is very useful in this operation. The possibility of changing the distance and safe positioning is very relaxing for the surgeon.

This work gave a new light to cochlea recovery processes. This method costs less than hearing aids.

The patient was very satisfied – no cosmetic impairments.

This is a very good operative method for hearing recovery in relatively young patients with good bone-conduction. Compared to other implantable systems it is much cheaper and it is followed by better audimetrical findings.

This method could be performed in all patients after radical trepanation of temporal bone for better hearing.

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"Hearing recovery using the TORP after radical trepanation of temporal bone"

Rancic D. S., Serbia (Abstract book number: A315), 1st Meeting of HYPERLINK "http://www. eaorl-hns2009.com/"the European Academy of ORL-HNS HYPERLINK "http://www.eaorlhns 2009.com/"in collaboration with EUFOS Mannheim, Germany, 2009

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Life in 3D: A 10 year review of literature on the application of cone beam computed tomography in dental implantology

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Abstract

This study reviewed the literature on the use of cone-beam computed tomography (CBCT) imaging specifically for its benefits regarding oral implantolgy over the past 10 years. A detailed online search of literature from February 2010 to 2000 was conducted. It revealed 96 papers. After a detailed screen 26 papers were found to be clinically relevant and analyzed in detail. An attempt was made to focus on how this relatively new technology has impacted the field of dental implantology and to what benefit is it being used and also what avenues need to be further explored so we can get the best out of this technology.

Key words: Cone Beam computed tomography, Implant logy, radiology

Introduction

Radiology is a priceless tool in the diagnostic assessment of the dental patient. The advent of the panoramic radiograph was as an excellent screening modality to recognize jaw structures allowed clinicians an expanded view beyond the capabilities of single film, periapical radiography but in this day and age, three-dimensional (3D) craniofacial imaging techniques have opened up a whole new dimension regarding use of radiology in different facets of dentistry.

Dedicated Cone-beam computed tomography scanners for the oral and maxillofacial (OMF) region were pioneered in the late 1990s independently by ARAI et al. in Japan and MOZZO et al. in Italy. Since then there has been an explosion of interest in this new imaging technique in the OMF region by different research groups. [1] These scanners are 3D in their acquisition of images and offer usable images from systems that are sufficiently compact and inexpensive to be installed in clinics and private dental, oral surgery, and orthodontic practices. With these special lowdose craniofacial CBCT scanners, the era of 3D digital imaging in dentistry began. [2]

The Cone-beam computed tomography technique allows more rapid data acquisition than traditional Computed tomography. Sophisticated software is available for every unit, allowing image processing and measuring. Many articles on Cone-beam computed tomography uses and benefits have been published. With a versatile range of applications in the dental specialties, Cone-beam computed tomography is becoming a valuable aid for diagnosis and treatment planning. Because it is a new technology, one can expect to see more articles on new applications and benefits soon. [3, 4, 5, 6, 7, 8, 9]

Although traditional computed tomography is still used in many clinical situations when 3D information is needed, its use has been limited in dentistry due to its high cost, low vertical resolution, and high dose of radiation. The cone-beam computed tomography scanner is intrinsically 3D in its acquisition of images and provides usable images from equipment that is compact and affordable for small diagnostic centers. [10,11]. The use of cone-beam CT in clinical practice has a number of potential advantages over conventional tomography, such as easier image acquisition, higher image accuracy, reduced artifacts, lower effective radiation doses, faster scan times, and greater costeffectiveness. [18]

Types of computed tomography scanners

Computed tomography can be divided into 2 categories based on acquisition x-ray beam Geometry; namely: fan beam and cone beam .In fanbeam scanners, an x-ray source and solid-state detector are mounted on a rotating gantry. Data are acquired using a narrow fan-shaped x-ray beam transmitted through the patient. The patient is imaged slice-by slice, usually in the axial plane, and interpretation of the images is achieved by stacking the slices to obtain multiple 2D representations.

As the name implies, cone-beam CT units emit a cone-shaped x-ray beam rather than the fan-shaped beam emitted by conventional CT technology. Because the beam covers the entire region of interest, images can be acquired in only 1 pass or less around the patient's head. After the x-ray beam passes through the patient, the remnant beam is captured on a 2D planar detector- either an amorphous silicon flat panel or an image intensifier/CCD detector. The beam diameter ranges from 4 cm to 30 cm and captures from 160 to 599 images which are used to compute a spherical or cylindrical volume from which planar or curved reconstructions can be extracted in any orientation. Voxels are isotropic and can be as small as 0.125 mm3. Cone-beam computed tomography can also be used to generate 3D images of bone and soft-tissue surfaces.[16,17]. As Cone Beam Computed Tomography (CBCT) scanners utilize a cone beam, which radiates from the x-ray source in a cone shape, encompassing a large volume with a single rotation about the patient the Images then can be reconstructed using algorithms to produce 3-dimensional images at high resolution.

Mainly cone-beam computed tomography systems have been designed for imaging hard tissues of the maxillofacial region. Cone-beam computed tomography is capable of providing sub-millimeter resolution in images of high diagnostic quality, with short scanning times (10–70 seconds) and radiation dosages reportedly up to 15 times lower than those of conventional computed tomography scans.[12].

Most systems have scan times of less than 20 seconds, and use personal computers as data processors. Cone-beam computed tomography is, however, not as well suited as traditional computed tomography for examining lesions involving both soft tissue and bone, because it is difficult to obtain good soft tissue detail. [15]

Use in dentistry

Cone –beam computed tomography was used in three major indication fields. [14]

Dental imaging: (a) Topography of impacted teeth, especially third molars, and their relation to the mandibular canal and the antrum of Highmore. (b) Extended cystic and inflammatory processes. (c) Shape of the mandibular condyles, pathologies of osseous structures of the temporomandibular joint. (d) Orthodontic indications. (e) Periodontologic indications.

Implantalogy: (a) Implant planning, data acquisition for navigated procedures. (b) Situation post implantationem.

Maxillofacial indications: (a) Trauma, pre- and postoperatively. (b) Imaging of local tumoros processes. (c) Imaging of paranasal sinuses, especially antrum of Highmore. (d) Osteomyelitis. (e) Clefts

Advantages and disadvantages of cone-beam computed tomography

The advantages of CT-based systems are (1) uniform magnification; (2) a high-contrast image with a well defined image layer free of blurring; (3) easier identification of bone grafts or hydroxyapatite materials used to augment maxillary bone in the sinus region than with conventional tomography; (4) multiplanar views; (5) 3-dimensional reconstruction; (6) simultaneous study of multiple implant sites; and (7) the availability of software for image analysis.

The disadvantages of computed tomography include (1) limited availability of reconstructive software; (2) expense; (3) higher doses of radiation compared with conventional tomography; (4) lack of understanding of the dentist's imaging needs by the radiological technologists and medical radiologists who acquire and interpret the computed topographic images; and (5) lack of usefulness for implant-interface follow-up because of metallic streak artifacts.[22]

Cone beam computed tomograhy and dental implants

It has been well documented that cone-beam computed tomography produces reliable data that facilitate the assessment of bone dimensions (both height and width) and/or the localization of important anatomical landmarks such as the mandibular canal, the mental foramen, the nasopalatal duct and the maxillary sinus [20]. Presently, cone-beam computed tomography is also being widely used for the examination of temporomandibular joint and sinus pathology, trauma in the maxillofacial region and, routinely, in oncology [21]. In the last few years, cone-beam computed tomography has become one of the most useful and significant examinations for the maxilla and mandible. Since implant treatment has become the preferred method in cases of partial or total edentulism, the use of cone-beam computed tomography has increased mainly due to its high diagnostic accuracy. [19]

Total 14 100% Implantology Planning 7, 48, 67, 109, 147, 164 6 55% Surgical guidance template 5, 122 2 18%, Other 21, 50, 180 3 11 (13%) papers dealt with the use of CBCT imaging in implantology. In 6 (55%) papers CBCT imaging was used to assess the region of interest (ROI) for dental implant planning 7, 48, 67, 109, 147, 164. 2 (18%) papers described the fabrication of surgical guidance templates with the use of CBCT data5,122, while in 1 paper CBCT imaging was used for navigation during implant placement 50. There were two case reports on the use of CBCT imaging for diagnosis of an antral floor perforation 180 and evaluation of a peri-implant defect21.

Planning

Munetaka Naitoh, et al., 2010 [23], compared the most common diagnostic imaging modalities for cross-sectional imaging in dental implant planning that are being currently used are cone-beam computed tomography (CBCT) and multislice CT (MSCT). These two diagnostic modalities were used for the location and course of various neurovascular bony canals, such as the bifid mandibular canal, accessory mental and buccal foramina, and median and lateral lingual bony canals in the mandible, which are of great important for dental implant fixture insertion and implant-related bone grafting.[24] However, the relative detection of these anatomic structures had not been fully clarified. Hashimoto et al., [25] reported that the image quality of cone-beam computed tomography images using the 3DX unit (J. MORITA Mfg. Corp., Kyoto, Japan) were better than that of multislice computed tomography images for all of the following: cortical bone, cancellous bone, enamel, dentin, the pulp cavity, lamina dura, and periodontal ligament space. Mischkowski et al., [26] and Dreiseidler et al., [27] reported that the mandibular foramen, mandibular canal, mental foramen, and incisive foramen could be observed and the diagnostic quality was the same between cone-beam computed tomography and multislice computed tomography. The study concluded that depiction of fine anatomic features in the mandible associated with neurovascular structures is consistent between cone-beam computed tomography and multislice computed tomography images.

(Niek L. et al 2010)[28] performed a study to investigate the reproducibility of 3 different tracing methods to determine a reliable method to define the proper anatomical position of the mandibular canal based on cone - beam computed tomography (CBCT) data. All mandibular canals were traced by 3 different methods using 3-dimensional image-based planning software. Method I was based on coronal views, also known as cross-sections. Panorama-like reconstructions were the starting point for method II. The third method combined methods I and II. Surgical procedures of the mandible, such as osteotomies, bone harvesting procedures, or placement of dental implants, are often involved with a possible unintentional impairment of the inferior alveolar nerve (IAN), causing a broad range in altered sensory perception.[29] This may result in either transient or persistent paresthesia, anesthesia, or even disabling dysesthesia, mostly affecting the lip and chin region. To avoid this complication cone-beam computed tomography is being and should be utilized to precisely locate the inferior alveolar nerve's anatomical location. The best reproducible method for mandibular canal tracing was found to be the combined method III.

L. Dubois et al 2010 [30] strongly recommend use of cone-beam computed tomography prior to implant placement in the anterior mandible. Upper airway obstruction secondary to massive hemorrhage in the floor of the mouth is a rare, but is a potentially life threatening condition, which can occur as a result of this type of surgery. Severe bleeding and formation of a large hematoma in the floor of the mouth are the result of vascular trauma. [31] Hemorrhage caused by damaging the sublingual arteries during implant surgery depends on the anatomy of the bone at the implant site, the diameter of the vessel, and/or the distance of the vessel to the bone. Therefore cone-beam computed tomography prior to such a surgery is invaluable.

Munetaka Naitoh et al 2009 [32] Assessed the accessory mental foramen using cone-beam computed tomography (CBCT) images. The paper implied that cone-beam computed tomography should be the preferred method to exactly locate any accessory mental foramina prior to implant surgery as the resolution obtained on cone-beam computed tomography images was reportedly higher than that on helical CT images. [33] Also, effective radiation doses with small exposure volume were lower in comparison with those for helical computed tomography.[34,35]

Rubelisa Cândido Gomes de Oliveira et al., 2008 [36] Assessed the trabecular bone density at implant sites on CT images. Two oft-mentioned factors that are considered important in the consolidation of the bone-implant interface and that can influence surgical technique, healing time, and progressive loading during prosthodontic rehabilitation are bone quality and bone quantity. The term bone quantity is most often understood as the amount of bone (e.g., height and width of the alveolar crest) available for implant installation, whereas bone quality is a far more comprehensive term with no clear definition, encompassing several aspects of bone physiology, degree of mineralization, and structural properties (architecture, morphology). The importance of each aspect in implant treatment is still not fully understood.[37] the study concluded that different qualities of bone can be found in any of the anatomical regions studied (anterior and posterior sites of maxilla and mandible), which confirms the importance of a site-specific bone tissue evaluation prior to implant installation. Also the paper emphasizes that cone-beam computed tomography appears to be the medium of the future due to its accuracy and lower radiation dose, thus, more research should be carried out to improve this dental imaging method.

Christos Angelopoulos et al., 2008. [38] Compared digital panoramic radiography and conebeam computed tomography for the identification of the mandibular canal as part of pre surgical dental implant assessment. The paper reinforced the view that cone-beam computed tomography seems to be a promising imaging modality which also reduces patient exposure considerably, compared with ordinary computed tomography. The report concluded that cone-beam computed tomography reformatted panoramic images were found to be superior to digital panoramic images for identification of the mandibular canal. The posterior third of the mandibular canal being better depicted, regardless of observer and imaging modality. Because the literature on the topic in question was limited, the report emphasizes that further investigation is required to confirm the results of this study and although present studies demonstrated that cone-beam computed tomography reformatted panoramic images are superior in diagnostic efficacy to digital panoramic images, cone-beam computed tomography images should not necessarily replace digital panoramic images as conebeam computed tomography studies cause higher radiation exposures (4 to 20 times greater).

Hatcher DC, Dial C, Mayorga C.2003 [40] in their study showed that pre-surgical assessment of proposed implant sites requires very specific and accurate data and cone-beam computed tomography is a valuable tool for this purpose. Imaging had always been used to assist with the implant site assessment but until the recent introduction of cone beam computed tomography scanners, the available imaging had a low value when considering the ratio between diagnostic potential, cost of study, and risk to the patient. Cone-beam computed tomography scanners were nearing the end of their first-generation that were dedicated maxillofacial imaging modalities and had proven to be an extremely useful imaging tool for pre-surgical assessment of implant sites. Cone-beam computed tomography scanners were and still easy to use and produce a 3-D image volume that can be reformatted using software for customized visualization of the anatomy. Protocols had been developed that optimized the visualization of image for implant site assessment and they required further research for the best possible outcomes/results.

Sato S et al., 2001 [40] Studied the clinical application of a cone-beam computerized tomography system to assess multiple two-dimensional images for the preoperative treatment planning of maxillary implants. It is a well known fact that accurate assessment of the location of the maxillary sinuses, incisive canal, and nasal cavity, as well as the height, width, and angulation of bone is essential for implant treatment planning. They also concluded that cone-beam computed tomography images provided useful information for evaluating the morphology of the maxilla and visualizing the location of the maxillary sinuses, incisive canal, nasal cavity, and the relationship of the radiopaque template to the bone.

Ito K, Gomi Y et al 2001. [41] In their study also proposed that 3-D computed tomography scanning data can be easily reconstructed to provide alternative images; i.e. conventional X-ray tomography-like or panoramic X-ray-like format, which can be used for presurgical examination for implant therapy. They also concluded that so far no control studies had been performed showing that computed tomography scans were actually needed before implant treatment planning and that in the future, well controlled studies should be carried out Terakado M et al., 2000. [42] The purpose of this study was to investigate the clinical usefulness of conebeam computed tomography which was very new at the time for the diagnosis of diseases in the oral and maxillofacial region. Apart from pre-surgical assessment of surgical implants they also focused on cone-beam computed tomography use in the imaging diagnosis of a radicular cyst of the upper first molar, mesiodense, tooth fractures in the upper anterior region, a fracture of the condylar process. They also concluded that because cone-beam computed tomography can take high-resolution 3-dimensional images at any tomographic layer with only 1 exposure, it is useful for the diagnosis of diseases in the oral and maxillofacial region.

Surgical guidance template

Georg Eggers et al 2009. [43] Researched the clinical use of navigation based on cone-beam computer tomography in maxillofacial surgery. Image-guidance in maxillofacial surgery has based predominantly on computed tomography images. Its main disadvantage was the considerable amount of radiation to which the patient was exposed, and dental metal artifacts. Cone-beam computed tomography has now become available, which allows for radiograph-based volume imaging of the maxillofacial area at reduced cost and a lower dose of radiation. [44]. The paper concluded on the note that the main application of cone-beam computed tomography to image-guided surgery is image-guided planning and placement of dental implants. There have been sporadic reports about the use of cone-beam computed tomography for image-guided maxillofacial surgery, and in all cases navigation based on cone-beam computed tomography data which were clinically successful. Cone-beam computed tomography is therefore considered to be a credible alternative to conventional computed tomography with the advantages of a lower dose of radiation and less cost, so its use is desirable whenever possible. The authors also remarked that cone-beam computed tomography imaging also shows most foreign bodies quite well. However, this does not necessarily mean that all anatomical structures that have to be strictly avoided during operation are displayed. For example, cone-beam computed tomography imaging showed foreign bodies in the cheek reliably, but the facial nerve and the parotid duct were invisible-as in conventional computed tomography. The surgeon must therefore not operate on data from images and navigation guidance alone, but still needs anatomical knowledge. However, even in such cases image-guided navigation can reduce the risk of collateral damage because the area in which the foreign body is sought is smaller. A directed procedure is possible and there is less exposure of anatomical structures.

Canseop Park et al., 2009. [45] Accuracy of implant placement using precision surgical guides. The paper identified that CAD/CAM-generated surgical guide in conjunction with cone-beam computed tomography have expanded the possibilities in terms of presurgical treatment planning and accurate implant placement and this area should be explored via further research.

T. Dreiseidler et al 2006. [46] Performed a study to describe surgical drill guides based computer-aided dental implant planning systems but their users need to have several pieces of software, follow specific radiological protocols and required data transfer from the radiologist. The aim of this study was to evaluate an integrated system for computer-aided implant planning consisting of a 3D cone beam scanner including software for planning and producing surgical drill guides. The conclusion of the paper was the use of CAD/CAM drill-guides showed to be precise and safe. Sur-

geons can place implants exactly as planned, avoiding surgical complications, reducing costs for individual abutments and opening up possibilities for immediate prefabricated prosthetics. 3D based computer aided planning also facilitates documentation and patient education.

Almog DM et al., 2006. [47] Described computerized tomography (CT)-based dental imaging for implant planning and surgical guidance carries both restorative information for implant positioning, as far as trajectory and distribution, and radiographic information, and also depth and proximity to critical anatomic landmarks such as the mandibular canal, maxillary sinus, and adjacent teeth can be analyzed. It was concluded on the notion that outcomes assessment in this area of dentistry is difficult, primarily due to bias and variability in clinical research. Therefore further research is required to study the quantitative relationship between successful outcomes in dental implant treatment and cone-beam computed tomography dental imaging, coupled with surgical template guidance as much is unknown and awaits discovery through large prospective clinical trials.

Pinsky HM et al 2006. [48] Did research regarding accuracy of three-dimensional measurements using cone-beam computed tomography. They commented that cone-beam computed is made recently available, with the potential to become a practical tool in dentistry, however, there is limited evidence to prove that defect osseous size and volume (especially with reference to oral implant surgery) can be determined accurately using cone-beam computed tomography. It was concluded that cone-beam computed tomography has the potential to be an accurate, non-invasive, practical method to reliably determine osseous lesion size and volume therefore further research needs to be carried out to optimize the use of this tool.

Other

Lutz Ritter et al 2009 [40] did a study dealing with the influence of body mass index, age, implants, and dental restorations on image quality of cone-beam computed tomography. No prior studies had been conducted on these lines. With regards to restorations including dental implants Exposure quality, amount of artifacts, and findings detection showed a positive correlation and the strongest correlation was found for bridges and artifacts. The study concluded that the patient individual factors size, weight, and gender seem not to influence the diagnostic quality of cone-beam computed tomography images obtained by the studied device. A negative correlation between age and diagnostic quality was detected, partly due to a larger amount of metallic dental restoration in elderly individuals. The image quality of the mandibular canal, the foramen mentale, and the nasal floor in was influenced negatively by the factor age. Also the question remains of whether the decrease in image quality for the factor age can be compensated by different exposure settings for cone-beam computed tomography. Further studies are required to identify more specific factors associated with age that may cause this effect.

Corinne Schouten et al 2009. [50] Studied the quantitative assessment of peri-implant bone responses using histomorphometry and micro-computed tomography. It is a well known fact that in oral implantology, the most important research goal is to design implants that induce predictable, controlled, guided, and rapid healing at their bone-implant interface. Obtaining such an optimal bone-implant interface depends on numerous factors, including implant-related factors (e.g. material, design, surface characteristics), biomechanical factors (e.g. mechanical loading), surgical factors (e.g. surgical technique, experience, implantation location) and patient variables (e.g. bone quantity and quality). The conclusion drawn from the study was, that bone volume measurements in a zone ranging from 0 to 500 mm around the implants, as calculated with micro-CT, was not reliable. Also, for the middle and outer peri implant zones this technique produced elevated bone volume numbers. On the other hand, micro-CT images show 3D information, which cannot be obtained using 2D histomorphometry. Consequently, conventional histologicaland histomorphometrical analysis and micro-CT are neither interchangeable, nor independent techniques, but need to be considered as complementary techniques. The results of this study clearly indicate that, due to the limitations of scanning at the tissue-implant interface, micro-CT analysis in its current application, is not the first technique of choice. More research is needed to optimize or even fully standardize the procedures utilized to assess
and analyze bone structure with micro-CT and therefore, the following part on effects of implant design and surface modification on peri-implant bone responses will only concern data obtained with histomorphometrical analysis.

HeilandM et al., 2008. [51] The purpose of this study was to Navigate implantation after microsurgical bone transfer using intraoperatively acquired cone-beam computed tomography data sets. The study concluded that although there is not yet evidence that implants placed with the help of surgical templates or intraoperative navigation, facilitating the transfer of meticulous preoperative planning to the surgical site, have a greater long-term success rate than implants placed 'free-hand', and the use of these supporting techniques in complex situations is well established now and cone-beam computed tomography data generated by mobile systems is sufficient for the planning of implant positioning. They can be used for navigated insertion using tools originally developed for spinal surgery.

Discussion

Since the introduction of dedicated dentomaxillofacial cone-beam computed tomography scanners in the late 1990s, there has been extraordinary amount of interest in these devices in the field of OMF surgery, orthodontics and dentistry. In the last decade, the number of cone-beam computed tomography related papers published each year has increased. With specific regards to oral implantology there has also been a surge of research since the birth of the machine but still many an avenue needs to be explored to setup specific guidelines for the ideal use of this technology in this field.

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Validity of the Turkish patient-doctor relationship questionnaire (PDRQ-Turkish) in comparison with the Europep instrument in a family medicine center

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Abstract

AIM: To establish the validity and concurrent reliability of the Turkish version of the PDRQ with an already validated questionnaire in Turkish, the EUROPEP-Turkish.

Materials & methods: The study was performed in a family medicine outpatient clinic from October 2009 until April 2010. The PDRQ-Turkish was administered to 405 outpatient volunteers, simultaneously with the EUROPEP-Turkish. The statistics were performed in SPSS 17 and Lisrel 8.3. Student's t- test and confirmatory factor analysis were applied.

Results: The mean age of the patients was $21.6 \pm$ 4.9 years (SD). The total scores for the PDRQ-Turkish and the EUROPEP-Turkish showed a moderate correlation (r=0.471, p=0.000) for all patients. Factor analysis of the PDRQ yielded two factors. However, the variance of the second factor accounted for 9.26% of the total variance, and the internal consistency Cronbach- α value of the second factor was 0.37. Thus, we deleted the items that loaded on the second factor (the 6th, 13th, 14th and the 15th items), and this change yielded an internal consistency Cronbach- α value of 0.91 and a large goodness of fit index (GFI) of 0.97 with the correlated factors model for the PDRQ-Turkish. The Cronbach-a of Europep instrument was found 0.91 also and there is no significant difference both them (p>0.05)

Conclusion: The PDRQ-Turkish can be used as efficiently as the Europep instrument for the patient and doctor relationship in primary care.

Key words: Patient-doctor relationship, validity, Turkish version, PDRQ

Introduction

The patient-doctor relationship is the mainstay of medical practice and the preferences, problems and emotions of patients must be taken into consideration in this relationship (1,2). The quality of a patient-doctor relationship is related to treatment success, treatment adherence and the consequence of 'bad practice' (3). A high quality patient-doctor relationship is characterized as a longitudinal relationship (4), agreement with regard to the clinical problem and the treatment (2,5), mutual confidence, and open, explicit communications. The most important patient expectations are diagnosis (94%), prognosis (82%), prevention (76%) and follow-up care (80%) (6). Regardless of their social-economic status or ethnic group, all patients generally want to be informed about the full details of their diagnosis and the possibility of a cure (7). Participation of the patient in the decisionmaking is also an important issue (8).

The doctor himself must be satisfied with his job before a good relationship with the patient can be achieved. Patient satisfaction is higher when doctors enjoy their work or work part-time (6). Moreover, the duration of a visit is also important. The average patient visiting a doctor in the United States is allowed 22 seconds in which to make a statement, and then the doctor take the initiative (9). If doctors allowed patients to talk as long as they wished the average spontaneous amount of time would be 92 seconds (10). Approximately, 50% of patients is satisfied after leaving the doctor's surgery (6). This satisfaction percentage increased to 63% when the same patients were asked about their satisfaction 3 months later (6).

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Peabody reported that medical students focus more on the mechanisms of disease than on medical practice itself. When medical education is diseaseoriented, patient reassurance decreased (11,12). The saying that "medicine is not a trade to be learned, but a profession to be entered" is very true. Medical professionalism requires commitment to provide patients with the best possible care (13).

As a reaction to high levels of specialization and sub-specialization, patient-centered medicine was first promoted by Balint et al. in the 1970s (14,15). Patient-centeredness involves perception of the patient's personality traits (16). However it has been found that when 'patient-centeredness' was increased patients were less trusting, regardless of their doctor's attitude (17).

Especially, doctor-patient communication is very important. Doctors who are more aware of their patients' emotions are noted to be more successful in treating them than their less perceptive colleagues (18). Assurance of empathy improves patient satisfaction (19), increases adherence to therapy (20), reduces complaints (21), and can also have beneficial physiological effects (22). Gender, age, and language are all correlated with communication skills, and training in communication skills is the core of the patient doctor relationship (23). Professional skills and the quality of interpersonal interactions are the major determinants of the satisfaction of doctors with regard to their professional activities (24). The quality of the doctor-patient relationship can affect diagnosis, treatment, and recovery, and there is a correlation between effective doctor-patient relationships and improved health outcomes (25).

Factors influencing patient-doctor agreement are: the number and the nature of the problems assessed during the clinical encounter, the level of education of the patient, the amount and type of prescribed and the number of tests ordered. Lack of trust and agreement between patients and doctors affects all aspects of the quality of care (26). In order to assess patients' opinions about the doctor-patient relationship, the PDRQ test was developed and validated for use in the primary care setting by van der Feltz-Cornelis et al. in 2004 (27). This questionnaire was derived from the Helping Alliance Questionnaire (HAQ), which was developed by Alexander and Luborsky. The HAQ is an important instrument for use in regular structured psychotherapeutic interventions but it is not intended for use in primary care. Van der Feltz-Cornelis et al. therefore adapted this questionnaire and developed the PDRQ which consists of 5 items rated on a Likert scale ranging from 1-5 (1=not at all applicable, 5=totally applicable), which are more appropriate for the primary care setting. Deleting the items that loaded on one factor that only accounted for a small part of the total variance, resulted in the PDRQ-9.

The PDRQ has been translated and validated in several languages and settings, i.e. the Spanish setting(1), the Arab psychiatric setting(28), and the Chinese general Hospital setting (29), however so far a Turkish version does not exist. The aim of our study was to develop a new Turkish version of this validated and reliable questionnaire, to assess the patient doctor relationship in Turkish speaking family medicine settings. Therefore, the PDRQ will be validated against, and compared with another questionnaire, the EUROPEP-Turkish (European Patients Evaluate General/ Family Practice).

This is a Turkish questionnaire, consisting of 23 items that was developed by the European Working Party on Quality in Family Practice (EQuiP) in 1999, and validated by Aktürk et al. (30).

Method

Translation

The translation of the PDRQ into Turkish was carried out by a group of four persons (3 medical doctors and one Assistant Professor of the Faculty of Education) all competent in English. The translated text was then back translated into English by the same group. Ambiguities in the text were corrected, taking into account the Turkish culture, based on consensus in the translation group.

After the PDRQ had been translated the study design was finalized, and the independent variables, such as age, gender, level of education and employment status were defined. We chose those independent variables whether a relationship is established or not with the dependent variables (PDRQ score=patient's satisfaction level).

Setting

The study was carried out in the family medicine outpatient center on the Uludag University

Campus, between October 2009 and April 2010 in Bursa, Turkey. Our outpatient center takes care of forty thousand university students and five thousand teaching staff and administrative personnels. Of the 600 patients who were invited to simultaneously complete the PDRQ and the EUROPEP-Turkish for the comparison of the two questionnaires only 405 patients of three family medicine specialists were willing to participate in the study. According to our sample size calculation, 384 patients were needed with a %95 confidence level and a confidence interval of 0.05. The statistical analysis was performed in SPSS 17 and Lisrel 8.3, and student's t- test and confirmatory factor analysis were applied. A wellfitted model for the confirmatory factor analysis was pre-defined as the $\gamma^2/df \leq 2$, the goodness-of-fit index (GFI) ≥ 0.95 , the comparative fit index (CFI) ≥0.95 and the Root Mean Square Error of Approximation (RMSEA) ≤ 0.05.

Results

Demographic and medical characteristics

The mean age of the patients was 21.6 ± 4.9 years (SD) (range: 17-65 years), and their demographic and medical characteristics are presented in Table 1. Only 52 patients denoted that they have a chronic disease (Type 1 diabetes, sinusitis, arthritis, thalassemia, renal disease e.g.). The level of education of the women was higher than that of the men (t=2.312, p=0.022).

Correlation between PDRQ and EUROPEP-Turkish

The total PDRQ mean was 4.5 ± 0.5 (SD) (95%CI=4.2-4.8), and the total EUROPEP-Turkish mean was 3.8 ± 0.7 (SD) (95%CI=2.9-3.9). The total scores for the PDRQ and the EURO-PEP-Turkish for all patients showed a moderate correlation (r=0.378, p=0.000). We found no statistically significant relationship between the total PDRQ scores and age, gender, level of education or the presence of chronic diseases, respectively.

Factor analysis

Factor analysis of the PDRQ, with principal component analysis by varimax rotation, yielded two factors: the first factor accounts for 44.0% of the total variance and the second factor accounts for 9.26%. The factors are shown in Table 2.

The total mean of factor1's was 1.8 ± 0.5 (SD) (95% CI=1.7-1.9), and the total mean of factor2 was 2.7 ± 0.6 (SD) (95% CI= 2.5-2.9).

According to the exploratory factor analysis, first factor includes: item no.3: dedication to patient, item no.2: trust, item no.4: talkative doctor, item no.1: understanding, item no.8: enough time, item no.9: benefit from doctor, item no.7: helping, item no.12: gratitude to doctor, item no.11: accessibility, item no.10: agreement, item no.5: patient satisfaction and item no.15: symptoms' disappear. All of them represent a good relation's properties. The first factor could be referred to as 'main elements of a good patient-doctor relationship'.

Table 1. Demographic and medical characteristics of the patients

		n	%
Condon	Male	229	56.5
Gender	Female	176	43.5
	Primary school	1	0.2
Level of Education	High school	356	3
	University	48	11.9
Monthly Income	<500TL	102	25.2
	501-1000TL	189	46.7
	1001-2000TL	88	21.7
	>2000TL e.g.military	26	6.4
Employment	Work (officer employee,)	59	14.6
	No work (e.g. student)	346	85.4
Chronic disease (s)	No	353	87.2
	Yes	52	12.8

	Factor1	Factor2	
3- My primary care physician is dedicated to help me	0.798	0.091	
2- I trust my primary care physician	0.783	0.136	
4- I can talk to my primary care physician	0.763	-0.060	
1- My primary care physician understands me	0.759	0.112	
8- My primary care physician has enough time for me	0.717	0.162	
9- I benefit from the treatment from my primary care physician	0.696	0.318	
7- My primary care physician helps me	0.688	-0.050	
12- Thanks to my primary care physician I feel better	0.660	0.423	
11- I find my primary care physician easily accessible	0.650	0.182	
10- My primary care physician and I agree on the nature of my medical symptoms	0.617	0.449	
5- I feel content with my primary care physician's treatment	0.587	0.124	
15- My medical symptoms will probably disappear	0.486	0.395	
14- I can handle my medical symptoms now (even if my primary care physician			
and I have no further appointments)	0.155	0.095	
13- Thanks to my primary care physician I gained new insight	0.452	0.629	
6- I think my primary care physician finds me hard to deal with	-0.302	0.592	

 Table 2. Explanatory factor analysis of the PDRQ

Rotated Component Matrix

The second factor contains: item no.14: handling of medical problems, item no.13: insight, item no.6: hard patient. These properties are related to a patient's behavior. Therefore, the second factor could be named as 'patient's feelings'. The internal consistency Cronbach- α of the sub-scale loaded on factor 1 was calculated 0.91, and the internal consistency Cronbach- α of the sub-scale loaded on factor 2 was 0.37. The internal consistency Cronbach- α value of the PDRQ scale, which applies to patients (without the deletion of items) was 0.87. In the confirmatory factor analysis of the PDRQ (without the deletion of items), the goodness of fit index (GFI) was 0.89 and the comparative fit index (CFI) was 0.89. These values indicate that the PDRQ (without the deletion of items) applied to patients is not sufficient for a good model. The internal consistency Cronbach-a of Europep instrument was found 0.91 also. This could indicates that there is no statistically difference (p>0.05) between two scales.

According to the factor analysis, the 15th item of the PDRQ has a difference in loading between factor1 and factor2 of less than 0.10 (Table 2). According to Nunnally, each variable should present a factorial load greater than 0.40 in its factor and less than 0.30 in the rest of the factors (31). Thus, the 15th item has to be deleted from the PDRQ, which is applied to subjects (without the deletion of items). The items loaded on the second factor could also be extracted because the factor2 explains only the 9.26% of the total variance. If we delete the 6th, 13th and 14th items, the internal consistency α -Cronbach value is 0.91. Moreover, we see that the 6th item has a low item vs. total score correlation coefficient, and for if it is deleted the internal consistency α -Cronbach value will increase, as shown in Table 3.

Table 3. Item vs. total score correlation diagram and Cronbach- α values if item was deleted

	Corrected	Cronbach's α if
	Item-Total Correlation	Item was deleted
PDRQ1	0.664	0.854
PDRQ2	0.701	0.853
PDRQ3	0.685	0.853
PDRQ4	0.585	0.857
PDRQ5	0.490	0.861
PDRQ7	0.517	0.860
PDRQ8	0.653	0.854
PDRQ9	0.697	0.852
PDRQ10	0.683	0.852
PDRQ11	0.587	0.857
PDRQ12	0.700	0.852
PDRQ6	-0.064	0.906
PDRQ13	0.601	0.856
PDRQ14	0.346	0.870
PDRQ15	0.526	0.860

Thus, for the PDRQ-Turkish was necessary to delete the 6th, 13th, 14th and 15th items, resulting in a PDRQ with 11 items, two more than in the Dutch PDRQ9. The final Turkish version is shown in Table 4.

Goodness of fit

We had two models for the confirmatory factor analysis of PDRQ-Turkish: 1) the independent factors model, 2) the correlated factors model. The χ^2 /df of the PDRQ-Turkish in the independent factors model was 4.94, the GFI was 0.91, the CFI was 0.92 and the RMSEA was 0.10. These data show that the independent factors model was not enough acceptable fitting for the Turkish sample since in a well-fitted model, the χ^2/df must be ≤ 2 , the GFI ≥0.95, CFI≥0.95 and the Root Mean Square Error of Approximation (RMSEA) < 0.05. Some unmeasured correlations could lie between the observed variables. Therefore, the Lisrel 8.3 advised a second model where the correlations between the latent variables are calculated. The second correlated factors model has the $\gamma^2/df=2.0$, the GFI=0.97, the CFI=0.98, and the RMSEA=0.05. The Figure 1 depicts the best-fitted correlated factors model for the confirmatory factor analysis of PDRQ-Turkish in the Turkish sample.



Figure 1. Graphical representation of the bestfitted correlated factors model of the PDRQ-Turkish for the confirmatory factor analysis, which is applied among Turkish patients addressing to a family medicine center

Discussion

Only a few articles about the PDRQ can be found in the literature. In the original Dutch PDRQ study carried out by van der Feltz-Cornelis et al., two factors were in the factor analysis. The second factor, focusing on medical symptoms, explained only 9% of the total variance. However, it seemed

Table 4. The PDRQ-Turkish (Hasta Hekim İlişkisi Anketi=HHİA in Turkish) resulting from confirmatory factor analysis

	Not at all applicable	Not Applicable	Not sure	Applicable	Totally Applicable
1. My primary care physician understands me	1	2	3	4	5
2. I trust my primary care physician	1	2	3	4	5
3. My primary care physician is dedicated to help me	1	2	3	4	5
4. I can talk to my primary care physician	1	2	3	4	5
5. I feel content with my primary care physician's treatment	1	2	3	4	5
6. My primary care physician helps me	1	2	3	4	5
7. My primary care physician has enough time for me	1	2	3	4	5
8. I feel content with my primary care physician's treatment	1	2	3	4	5
9. My primary care physician and I agree on the nature of my medical symptoms	1	2	3	4	5
10. I find my primary care physician easily accessible	1	2	3	4	5
11. Thanks to my primary care physician I feel better	1	2	3	4	5

that it would be incorrect to use the second factor in the primary care setting. Because of the lower variance percentage of factor2, the items concerning the second factor (6th, 9th, 12th, 13th, 14th and 15th items) were deleted, which resulted in the PDRQ-9. The PDRQ-9 is suitable for the Dutch population, but for the Turkish population the 6th, 13th, 14th and 15th items should be deleted, but the 9th and 12th item can remain in the questionnaire. The number of patient in our study was greater than in the Dutch study (27), but still the results of the factor analysis seemed to be similar in both studies. There were some cultural differences. Another difference between our study and the Dutch study concerned the means of the factors. Our factor1 and factor2 means were lower, which could be due to the fact that there are generally more patients per doctor in Turkey, and the lack of sufficient time to make a comprehensive medical examination. By WHO's report on the global health data, while 3.9 doctors are needed for 1000 persons in the Netherlands; 1.5 doctors are needed for 1000 persons in Turkey. This implies that the Turkish doctors must work 2.7 times harder than the Dutch colleagues (32). This data supports our results. In a Spanish PDRQ study, the patients were screened by six internists for 5.7 years (1). In that study the PDRQ yielded two factors in the explanatory factor analysis, as in our study. The 6th and the 15th items were deleted because factor2 had a variance of 7%, and 15th item had a weight of 0.40 in factor1 and 0.30 in factor 2. Therefore, the validated Spanish version of the PDRQ consists of 13 items.

In another Spanish study in which the PDRQ-9 was administered to 451 patients in six primary care health centers, an average factor index of 4.41 was found, which is similar to the findings in our study (33). However, the total variance in that study was 75.3%, which is greater than our variance. Moreover, the study carried out α -Cronbach value was 0.952, which is similar to the results of the Spanish PDRQ validation study by Adan Mingote et al. (1), but greater than the α -Cronbach value found in our study.

The Arabic translation study of PDRQ recruited 1054 patients aged 18 to 65 years old participated to the study in Katar, in 2009. The internal consistency Cronbach α was 0.92 representing a good reliability. In the exploratory factor analysis,

2 factors found representing the 60% of the total variance. The Arabic version is a 13 itemed form of PDRQ. But in the study, why because they had eliminated two items, is not well explained (28).

In a study carried out among 3rd year medical students in Singapore with a similar questionnaire, the Patient–Practitioner Orientation Scale (PPOS), the patient-centered attitude of the students was assessed (15). At the beginning and at the end of the 3rd year of their medical studies, the 'sharing' and the 'caring' medical attitude of the students were assessed. It was found that the 'caring' attitude of the students had increased at the end of the 3rd year, but that the 'sharing' attitude had decreased. Nevertheless, in a similar study in the USA, the same study among medical students it was found that the 'caring' attitude of the students increased and the 'sharing' attitude remained unchanged (12). This could, however, be due to cultural differences. Sharing attitude could be observed in our trial mainly in the first factor's dimension which we named also "main elements of a good patientdoctor relationship" and which was relating with the 'sharing attitude' of a medical visit. Moreover, in our study, factor1 in the PDRQ concerned 'patient-centered' questions, for which we obtained a low mean (1.83 ± 0.5) per patient. We could therefore say that medical practice in our sample was still doctor-centered, and the 'caring' attitude was greater than the 'sharing' attitude.

In sum, doctor-patient relationship is an important and fragile one to restore and maintain. Because of it communication, empathy, professionalism which are the main skills of "a good doctor" should be discussed and should be the part of the medical education beginning from the freshmen (34,35,36).

Limitations

The patients in our study were not monitored for a long period of time by the same doctor, which implies that the patients had to make a rapid appraisal of their doctor. Of 600 patients, 405 (67,5%) consented to participate in the study. Moreover, the patients visiting our family medicine center are mainly young, and therefore the sample may not have been representative of the general population of Turkey.

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Predicting Heart Health: Near-Future Impact of Activities on Heart Rate

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Abstract

In this paper we demonstrate the ability to predict changes to heart rate due to changes in levels of activity. The predicted changes are up to an hour into the future. Activity levels are calculated from data collected by a worn accelerometer for a person performing daily activities. For people with congestive heart failure it can be a challenge planning everyday activities as it is hard to estimate how much stress an activity exerts on the heart. We propose to model the relationship between motion and heart rate. This approach enables the prediction of heart rate changes prior to performing an activity. We explored four methods to predict current and future heart rate from activity level: a continuous state Kalman Filter, two simple linear models, a continuous nonlinear model, and a nonlinear discrete Hidden Markov Model. The results from subjects with congestive heart failure and healthy subjects show that using the proposed models, the heart rate can be predicted an hour into the future using accelerometer data.

Key words: Heart Rate, activity level, nonlinear models, Kalman, Filter, prediction, Hidden Markov Model

Introduction

The heart rate (HR), measured as the number of beats per minute (bpm), is the most informative and simplest ECG feature for heart health. The increase in HR during an activity reflects the additional work performed by the heart to meet increased demands on the body. A person's HR varies with age, gender, physical fitness, experienced emotions, physical strain, and disease. Further, HR variations correlate with autonomic nervous system fluctuations, and studies have shown a connection between HR variations and patient mortality/morbidity [1]. Particular effort has gone in the area of modeling heart rate response during exercise and recovery after exercise, as it is believed that such knowledge would be beneficial to predicting heart disease mortality [2]. The models predominantly consist of feedforward and feedback components [3], or use a static nonlinearity cascaded at the input of a linear system and performed well for short duration exercises [4]. An exception is a nonlinear model by Cheng at al [5], which associates a transient response with the intensity of the exercise, measured as the speed of a treadmill, thus making the model applicable to long duration exercises. Critchley and al. showed the human brain activity that responds to emotional facial expressions can be used to predict differential heart rate response [6]. In the same vein, measured response of beta-adrenergic receptors to brain stimuli may be used to predict heart rate [7]. However, all these variables are not easily accessible in a non-laboratory environment.

A major focus of cardiac health research is the detection of possible catastrophic events [8], thus centering research goals on the detection of anomalies that already exist [9]. Cardiac health may begin to deteriorate long before a person experiences heart related problems. The moment of change is not detectable from the ECG exam taken during a patient's ambulatory exam. Continuous data collection opens the possibility of a personalized model that enables comparison between the actual and predicted state of cardiac health. A personalized model could potentially be used to monitor and detect minor but significant long-term changes in a person's continually monitored cardiac health that would be otherwise imperceptible during brief clinical observations. This model could help cardiac patients to get input to the efficacy of their treatment sooner, or assist in early diagnostics of otherwise healthy

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people. Advances in technology are enabling continuous monitoring, particularly in patients at risk. However, continuous monitoring of the ECG signal may involve additional problems such as allergies to contact gel, the number of electrodes needed, and wires. Also, a subject made uncomfortable by the numerous sensors placed on them is unlikely to act in a natural fashion, possibly compromising results. In addition, the discomfort may cause the subject to decline participating in future studies or agreeing to be monitored to improve their health. Further, such burdensome equipment is unlikely to be adopted on a large scale study or for commercialization. The problem can be resolved by mapping the ECG features to other more easily observed variables from compact wireless sensors [10], which also can be interesting for telemedicine processing [11]. Although subtle ECG differences might not be directly visible in short observations from simpler sensors like accelerometers, the ability to acquire data over a long period may reveal substantial information about a person's heart health. Potentially, a personalized model can add to quality of life of chronic patients with an additional insight to consequences of an activity before it is performed. In this preliminary study, we examine whether accelerometers can be used to extract and predict a person's heart rate during structured activities, and also how far into the future we can reliably predict heart rate from unstructured activity.

Data Collection and Processing

We used two sets of devices to collect data. In one we employed an Alive Heart monitor [12] positioned on a hip of a subject, a device which records both one channel ECG with a sampling rate of 300Hz and three axis acceleration with a sampling rate of 75Hz. The second set of devices consisted of three channels commercial holter device, with a sampling rate 255Hz, and the ADXL330 three axis accelerometer (sampling rate 20Hz) mounted on a TMoteSky [13] in custom made casing. The casing is worn on the hip. The ECG data is taken across the heart with one electrode placed on the top of the bone directly between the collarbones and below the throat. A second electrode is placed on the lower left rib area, so that an imaginary line that connects two electrodes passes directly through the heart. Although the holter device has three channels, for our purposes we used only the channel that corresponded to the electrode placement described above.

We collected 20 hours of continuous data from 10 subjects with New York Heart Association class 2 or 3 diastolic heart failure and 10 healthy controls, performing their everyday activities. We also collected data from healthy subjects performing structured activities during 20 minutes: slow and brisk walk, climbing stairs, jog, and run, averaging three minutes per activity with a minute rest in a standing position. The signals were additionally processed to accommodate for different sampling rates. For each subject we had multiple runs, not less than three, collected at least two weeks apart.



Figure 1. The top plot shows a segment of 3-axis acceleration data recorded by the Alive Heart Monitor during a walk. The second plot shows the magnitude of acceleration calculated according to Equation 1. In the next step we calculate the velocity of acceleration i.e. the magnitude difference per sample which is shown in the third plot. This is integrated over a one second window shown in the fourth plot providing a measure of activity level (Equation 2).

Acceleration data is recorded for 3 axes: x, y, and z. A sample of acceleration data is shown in Figure 1, top plot. The marked axes are in relation to the device. The offset of the x-axis from the other axes is caused by the force of gravity creating a constant acceleration in the vertical axis, in this case corresponding to the x-axis.

The key interest in acceleration is to detect if the subject is moving and the intensity of the movement. Analysis of each of three axes of acceleration is unreliable in cases where an accelerometer is loosely secured to a subject, and also unnecessary for this application. Therefore the magnitude of acceleration a, is calculated from the three acceleration components (also shown in Figure 1, second plot).

$$a = \sqrt{x^2 + y^2 + z^2}$$
 (1)

The line integral of the acceleration vector is then computed to measure the total changes in acceleration over a time window of one second.

ActivityLevel =
$$\sum_{i=t-1}^{t} \sqrt{\Delta a^2 + \Delta t^2}$$
 (2)

where Δa is the change in acceleration over a small time change Δt , equal to one sample (Figure 1, third plot). The activity level (Figure 1, last plot) provides an estimate of the average energy involved in movement occurring over a short period of time. It shows when the subject is stationary and when the subject is moving, along with the intensity of this movement. Figure 2 shows the activity levels associated with a variety of different activities.

We applied an algorithm given in [14], to detect times associated with R-peaks from ECG signal. The steps of the algorithm are shown in Figure 3. The HR is then calculated as follows:

$$HR = \frac{60}{t_{R-R}} [bpm] \qquad (3)$$

Where, t_{R-R} is the time difference between two adjacent peaks.

Although there may be simpler algorithms to detect the most prominent peaks of the ECG si-

gnal, we decided to use this algorithm because it works well with noisy data collected from nonstationary subjects.



Figure 2. The three stationary activities (lying down, sitting, and standing) at the beginning and the end show close to zero activity level as expected. The moving activities (walk 1 and 2, jog and run) are clearly distinct from stationary activities and also distinct from each other. The two walks performed at different speeds have different activity levels associated with them as do the jog and run. This activity level method provides a clear picture of the relative difference between different activities.

Models

We considered both continuous state and discrete state models for capturing the underlying relationship (f) between heart rate (x) and activities (u) from examples $\{(x_1,u_1), (x_2,u_2)...\}$. The methodology is standard: split the data into training and testing sets, use training data to find a function f, and then use testing data to evaluate f. All models are personalized, i.e. trained and tested per each subject, except for the nonlinear model given by Cheng *at al.* [5].

The Kalman filter [15] is described by following general equations:

$$x_{t+1} = Ax_t + Bu_t + n_t \quad \dots \qquad (4)$$

$$y_t = Cx_t + v_t \tag{5}$$



Figure 3. A sample of the ECG signal (a) is passed through a bandpass filter to remove baseline wander and power line noise (b). This is followed by differentiation (c), squaring (d), and integration (e). The R-Peak must occur during the rising slope of the integrated value, so the filtered ECG signal is examined during this period to detect the maximum (f). The peak times of the ECG signal are adjusted for delay introduced by filtering (g)

Here x is the hidden state, y is the observed heart rate, A and B are general form matrices, n and v are normally distributed Gaussian noise parameters, u is activity level, and t is the current time step. The state x contains the unobserved true heart rate and C is a fixed matrix (not learned) that selects this component (Figure 4).



Figure 4. Continuous system flow: the Kalman filter.

We considered four different models.

Model 1: The hidden state consists of the person's true (unobserved) heart rate.

$$x_t = h_t \quad \dots \quad (6)$$

$$h_{t+1} = a(h_t - \overline{r}) + \overline{r} + bu_t + n_t \quad \dots \dots \quad (7)$$

where \mathbf{h}_{t} is heart rate, and , is an absolute resting heart rate

Model 2: The hidden state contains the true (unobserved) heart rate, and the person's resting heart rate.

$$\boldsymbol{x}_t = \begin{pmatrix} \boldsymbol{h}_t \\ \boldsymbol{r}_t \end{pmatrix} \quad \dots \qquad (8)$$

$$h_{t+1} = a_1(h_t - r_t) + r_t + b_1u_t + n_{1t} \quad \dots \qquad (9)$$

$$r_{t+1} = a_2(r_t - \overline{r}) + \overline{r} + b_2 u_t + n_{2t}$$
(10)

where r_t is a slowly varying resting heart rate **Model 3**: The heart rate is a constant.

$$y_{t} = \overline{r} + n_{3} \quad \dots \qquad (11)$$

Model 4: Heart rate is an affine function of activity only.

$$y_t = a_3 u + b_3 + n_4$$
 (12)

Models 1 and 2 are simple models of a heart, but seem to work well. Models 3 and 4 are used as additional baselines. The parameters are determined using linear regression from the training data.

Nonlinear Model: Cheng *et al.* [5] present a nonlinear model that is defined similarly to the models above, but is designed to work across multiple subjects for a single activity - walking on a treadmill over an extended period of time. The primary benefit of their model is the ability to model a nonlinear HR response to different walking speeds, i.e. walking at 5 km/h and 6 km/h changes the HR by a constant offset while walking at 7 km/h yields a linear change in HR over time. Using v to denote the

treadmill speed, $z_t = h_t - \overline{r}$ for the elevation of heart rate over baseline, and q_t for the long term perturbation of the HR, their system model is as follows:

$$dz_{t} = -a_{1}z_{t} + a_{2}q_{t} + a_{2}v_{2} \quad \dots \qquad (13)$$

$$dq_{t} = -a_{3}q_{t} + a_{4}\sigma(z_{t})z_{t} \quad \dots \quad (14)$$

where $\sigma(z_t) = (1 + e^{-z_t - a_s})^{-1}$ is a nonlinear sigmoid function. The parameters for this patient-independent model were found by the Levenberg–Marquardt method from six healthy patients across three trials. As such, this model is neither personalized nor directly applicable to a person's life off a treadmill. For more details see [1]. Parameter values are given in table 2.

Table 1. Parameter values for nonlinear model

<i>a</i> ₁	<i>a</i> ₂	<i>a</i> ₃	<i>a</i> ₄	<i>a</i> ₅
1.84	24.32	6.36 10-2	3.21 10-3	8.32

A Hidden Markov Model (HMM) [16] is a model that can capture nonlinear behavior through the use of discrete hidden states and discrete observations. An HMM is a generative model that assumes that the state evolves probabilistically with a fixed *transition* probability T_{ij} from state *i* to state *j* and a fixed *emission* probability E_{ia} for each observation *a* from each state *i*. Computing the next state and observation from a current state involves running the model forward by one step according to the following equations. We use discrete ranges of heart rates for the state *x*, and discrete ranges of activity levels for the observations y_t . Then the probabilities of states and observations are given by the recursive equations (Figure 5).

$$Pr(x_{i+1} = j) = \sum Pr(x_i = i) \times T_{ij}$$
 (15)

$$Pr(y_i = a) = \sum Pr(x_i = i) \times E_{i_i} \quad \dots \quad (16)$$

To define the discrete HMM structure from the training data, for each patient we manually discretized the continuous heart rate into 5 bins, and the activity levels into 8 bins. The transition and emission probabilities were set to the frequency counts observed in the training data. The models were evaluated by predicting the bin of heart rate at a fixed point in the future, given the sequence of future observations to that point. This prediction is given by the standard HMM forward algorithm on the future observations that yields the most likely state (bin of heart rates) for the given time.



Figure 5. Flow of the HMM. x_t is a hidden state (heart rate), y_t is a discrete observation (activity level). Arrows indicate probabilistic generation: value of x_{t+1} is generated from x_t value of y_{t+1} is generated from y_t

Results

We tested the models on both the 20 minute runs with structured activities and 20 hour runs for a person's daily life, see Figures 6 and 7. The Kalman filter model parameters were estimated from the training data and evaluated on the separate test data.

The nonlinear model from the literature requires velocity information. Thus, it was only applicable to the 20 minute run, for which velocity information could be estimated from the accompanying GPS data. Furthermore, the literature model proposed a fixed value for resting heart rate calculated as an averaged resting heart rate of all subjects in the study and set to 74 bpm. In our study, as subjects had widely varying resting heart rates, we adjusted the resting heart rate for each individual from the training data.



Figure 6. Nonlinear model applied to a 20 minute data, zoomed in during walk and brisk walk of a healthy female subject. It is easy to observe that predicted and real heart rate have high correlation



Figure 7. Zoomed detail of the cardiac patient using 20 hour data and model 1. It is easy to observe that predictions are highly correlated with HR. The horizontal axis is time in minutes, and the vertical is HR [bpm]. For clarity the same segment is zoomed with lines showing prediction 10, 20 and 60 minutes in the future (upper plot), and zero and 5 minutes (lower plot)

The HMM model was applied only to 20 minute data sets. The HMM model was trained on two trials of data of 20 minutes structured activities and tested on third trial for each person. For the entire 20 minute trial the prediction was 60%. However, if restricted to activity periods the prediction was 94%.

To evaluate the predictive performance of other models, we assume the model state variables are updated at each time step with the observed heart rate and activity level, and then the models are used to predict the patient's heart rate at some point in the future given only the activity level. The Figures 8, 9, and 10 show the average root mean squared error (RMSE) from computing the difference at each point in time. The results from the 20 hour run are shown in Figure 8 and 9. Model one and two, substantially outperform baselines three and four. Predictions for the cardiac patients are comparable to those for the healthy subjects, showing that this approach is appropriate for the target patient population. The results for the 20 minute trials are shown in Figure 10. Models 1 and 2 outperform the nonlinear model. Figure 6, shows that the nonlinear model can do a good job of walks and brisk walks, but it does not generalize to the broader set of activities tested here.



Figure 8. RMSE of 20 Hour Kalman models for Healthy Subjects

The results in Figure 10 for nonlinear model are restricted to the non-strenuous activities, otherwise the RMSE jumps from 15.03 to over 40 bpm.



Figure 9. RMSE of 20 Hour Kalman Models for Cardiac Patients.



Figure 10. RMSE of 20 minute trials with structured activities.

Discussion

This study has shown different methods to predict changes in a subject's heart rate based on given pattern of changes of activity level. With the exception of the Cheng's and al. nonlinear model, the parameters of the models are personalized, i.e. calculated per subject, instead of being averaged per demographic group. The Cheng's model was optimized for average healthy subjects with limited activity levels, and as expected this model yielded questionable results for non-healthy subjects and activities that are out of scope of brisk walk. However, it can be seen from the RMSE that the performance of the model does not vary with the depth of future prediction. Note that we applied parameters given in [5], also presented in table I. The only deviation from the given model is adaption of resting heart rate per subject, which was set to 74 bpm in [5]. This leaves room for improvements, such as broadening the spectrum of activity levels and personalization of the parameters instead of averaging. We expect that our future work will prove this model to be very powerful for our research goals. The Kalman filter in Models 1 and 2 is effective for predicting heart rate from activity level, for both healthy population and cardiac patients, and these results were fortified by poor performance of "placebo" models 3 and 4. The real goal is to predict the consequences of an activity before it is performed. The use of a holter is for verification, and even a low-cost pulse watch could be deployed in practice. Planning and models are limited, so distant forecasts are bound to have error. Still, the ability to perform any prediction has potential benefits and is a promising direction for future research.

The Kalman models presented above can be run to predict future observations many steps into the future, the prediction of more than an hour is still poor. The reason could be that the models are based on strong assumption of linear relation between heart rate and activity. Nevertheless, the graphs of the models show good capture of the shape between predicted and real curves. However, as the heart is known to be non-linear future research focus should be directed to nonlinearity. On the other hand, the hidden Markov model can account for some non-linear aspects and showed that heart rate is well predictable for single activities, the model was less accurate between activities.

Continuous models can account for slow small changes, while discrete models for single activities look promising for long-future predictions. Discrete activities can be associated with reliable changes in heart rate. Combining discrete activities with activity recognitions [17] with continuous models can lead to better heart rate predictions.

There are many studies involved with activity classification methods. These techniques can be applied to the acceleration data, and would certainly prove useful in a long-term study with a subject performing undocumented activities. However, the activity level method provides enough information to pinpoint changes between certain activities, and clearly shows difference between stationary and moving activities.

Conclusion

We are at the brink of the "Star Track tricoder" technologies era that shrink in size and expand in possibilities. Consumers can buy all sorts of technical gadgets which gather statistically significant collection of data per person, from which signal processing tools may reveal trends and predict health changes that are intrinsic to the individual. An at-risk patient can wear sensors from which data can be processed in real-time via a cell-phone. From a retrospective perspective it aids patient-caregiver interaction, from an introspective perspective it enables status monitoring for patients, and from prospective perspective it can answer a patient's question: what are the consequences of walking for an hour? Such an ability would allow a patient to better tailor their activities to those they can successfully perform.

Development of biomedical devices that will be used to treat a person's possible and existing health issues follows the P-4 (Personalized, Predictive, Preventative, and Participatory). Continuous monitoring enables personalized models, and detection of changes in model parameters per subject, which may aid to either to detect or foresee future heart problems.

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Prevalence of Temporomandibular dysfunctions symptoms in children and in adults

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Abstract

The term temporomandibular dysfunction (TMD) usually defines a number of symptoms and clinical signs occurring in the masticatory muscles, temporomandibular joint and structures associated with it, or in the muscles and joint simultaneously.

Etiologically, temporomandibular dysfunctions are viewed as multifactorial disorders, involving a significant number of both direct and indirect causal factors. Temporomandibular dysfunctions are widely present in adolescents and adults, as well as in children. The symptoms of temporomandibular disorders have been reported in 20-25% of individuals.

Nine epidemiologic studies have been analyzed in order to assess the prevalence of symptoms of TMD in the population of adults. The results demonstrated that the prevalence of TMD symptoms significantly varied in the population. At least one of the symptoms in adults occurred at the prevalence of 30-49.9%. As for the gender, most studies showed a higher prevalence of TMD in women compared to men.

Six epidemiologic studies were analyzed in order to assess the prevalence of TMD symptoms in children. The analysis demonstrated that the prevalence of TMD symptoms greatly varied in children. At least one of the symptoms occurred at the prevalence of 12.2% to 67.5%. The most common symptom in children was the sound in the TM joint during mouth opening.

The results of numerous epidemiologic studies were hardly comparable because of different methodologies utilized. We thus recommend the use of more universal methods in epidemiologic studies. The picture of the population prevalence of TMD symptoms could thus be made much clearer.

Key words: temporomandibular dysfunction, prevalence, symptoms, adults, children

Introduction

The term temporomandibular dysfunction (TMD) usually defines a large number of symptoms and clinical signs occurring in the masticatory muscles, temporomandibular joint (TMJ) and structures associated with it, or in the muscles and joint simultaneously¹. These dysfunctions form the most common clinical entity affecting the mastication apparatus, which is also the principal cause of pain of non-dental origin in the orofacial region.

Etiologically, TMDs are viewed as multifactorial disorders involving a large number of direct and indirect causal factors. These factors can be divided into predisposing, initiating or precipitating, and permanently present ones. The predisposing factors involve structural, metabolic, and/or psychologic conditions which affect adversely the mastication apparatus. These factors, in fact, increase the risk of TMD. The initiating factors, leading to TMD symptoms, are primarily associated with traumas or with constant, deleterious burdening of the mastication system. Various types of traumas to the head, neck, or jaw, can result in the TMJ injury and consequential TMD. However, traumas to the joint may be incurred during eating, jawning, or longer opening of the mouth, eg. during dentistry interventions. The second group of traumas, associated with constant harmful burdening of the TMJ, occur as the result of parafunctions (bruxism, gum chewing). Permanently present factors are hormonal status, psychosocial factors, but also parafunctions. These factors can have harmful effects upon the already present TMD, and can also be associated with any of the predisposing or precipitating factors.

Numerous epidemiologic studies have shown that the problem of TMD is very prevalent in most of the countries, especially in Scandinavia and Central Europe. TMDs are widely present in adolescents or adults, and in children as well. It has been reported that in 50-70% of individuals of each of the above groups, there occurs at least one sign of the disturbed function of the orofacial system, and that in 20-25% of individuals TMD symptoms occur. These diseases affects individuals aged 30-50 years of age, i.e. in their most active period of life².

There are numerous classifications of these diseases, but most important is the one given by Dworkin and LeResche³. They suggested the system known as the "Research Diagnostic Criteria for Temporomandibular Disorders." The system incorporated two classification directions. The first direction involved three groups: 1) muscle diseases; 2) discus movement in the joint; 3) arthralgia, arthritis, and arthrosis. The second direction described joint disorders caused by the patient psychologic condition.

The symptoms associated with TMD are most commonly the pain, presence of joint sounds during mouth opening, limited joint mobility, and so on. TMD pain can be the pain in the masticatory muscles or TMJ pain. Clinical signs characterizing TMDs are disturbed mobility of the lower jaw, pain in the TMJ and masticatory muscles under palpation, pain during mandibular motions, limited mouth opening, deviations during mouth opening, etc. The symptoms and clinical signs can occur both individually and associated one with another.

Aim of study

This paper aims to analyze the results of epidemiologic studies dealing with the prevalence of TMD symptoms in both adults and in children.

Prevalence of TMD symptoms in adults

Nine epidemiologic studies were analyzed in the assessment of prevalence of TMD symptoms in adult population. In each of them, the data about the TMD symptoms were analyzed. The data were obtained during anamnestic inquiries, i.e. during the analysis of appropriate questionnaires filled in by the examinees.

In 2010, the study was performed to assess the prevalence of TMD symptoms related to gender and age in the representative sample of urban population of Brasil⁴. By way of random phone calls, 1230 individuals aged 15 to 65 years were selec-

ted. TMD symptoms were evaluated based on the recommendations of the American Academy for Orofacial Pain. Out of the total number, 39.2% of examinees reported at least one of the TMD symptoms. The most common symptom was the sound in the TMJ, then pain in the TMJ, and lastly pain in the masticatory muscles. All of the symptoms were more common in women.

During 2007, TMD-associated symptoms were investigated in Italy as well⁵. The criterion utilized was based on the diagnostic criteria for the assessment of TMJ dysfunctions⁶. The study sample consisted of 2005 examinees aged 15-70 years. The results showed that as high as 33.6% of examinees had TMJ sounds on mouth opening, while jaw clenching was established in 16.7% of the studied population. Gender-specific, significant differences were not discovered. However, regarding the difficulties during mouth opening (11.7%) and TMJ pain (4.9%), these were most commonly associated with women, with a statistically significant difference compared to men. Difficulties during mouth opening were present in 8.4% of women vs 3.6% of men, while joint pain was present in 6.5% of women vs 3.1% of men. As for age distribution, statistically significant differences were not found for any of the studied symptoms.

A similar study of symptoms was done in Turkey as well⁷. A sample of 1253 examinees (Istanbul inhabitants, aged 18 and more years) was studied. Random phone calls were used to reach the examinees. The criterion for pain used in the study was based on the study by Goulet et al.⁸. Out of the total number of examinees, 31.0% reported pain in the TMJ region, out of them 26.2% of men and 35.6% of women (the gender-related difference being of statistical significance). Other TMD-associated symptoms were also studied. It was established that there were TMJ sounds on mouth opening in 27.3%, teeth clenching in 23.0%, and difficult mouth opening in 8.4% od examinees. As for these symptoms, neither age-, nor gender-related statistically significant difference was observed.

A population health study in the region of Pomerania, Germany, has been used to establish the prevalence of TMD symptoms in individuals aged 21-81 years⁹. The examinees were randomly chosen in the smaller towns of northeastern Germany. Study participants were anamnestically and clinically examined using the research criteria for TMD diagnosis⁶. The total number of subjects enrolled was 4289. The results showed that as high as half of the examinees (49.9%) had one or more TMD symptoms. TMJ sounds were found in 9%, while TMJ pain was found in 3%. Both symptoms were more common in women, although without statistical significance.

A study was done in 2001 in the population of China as well. The study was done by a group of scientists from the Faculty of Dentistry, University of Hong Kong¹⁰. The study enrolled 1526 randomly selected individuals from the Canton region, aged 18 years or more. The symptoms of TMD were defined based on the recommended diagnostic criteria⁶. The results demonstrated the overall prevalence of at least one TMD symptom of 33%, with only 5% of subjects reporting TMJ pain. As for other symptoms, TMJ sounds were present in 1.8%, and difficulties opening mouth in 0.3%. The study did not detect any statistically significant gender difference in the prevalence of symptoms.

A study performed in Okayama, Japan, tried to assess the prevalence of TMD symptoms¹¹. The study enrolled 672 randomly chosen individuals aged 20-92 years. The most common reported symptoms were TMJ sounds (24%) and TMJ pain (11%), with the prevalence of crepitation higher in women (28.2% vs 20.3% in men, the difference being of statistical significance). As for age, the symptoms were more conspicuous in younger examinees, though without statistical significance.

A significant study was done on the sample of 897 adults from the Quebec province in Canada¹². The examinees were randomly chosen by way of phone calls. The study enrolled individuals aged over 18 years. In 30% there was at least one of the TMD symptoms. Most common were TMJ sounds (9%), TMJ pain (7%) and more difficult mouth opening (4%). These symptoms were more common in women of all ages (the difference being statistically significant). The symptoms were also less prevalent with advancing age.

A study with 2033 student participants aged 18 to 26 years was performed in Taiwan in 1992^{13} . At least one TMD symptom was observed in 42.9% of students, with a female predominance of statistical significance (47.5% vs 39.2% in men). TMJ sound was the most common symptom (5.6%), without a statistically significant gender difference.

In Denmark, 4496 individuals aged 15 to 74 years were studied using anamnestic and clinical identification of signs and symptoms of TMD¹⁴. Joint crepitations were present in 11.3%, i.e. in 14.8% of women and 8.8% of men, the difference being of statistical significance. TMJ pain during mastication was identified in 1.9% of examinees. Statistically significant differences were not reported.

The results of the analyzed studies are presented in Table 1.

The analysis of these studies showed that the prevalence of TMD symptoms greatly varies in the population. It was also established that 30-49% of adults had at least one of the symptoms. The range was very wide for the prevalence of TMJ pain, 1.9% to 31%, as well as for the prevalence of TMJ sound, ranging from 1.8% to 33.6%. The reason for this phenomenon most probably were not the differences between the examinees, but the usage of different criteria for the formulation of questionnaires to be filled in by the examinees. The deviations could also be explained by different modes of sample selection, different assessment of TMD symptoms, but also by the specificities of the population groups regarding the occlusion status and emotional conditions.

Gender-related distribution of TMD symptoms was significant. Most studies demonstrated higher prevalence of TMD in women compared to men, which was in accordance with numerous studies showing that endogenous hormones, especially estrogen, can have an important role in these painful conditions. Biologic effects of estrogen can be explained by the presence of estrogen receptors in the TMJ. These receptors are situated on the synovial membrane, articular disc, and mandibular condyle. Estrogen binding to these receptors can induce ligament slackening in the TMJ which is of relevance regarding TMD development. Studies have shown that pain frequency in the TMJ area increases in those on hormonal therapy. The increase amounts to 30% in women on hormone (estrogen) replacement therapy in menopause, and 20% in those on oral contraception¹⁵. Moreover, it has been shown that estrogen is able to modulate pain pathways in two ways¹⁶. First, it can increase the expression of several neuropeptides in the sensory neurons, which can modulate pain receptor response. Second, estrogen can lower the pain threshold.

First author	Sample size	Age (years)	Country	Symptoms (%)	
Gonçalves (2010)	1230	15-65	Brazil	One of TMD symptoms	39,2
Mobilio (2007)	2005	15-70	Italy	TMJ sounds Teeth clenching Difficult mouth opening Women TMJ pain Women Men	33,6 16,7 11,7 8,4* 3,6 4,5 6,5* 3,1
Nekora-Azak (2006)	1253	<18	Turkey	TMJ pain Women Men TMJ sounds Teeth clenching Difficult mouth opening	31 26,2* 26,2 27,3 23 8,4
Gesch (2004)	4289	20-81	Germany	One of TMD symptoms TMJ sounds TMJ pain	49,9 9 3
Pow (2001)	1526	<18	China	One of TMD symptoms TMJ pain TMJ sounds Difficult mouth opening	33 5 1,8 0,3
Matsuka (1996.)	672	20-92	Japan	TMJ sounds Women Men TMJ pain	24 28,2 20,3 11
Goulet (1995)	897	<18	Canada	One of TMD symptoms TMJ sounds Women Men TMJ pain Women Men Difficult mouth opening Women Men	30 9 12* 6 7 9* 5 4 6* 3
Shiau (1992)	2033	18-26	Taiwan	One of TMD symptoms Women Men TMJ sounds	42,9 47,5* 39,2 5,6
De Kanter (1986)	4496	15-74	Danmark	TMJ sounds Women Men TMJ pain	11,3 14,8* 8,8 1,9

Table 1. Prevalence (%) of TMD symptoms in adults

* Observed statistically significant difference

Prevalence of TMD symptoms in children

Six epidemiologic studies were analyzed in the assessment of prevalence of TMD symptoms in children. In each study, the data about TMD symptoms were analyzed. These data were obtained during anamnestic evaluation, i.e. by way of analysis of patient questionnaires.

In a clinical study in Saudi Arabia (2006) 385 school children aged 12-15 years were analyzed¹⁷. Selection stratification technique was used to determine the schools to be involved. The results showed that in 33% of children there was at least one of the TMD symptoms, which was of statistical significance in girls compared to boys (35.1% vs 21.9%). The most common symptom was mastication pain (14%). Pain was significantly more common in girls (15.6% vs 3.1% in boys). TMJ sounds during mouth opening were found in 8.7% of children, and difficult mouth opening in 2.5%.

A similar study was performed in Brazil¹⁸. The study enrolled 217 children aged 12 to 18 years. The study aimed to establish the prevalence of TMD symptoms in children related to gender. The authors concluded that most common symptoms were TMJ sounds (26.7%), then pain in the joint (12.9%), and difficulties opening mouth (3.2%). All symptoms were more severe in girls, although without statistical significance.

In a study of prevalence of TMD symptoms in Saudi Arabia, 1976 children aged 3 to 15 years were enrolled. The children were from the state schools from 4 districts of Jeddah City. The study was performed in 2003¹⁹. In 24.2% of children there was at least one TMJ symptom. Pain in the joint occurred in 11.1%, TMJ sounds in 4.5%, and difficulties opening mouth in 2.1%. The study did not report any statistically significant difference in the prevalence of symptoms related to gender.

In a study in Greece in 2002 the authors enrolled 314 children aged 6 to 8 years²⁰. Out of the total number of children, 28.9% reported at least one of the TMD symptoms. The overall prevalence of pain during mouth opening was 21.6%, TMJ pain was present in 4.46% overall, and TMJ sounds were reported in 4.1% of children overall. All the symptoms occurred in a higher proportion in girls, though without any significant difference.

A study in Turkey also in 2002 tried to establish the association of TMD, bruxism, and oral

parafunctions in children aged 9 to 14 years ²¹. The study enrolled 203 children. At least one of the TMD symptoms was reported by 67.58% of children. Out of the other symptoms, most common were pain in the joint (29.6%), then TMJ sounds (18.1%), and limited mouth opening (9.8%). There were no significant gender-related differences.

In Japan, a large study was organized, enrolling 7337 school children aged 6 to 18 years ²². The study was performed on the occasion of regular yearly systematic check-up of school children, asking children the questions about possible pain, sounds, and abnormal motion in the TMJ. Overall, 12.2% of children reported at least one of TMD symptoms, with an increasing number of symptoms with advancing age. Sounds were reported by 89.3% of children, pain in the joint by 2.2%, and abnormal TMJ motion (difficulties opening mouth) by 0.9% of examined children.

The results of the analyzed studies are presented in Table 2.

The analysis of these studies demonstrated that the prevalence of TMD symptoms varied very much in children. It was established that at least one of the symptoms was reported by 12.2% to 67.5% of children. The range was very wide for the prevalence of TMJ sounds on mouth opening (reported in 4.5% to 89.3% of cases), as well as for the prevalence of TMJ pain (reported in 2.2% to 29.6% of cases). The reason for this phenomenon most probably were not the differences among the examinees, but the study of different types of samples and use of different methodologies in the study.

However, we cannot overlook the fact that TMJ sounds on mouth opening were found in a high percentage in children. Perhaps this could be explained by occlusal disorders and occlusal instability occurring in children with mixed and those with initial permanent dentition. Moreover, the sounds can be produced as the result of temporary incompatibility of shape of the disc, occurring as the consequence of different speed of growth and speed of bone calcification in children.

The impact of gender on the prevalence of TMD symptoms in children is not so striking as in adults, which can be explained by a reduced impact of sex hormones, i.e. estrogen, in preadolescence.

First author	Sample size	Age (years)	Country	Symptoms (%)
Feteih (2006)	385	12-15	Saudi Arabia	Total33 GirlsGirls35,1* BoysMastication pain14 GirlsGirls15,5* BoysJofficult mouth opening2,5
Bonjardim (2005)	217	12-18	Brazil	TMJ sound26,7TMJ pain12,9Difficult mouth opening3,2
Farsi (2003)	1976	3-15	Saudi Arabia	Total24,2TMJ pain11,1TMJ sound4,5Difficult mouth opening2,1
Vanders (2002)	314	6-8	Greece	Total28,9Mouth opening pain21,6TMJ pain4,46TMJ sound4,14
Sari (2002)	203	9-14	Turkey	Total67,5TMJ pain29,6TMJ sound18,13Limited mouth opening9,89
Motegi (1992)	7337	6-8	Japan	Total12,2TMJ sound89,3TMJ pain2,2Difficult mouth opening0,9

Table 2. Prevalence of TMD symptoms in children

Conclusion

The results of many epidemiologic studies can hardly be compared due to different methodologies utilized in them. That is the reason why we recommend the use of universal methods in epidemiologic studies. The picture about the prevalence of TMD symptoms could thus be made much clearer.

The prevalence of most TMD symptoms is significantly higher in women. Adequate treatment of these dysfunctions is thus of great importance in women, especially in their reproductive age of life.

The prevalence of TMD symptoms is high in children as well, indicating the necessity of their early diagnosis, so that proper growth and development of the stomatogenous system may take place.

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Neuroscience of music and musicotherapy

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Abstract

The effect of music on human physiological functions is a very fruitful field of scientific study, both theoretical and empirical. The aspects of musical experience may be analysed by breaking the perceived sounds into notes and tones with complex interrelationships. The experience of music somehow goes beyond this, probably because a unified qualitative impression arises from complex sequences, such as chords, but not from randomly selected notes. This paper discusses the perceptual dimensions of hearing used to represent high-level musical features in the brain, as well as the areas of the brain and their roles in music perception and performance. Music was considered capable of restoring the balance between the soul and its faculties, thanks to its great emotive power. The relationship between the physics of sound and the psycho-neuroimmuno-endocrinologic system has been analyzed in many studies trying to investigate the methodology of the use of music, the evaluation systems, and scientific and applicative research in the field of prevention, rehabilitation, and therapeutics. A basic concept underlying the use of music as a therapeutic agent is that music can relieve stress and promote relaxation. Emotional states and pain sensitivity are also susceptible to modification through music. Facilitated by trained musical therapists, by either actively making music or listening to it, many patients can achieve significant therapeutic goals.

Key words: music, emotion, cognition, brain, therapy

Introduction

The sound phenomenon is studied from the perspectives of diverse disciplines: psychology, medicine, education, musicology, sociology, an-

thropology, biology, philosophy, physics and their sub-disciplines. There are many interdisciplinary fields whose central aim is to comprehend how humankind perceives music, focusing on emotional, cognitive and physical processes: affective science (emotions and music), music cognition, music perception, music performance, music theory and finally, not the least, music therapy (1,2). The study of the biological foundations of music, likewise, is trying to bring together the fields of genetics, developmental and comparative research, neuroscience, and musicology. By studying the development of probably most demanding tools, musical instruments, we can infer something about the precise execution of very fast, and in many instances, extremely complex movement patterns, characterising the skills of professional musicians. Some examples of interdisciplinary integration and collaboration extend far back into the history of mankind. One of them is a bone flute found in Divje Babe, a site in Slovenia, dating back to the middle Paleolithic (50,000-35,000 years B.C.); another has been found in the French Cave of Isturitz, and dates back to the Aurignacien (35,000-15,000). The flute is played with the index, middle, and ring fingers. A typical forked movement pattern is the combination of the fingerings no. 3 and 6 (from the left in Figure 1.), requiring the index and forth finger to be extended, whilst the middle finger is synchronously flexed (3). Clearly, these kind of forked finger movements were not common tasks in ancient hunter-gatherer societies. Even today, about 2% of people are unable to properly execute synchronous antagonist movements of adjacent fingers. Skilled movements do not only rely on anatomical properties, but more critically on central nervous processing. Such movements are associated with a very variable pattern of muscular co-contraction of many different, partly antagonist muscles with different levels of activity organized into a specific pattern. Furthermore, the processing of three-dimensional body coordinates and object coordinates, knowledge about the mechanical properties of the handled objects, precision of motor programming and rapid reciprocal visual, somatosensory and motor information transfer are necessary. Finally, the mental representations of all these properties have to be maintained in procedural memory. All of this suggests that the neural bases of cognitive processing and especially of 'modern' skilled behaviour were present long before the documentation of elaborate sensorimotor problems became available.



Figure 1. Fingering table and obtained tones from a reconstruction of the Divje babe flute (modified according to 3)

Psychophysiology of musical emotions

Emotions are difficult to define and measure, since they are commonly regarded as a multicomponent phenomenon. One of the definitions is that emotions are fairly brief and intense reactions to goal-relevant changes in the environment, which consist of several sub-components: cognitive appraisal, subjective feeling, physiological reaction, expression, and action tendency and emotion regulation (4). In contrast to emotions, moods are commonly understood as diffuse affective states of low subjective intensity but relatively long duration, often without an apparent cause. It is possible that the distinction between emotion and mood may be particularly central to musical emotions. Emotions can be viewed as phasic perturbations that are superimposed on the tonic affective background prodded by mood. Inclusion of measures of different sub-components might increase the ability to decide exactly what kind of reaction to a musical event has occurred.

The primary structural rules relating music and emotion may be presented as a graph on the Two Dimensional Emotion Space: valence (negative vs. positive) and arousal (passive vs. active). A meta-analysis (5) of attributes of music and commonly reported emotions, showed, for example, that happy upbeat music tends to have a faster tempo (20 studies), be composed in a major mode (19 studies), have above average loudness (10 studies), staccato articulation (5 studies) and above average pitch (4 studies).

The conveying of emotion is considered to be the essence if not the purpose of music and the reason that most people report spending large amounts of time listening to it (6). Musical emotions are a short term for "emotions that are induced by music." Emotion is essential in the arts (literature, drama, music and fine art), which might be described as being concerned with the basic expression of emotion and the manipulation of the emotion of others (7). The ability of music to modify mood is a fact of everyday life. The fact that music would have fairly robust effects on various body parameters is to be expected, simply from the fact that music arouses emotions, and emotions are characterized by many autonomic changes. The cochlea translates the initial acoustic information into neural activity that reaches the auditory brainstem. Then, in the auditory cortex an initial features extraction from this information is carried out. This activity is followed by: the grouping of these features (pitch height, timbre, etc.) using gestalt principles and the analysis of intervals (pitch relation, time relations, etc.). Meaning and emotions are essentially induced when musical structures (harmony, meter, rhythm and timbre) are built. After all these processes body reactions and immune system variations are induced via the autonomic nervous system (ANS). ANS is the nervous system that influences the physiological responses according to specific (musical) stimuli.

One good example of investigation (8) are measurements of heart rate (HR), electromyogram (EMG), respiration depth (RESP), electrodermal response, and skin temperature during positron emission tomography (PET) scans. After each PET scan, subjects rated their emotional reactions to each stimulus with ratings for "chills intensity" (0 to 10), "emotional intensity" (0 to 10), and "unpleasant versus pleasant" (-5 to +5).

Music has been shown to be effective in positively affecting physiological stress parameters such as pulse rate, blood pressure, respiration, galvanic skin resistance (GSR), and electroencephalography (EEG). Music can reduce stress hormones (ACTH, cortisone) and increase the emotional neurohormone, beta endorphin, acting as a protection mechanism against emotional excitation. Levels of neurohormones and neurotransmitters such as dopamine, norepinephrine, endogenous morphines, enkephalin and phenylethylamine can be elevated through music. For example, music (Mozart K.205) leads to increased calcium/CaM-dependent DA synthesis in the brain, thus causing a reduction in blood pressure. Music might regulate and/or affect various brain functions through dopaminergic neurotransmission, and might therefore be effective for the rectification of symptoms in various diseases that involve DA dysfunction (9).

The influence of musical features on emotional types and psycho-physiological changes characteristic for those emotions are shown in Table 1.

Investigation results (10) showed that happy and sad music were significantly differentiated (happysad) by diastolic blood pressure, electrodermal activity, and zygomatic activity, while the fast and slow rhythmic and tempo control versions did not elicit such differentiations. In contrast, respiration rate was faster with stimuli presented at fast tempo relative to slow stimuli in the beat-alone condition. It was thus demonstrated that the psycho-physiological happy-sad distinction requires tonal variations and cannot be explained solely by entrainment to tempo and rhythm. The tempo entrainment exists in the tempo alone condition but these results suggest that this effect may disappear when embedded in music or with the rhythm.

Important consideration regarding the nature of musical emotions concerns the "locus" of the emotion: Is it in the music, in the listener, or in both? This question invokes the idea - known since ancient Greece - that music may both "represent" emotions (that are perceived by listeners), and "induce" emotions (that are felt by listeners) (1, 12).

Several methodological problems such as language issues, social and personal modesty and disturbances introduced by the presence of the analyst are present in investigating the cross-cultural perspective of emotions created by music. One way of objectivising and analyzing the emotional expression in music performance and body motion is a real time algorithm i. e. fuzzy analyzer (13). The fuzzy mapper translates the cue values (tone parameters such as tempo, sound level and articulation from audio input or overall quantity of motion and vertical/horizontal motion from video input) to three emotion outputs: happiness, sadness, and anger. A recent system provides real-time expressive visual feedback of music performance and allows mapping between the acoustic cues and the expressivity dimensions of

Table 1. Musicians' use of acoustic cues when communicating emotion in music performance (modified according to 6) and relations between emotions and psychophysiological responses (modified according to 11). Abbreviations: c- change; n-normal

		Acoustic cues]	Psyc	ho-j res	ohys pon	iolo ses	gical	I
Emotion	mean tempo	tempo variabil.	sound level	articulation	duration contrasts	timbre	tone attacks	micro-intonat.	vibrato	ritardando	heart rate	blood pressure	skin conductance	temperature	respiration	rate of blood flow	amplitude of blood flow
Sadness	slow	large	low	legato	soft	dull	slow	flat	slow	final	с	c	c	c	n	n	n
Fear	fast	small	high	staccato	sharp	sharp	abrupt	accent unstab. notes	large extent	no	n	n	n	n	n	с	c
Happiness	fast	small	high	large variability (staccato)	sharp	bright	fast	rising		small	n	n	n	n	с	n	n

the face. As the music expressivity changes, the facial expressions and the quality of movement of the agent get modified accordingly (14). The coupling of theoretically precise psychological predictions with modern brain imaging techniques promises to be one of the most important domains of research in this millennium (12).

Music and cognition

Music is a biologically deeply ingrained function of the human brain and, as such, basic to cognitive structure. Music and language constitute complementary components of the human communicative toolkit (15). The brain can respond in highly plastic ways to musical input and production, and the continued and intense practice of music can lead to significant structural and functional adaptations in the brain. For example, the neural reshaping of central nervous hand representations begins after such short time intervals as 20 minutes of the dissolution of the practice (16) and continues during practice. This activity results in enlarged cortical representations of, for example, specific fingers within existing brain structures. Listening to music involves not only hearing but also visual, tactile and emotional experiences. Each of us processes music in different regions of the brain (17). The musicians' brain is an excellent paradigm to study the short-term and long-term effects of central nervous neural plasticity and long term adaptation in sensorimotor systems, even in macroscopic brain structures.

Emotional reactions to music may come, among other ways, through cognition, so it is suggested that we recognise what is familiar and we like what we know (recognise). Emotional reactions to music may be explained in evaluative cognition and arousal. Some emotional impact of beautiful music may be caused either by the form of the music, which reflects Gestalt laws, or by music as a language, which expresses emotions and musical events similar to other events of the world.

For just one example, music made by a special instrument, bagana, can "attract the mind and control the emotions", probably due to the religious character of the instrument. Bagana performances arouse a specific kind of emotional reactions with specific vocal and instrumental timbres and low loudness of the instrumental sounds decreasing a lot with distance (18). Repetitiveness is typical of music with a strong influence on the state of consciousness among many musical traditions, and even among Western-trained listeners.

Brain areas involved in music processing: a link between emotion and cognition

The perceptual dimensions of hearing (pitch, timbre, consonance/roughness, loudness and auditory grouping) are used to represent high-level musical features (melody, harmony and rhythm) in the brain. The areas of the brain and their roles in music perception and performance are presented in Figure 2.



Figure 2. Brain areas and their roles in music processing (modified according to 19)

Several animal models have recently been used to elucidate how vocalizations are processed in the brain, specifically in the auditory pathway. The most frequently used animals are songbirds and mammals such as bats, rodents, cats and primates. Guinea pigs represent a suitable model for studying the representation of communication signals in the neural system due to their rich repertoire of communication calls and the characteristics of their hearing, with an audible range from 50 Hz to 50 kHz (20-22). The neural coding strategies in the guinea pig are likely applicable to the auditory system of other mammals, and data from the guinea pig model can be compared to studies performed in other species that describe the transformation of the neural representations of vocalizations and other complex stimuli from the inferior colliculus (IC) to the auditory cortex (AC). The selectivity of neuronal responses for individual calls in higher centres of the auditory system is usually low most neurons respond to calls as well as to artificial sounds; the coding of complex sounds in the central auditory nuclei is apparently based on the representation of temporal and spectral features of acoustical stimuli in neural networks.

Music can arouse basic emotional circuits at low levels of auditory input. Intrinsic emotional sounds may be decoded within the brainstem. For instance, the inferior colliculus, richly endowed with opiate receptors, is the station of the auditory pathway, where the mother's voice may leave its first affective imprints and may mediate attachments which are developed to certain sounds (e.g. the voices of those we love) and hence, by a parallel line of reasoning, to certain types of music (23, 24). Periaqueductal gray matter (PAG), an area adjacent to the inferior colliculus, is the place where all emotional systems converge upon a coherent self-representation of the organism, a primordial core consciousness (23), and affective consciousness (i.e. the generation of valenced feelings, generated largely by the neurodynamics of the subcortical emotional/instinctual system that we share with other animals). Music is not a uni-dimensional process, and many distinct, but widely distributed, brain areas participate in the neural coding of music.

The auditory processing of musical information could easily access the higher reaches of various emotional systems through temporal lobe inputs into the amygdala, frontal and parietal cortical inputs into other basal ganglia such as the nucleus accumbens as well as more direct inputs to limbic areas such as the cingulate and medial frontal cortices (8). The neural basis for musical rhythm is a highly complex and modular network system (25).

A novel theoretical framework has been proposed, featuring six additional mechanisms through which music listening may induce emotions: brain stem reflexes, evaluative conditioning, emotional contagion, visual imagery, episodic memory, and musical expectancy (26). Music evokes emotions through mechanisms that are not unique to music. The study of musical emotions could benefit the emotion field as a whole by providing novel paradigms for emotion induction.

"Emotional" brain processing of non-musicians in reaction to classical music, recorded by fMRI, occurs in this particular order: the auditory cortex, then frontal regions, followed by mesolimbical system. The subcortical regions that became involved include nucleus accumbens, VTA and the hypothalamus. The cerebellum and basal ganglia are activated throughout. There is the feeling of reward and satisfaction as the brain, through the activity of the cerebellum, synchronizes neural oscillators to the pulse of the music (27). Rhythmical aspects of the musicking entrain neural oscillators and this facilitates the synchronization of perceptions and bodily action with the rhythm. This entrainment results in the coupling of the individual's nervous system and in the process a uniquely human social space is created. Secretion of the neurohormones such as oxytocin leads to the dissolution of the solipsistic barrier and fulfills the need for increased social bonding.

Humans activate a circuit composed of temporal, parietal and frontal neurons while observing the actions of others. The frontal and parietal nodes of this circuit are active both when the subjects perform an action and when they perceive someone else perform a similar action. When skilled pianists listen to piano tunes, the primary hand area of the precentral area is active, revealing an unconscious corepresentation of heard tunes as movement patterns. Furthermore, an auditory association area between the temporal and the parietal lobe lights up (28). Compared with nonpianists, the pianists demonstrate stronger activations of brain areas 6 and 44 (BA6/44), rostral inferior parietal lobule (IPL) and middle temporal gyrus (MTG) while listening to piano pieces (Figure 3).



Figure 3. Lateral view of the human brain with the location of brain areas (BA) 6/44, inferior parietal lobule (IPL) and middle temporal gyrus (MTG) together with their anatomical connections (arrows) (modified according 29)

The acquisition of the novel motor skill of piano playing also enhanced the auditory mirror representation of these actions while listening. This observation might relate to the fact that pianists often find it harder to keep their fingers still while listening to piano pieces (30). Also, dance can be conceived of as an extension or complementary correlate of the movements required to create music. The connection between music and dance can be thought of as an extension of the movements required for vocalizing simply applied to other body regions (31).

Auditory features of the musical signal are processed primarily in the superior temporal gyrus (STG) and combined with synchronous structural features of the 'motion' information conveyed by the musical signal in the posterior inferior frontal gyrus (BA 44) and adjacent premotor cortex. The anterior insula forms a neural conduit between the mirror neuron system and the limbic system, allowing this information to be evaluated in relation to one's own autonomic and emotional state contributing to a complex affective response mediated by the limbic system.

Possible feedback mechanisms may influence the subsequent processing of the musical signal at the immediate and more long-term timescales. The shared recruitment of this neural mechanism in both the sender and the perceiver of the musical message allows for co-representation and sharing of the musical experience (32).

Functional asymmetry of the brain hemispheres for music processing

The music is built upon the prosodic mechanisms of the right hemisphere that allow affective emotional communications through vocal intonations, while skills (which are not essential for everyday enjoyment of music) needed to deal with musical information in more cognitive ways are elaborated by the left hemisphere (33, 34). Electroencephalography (EEG) showed frontal brain electrical activity in healthy controls during their rating of valence and intensity of four orchestral pieces. A greater activity relative to the left frontal EEG in response to positive stimuli and greater activity relative to the right frontal activity for negative stimuli was found (35). A similar lateralization pattern was shown (36) for positive emotional attributions accompanied by an increase in the left temporal activation and negative emotional attributions by an increase in the right frontotemporal cortex.

An emotion processing network in response to music integrates the ventral and dorsal striatum, areas involved in reward experience and movement; the anterior cingulated cortex (ACC), which is important for targeting attention; and medial temporal areas, traditionally found in the appraisal and processing of emotions (37). Happy musical stimuli were associated with increased activation in the bilateral ventral and left dorsal striatum, left ACC and left parahippocampal gyrus. Sad musical stimuli led to increased activation in right medial temporal structures. Presentation of neutral music was associated with increased BOLD signal responses in the insula and auditory association areas.

The investigation (25) showed that the pitch/ melodic contour system is separate from the rhythm perception system in the brain. In nonmusicians, pitch/melody discrimination activated right auditory cortex regions. Each rhythm component showed a different neural brain network subserving the different rhythmic elements. Meter prominently activated inferior frontal gyrus regions, pattern discrimination was mediated by activations mostly subcortically in midbrain regions, tempo discrimination activated prefrontal areas, and the duration judgments activated additional areas in the inferior prefrontal gyrus region. All tasks showed a significant involvement of the cerebellum, demonstrating that the cerebellum is not only important for motor control but also for complex sensory perception without any movement. One of the most interesting insights from this study may be that the partial separation of networks in the brain subserving each rhythm function constitutes the neurological basis for the brain to be able to create very different rhythmic languages and vocabularies across music cultures.

Emotional responses to unpleasant music in healthy volunteers were associated with a significant increase of cerebral blood flow in the right parahippocampal gyrus and a decrease of blood flow in the orbitofrontal cortex and the subcallosal cingulum. Regions associated with reward/ motivation circuitry, such as ventral striatum, dorsomedial midbrain, amygdala, and hippocampus, correlated with chills intensity, but not with the more mildly pleasant emotion associated with consonance. These discrepancies provide further evidence that different emotions are associated with activity in different groups of brain structures. In contrast, ventral medial prefrontal cortex (VMPF) and orbitofrontal cortex (OfC) activity changes were seen in correlation with pleasant emotion, although VMPF subregions differed between studies. These regions may subserve multiple emotional functions and therefore may respond to more than one type of emotion.

Music therapy

Music recruits neural systems of reward and emotion similar to those known to respond specifically to biologically relevant stimuli. The involvement of dopamine in the nucleus acumbens and ventral tegmental area is a key factor in the regarding effect of food, sex, psychoactive drugs of abuse and also music (27, 38). Perhaps as the formation of anatomical and functional links between phylogenically older, survival-related brain systems and newer, more cognitive systems increased, the general capacity to assign meaning to abstract stimuli, and the capacity to derive pleasure from these stimuli, also increased. The ability of music to induce such intense pleasure and its putative stimulation of endogenous reward systems suggests that, although music may not be imperative for the survival of the human species, it may indeed be a significant benefit for mental and physical well-being (8, 39).

The question about the nature of music has implications for how caregivers raise children, how educators teach students and how clinicians diagnose and treat patients (40). Music has positive effects during pregnancy, harmony labor, and delivery in various stressful contexts, such as the operating room. The choice of music by the patient may not necessarily coincide with the preferences of the physician. The use of music with specific components of rhythm, tone, pitch, dynamics, melody, and harmony may successfully control the sensitive environment of the neonate. Music therapy is especially effective when applied to neonates, children with autism, and children and youth with psychopathological problems. The physiological impact of music in medical treatment, determined by both research and clinical work (Table 2) is obvious in physiological parameters like heart rate, arterial blood pressure, salivation, skin humidity, blood levels of stress hormones like adrenocorticotropic hormone (ACTH), prolactin, human growth hormone (HGH), cortisol, betaendorphine, which show a significant decrease under anxiolytic music compared with usual pharmacological premedication. EEG studies have demonstrated sleep induction through music in the preoperative phase. Music reduces arousal states, and length of hospital stays by an average of 5 days, while increasing weight and caloric and formula intake in low-birth-weight neonates. The results of the experiment with animals (24) confirmed that extended early exposure to classical music could have complex effects on brain biogenic amine levels and metabolism in an avian species. Exposure to classical music elevated whole brain norepinephine (NE) by 31% and reduced the dopamine (DA) metabolites dihydroxyphenylserine (DOPAC) by 28% and this last effect was significantly larger in social than isolate animals. These results suggest one reason why Auditory Integration Training (AIT) may have had beneficial effects on young autistic children in certain studies where the music tends to promote certain brain neurochemical, especially brain NE, activities, and hence facilitating attentional proc-

esses. Psychoneuroimmunology is documenting the effectiveness of music therapy in terms that are important in the context of a biological medical model (41). Recent imaging studies have shown that some of music's effects are specifically elicited by the sites and ways in which it is processed by the brain's neuronal network. Such processing can influence and alter our emotional experiences and the perception of pain (42, 43). Music can provide some relief from pain through the release of endorphins and promotion of relaxation. It can also provide an opportunity for the patient to reminisce and talk about the fears that are associated with death and dying. Music may help regulate the rapid breathing of a patient who is anxious, and soothe the mind. After listening to relaxing music for 20 minutes, patients with myocardial infarction exhibited significant reductions in myocardial oxygen demand, heart rate, respiratory rate, and anxiety (44).

Music is used within a therapeutic relationship to address individuals' physical, emotional, cognitive and social needs. The common roots of music-making were the establishment and maintenance of social bonds, the need for communication, among other things, the need to express and share emotions. Exclusion from the engagement in social functions represents an emotional stressor, and has deleterious effects on health (45). The explanation of music's effect on health is through activity involving at least seven social functions, which are important for the survival of the individual and thus for the human species. Music always involves communication. Making music presupposes making contact with other individuals, it engages social cognition and increases the social cohesion of a group, involves coordination of actions and cooperation between players, where inter-individual emotional states become more homogenous. Music making, a new music therapy method (46), increases the mood of individuals and it is promising in encouraging further development for the treatment of affective disorders.

Music therapy is recognized as an effective psychotherapeutic approach. A distinction needs to be drawn here between music therapy, which always involves the participation of a qualified music therapist, and the concept of music medicine, in which music is employed as an ancillary therapy by those who are not necessarily specialized in the field. The areas in which music therapy can be applied can be broadly subdivided into clinical, pedagogic and gerontologic applications. Some of the relaxing properties of music, for example some slow movements from Mozart's piano sonatas, can elicit stress-reducing effects, through a biochemicaly measurable reduction of inflammatory markers and improved activation of the immune system natural killer cells (47, 48). A group of Japanese scientists (49), working in a geriatric nursing hospital, observed in a group of 87 elderly patients with cerebrovascular disease and dementia a decrease in biochemical parameters such as cytokine and catecholamine levels, as well as a decrease in congestive heart failure events.

There is evidence suggesting a strong benefit of music, including that as a mnemonic device, in a variety of clinical settings (50). The mechanisms underlying successful musical mnemonics are not well understood, but may relate generally to a shared cognitive architecture for both music and linguistic processing (15, 51). Patients with Alzheimer's Disease (AD) performed better on a task of recognition memory for the lyrics of songs when those lyrics were accompanied at encoding by a sung recording than when they were accompanied by a spoken recording (52). The authors propose two possible explanations for these findings: first, that the brain areas subserving music processing may be preferentially spared by AD, allowing a more holistic encoding that facilitates recognition, and second, that music heightens arousal in patients with AD, allowing better attention and improved memory.

Table 2.	Clinical fields and conditions suitable for
treatmen	t with music therapy

Clinical field	Selected conditions/goals				
Palliative	Audioanalgesia, anxiety reduction,				
medicine	terminal care				
Description	Autism, anxiety reduction,				
r actilations	migraine, neonatology				
	Stroke with hemiparesis, memory				
Neurology	performance, fine motor action,				
	fine motor function in speech				
Psychiatry	Depression, schizophrenia				
Psychosomatic	Tinnitus, pain, burn out, stress				
Gerontology	Dementia, reduction in agitation				
	Illness adjustment, audioanalgesia,				
Oncology	anxiety reduction, life quality,				
	expression of emotions				

There are two fundamentally different types of music therapy: active and receptive. In active music therapy, the patient makes music either alone, with a therapist or within a group. In receptive music therapy, the therapeutic goals are pursued exclusively by listening to music. A striking difference between the two forms, however, is that receptive music therapy encourages the patient to recall past events while active music therapy urges the patient to create - rather than recall - an experience, and this creation is an implicitly forwardlooking exercise. Active and receptive therapeutic modes are recommended in combination, but active therapeutic models are recommended for all selected conditions, except for oncology and palliative medicine where receptive therapeutic modes are highly recommended as well.

Conclusion

The processing and production of music are highly complex activities that place great demands on our brains. Music is processed in different regions of the brain and it has short- and long-term effects on central nervous neural plasticity. Music elicits and conveys emotions, which is the reason why most people spend large amounts of time listening to music. Music has been shown to be effective in positively affecting many physiological stress parameters. It can reduce stress hormones and increase the emotional neurohormone acting as a protection mechanism against emotional excitation. Simply consuming music is unlikely to promote mental abilities without additional individual input or initiative. For example, making music challenges humans at many levels, including fine motor skills, memory and responsiveness to stimuli. It trains not only human cognition, but on the level of the personality, it affects how humans deal with own emotions. As such, it is an important resource for learning self-discipline.

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Knowledge and awareness of tuberculosis among medical and dental students in Belgrade, Serbia

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Abstract

Aim: Tuberculosis (TB) continues to be an important health problem in Serbia, as a country with numerous socioeconomic problems. Health care workers, especially medical and dental students could be key persons to engage in prevention of TB.

The aim of our study was to compare the knowledge level and awareness of TB among medical and dental students.

Methods: Cross-sectional study was conducted at the School of Medicine and the School of Dentistry, University of Belgrade, Serbia. A sample of 350 students was selected by stratified sampling. Data about knowledge and awareness of TB was collected through the anonymous (self-administered) questionnaire.

Results: 300 questionnaires were returned; response rate was 85.7%. Medical students gave significantly higher correct responses about modes of transmission of TB (p<0.001). Significantly higher proportion of medical students (p=0.003) knew that age above 65 years is risk period of life for getting TB, but only 6.5% of them noted that the age of puberty is the risk period too. High proportion of both groups agreed that alcoholism and AIDS are the conditions, which can increase risk for getting TB. Medical students have better knowledge about therapy of TB, but there were no differences concerning questions about diagnosis.

Conclusion: In spite of valid basic awareness of TB, there were some gaps in the knowledge, more frequently among dental then medical students. This study suggests that students need more training and more practice.

Key words: tuberculosis, knowledge, students, medical education, TB treatment, awareness

Introduction

Tuberculosis (TB) has re-emerged as one of the highest burden communicable disease (1). It is one of the most common infectious diseases nowadays, responsible for the largest number of deaths from a single infectious cause. Due to global migration and an increasing number of immunocompromised persons, the probability of getting infected with Mycobacterium tuberculosis is increasing. TB incidence rates have increased in the Eastern European countries in the last decade. Contrary to these countries, the total TB incidence rates in Serbia had been moderately decreasing during the same period. Average annual TB incidence rate in the general population was 33.9/100 000 (2). However, in spite of this fact, TB continues to be an important health problem in Serbia, as a country with numerous socioeconomic problems. There is need to establish the prevailing awareness towards TB. Health care workers, especially medical and dental students could be key persons to engage in prevention of TB. Their knowledge about it is important for later differential diagnosis, primarily for medical students in their future clinical practice. Dental students are also important. In their practice they could be exposed to the infection. Also, as health care workers they should have a role in early case detection.

TB is thought within several subjects at the School of medicine and School of dentistry, mostly within Internal medicine. Until 30 years ago, much attention was paid to TB in the program of Internal medicine. Students were obliged to pass oral exam in TB in order to take the exam in Internal medicine. In late 80's the interest in TB in Serbia declined, due to decreased prevalence and mortality rates. Therefore, separate exam in TB was abandoned,

and knowledge about TB was tested during oral exam in Internal medicine, as students obligatory had one question related to TB. Fifteen years ago the obligatory question related to TB within the exam in Internal medicine was abandoned. In the same time, the number of hours dedicated to TB was reduced. At the School of Dentistry the number of hours dedicated to TB was mostly within Internal medicine, but also within Oral surgery and Radiology. However, TB was never so significant issue and was never obligatory question at any exam.

The aim of our study was to assess general knowledge level and awareness of TB, knowledge about risk factors, diagnosis and treatment of TB among medical and dental students.

Methods

Cross-sectional study was conducted at the School of Medicine and the School of Dentistry, University of Belgrade, Serbia, during November of 2006/2007 academic year. A sample of 350 students was selected by stratified sampling. Students currently enrolled in their last year (after exam of internal medicine and epidemiology). Data about knowledge and awareness of TB was collected through the anonymous (self-administered) questionnaire. Study participants were instructed to choose only a single answer to each question. The questionnaire was consisted of four parts. The first part referred to demographic data; the second part consisted of etiology and transmission; the third of symptoms, diagnostic procedures and treatment; the fourth of risk factors for tuberculosis. It has taken them approximately 15 minutes to complete the questionnaire. Statistical analysis was performed using Fisher's Test. A p level < 0.05 was considered statistically significant.

Results

Questionnaires were completed and returned by 300 students (a response rate of 85.7%). There were 199 medical and 101 dental students; 183 (61%) of total were females and 117(39%) males, the gender ratio was not significantly different between medical and dental students. The overall mean age of respondents was 24.7 (\pm 1.2) years.

There were 5 questions on general knowledge about TB. Medical students gave significantly higher correct responses in comparison with dental students (Table 1). Only about one third of dental students knew that a cough longer than three weeks is the most important symptom of the disease and that close contact with patients who have Mycobacterium tuberculosis infection does not regularly cause the active TB. Knowledge about risk factors included questions about the risk period of life for getting TB (Table 2). Significantly higher proportion of medical students knew that risk period is above 65 years. Low proportion of medical (18.6%) and dental students (18.8%) recognized that women are more susceptible to TB during pregnancy and in post pregnant period. Only 6.5% of medical students noted that the age of puberty is the risk period too. High proportion of both groups agreed that alcoholism and AIDS are the conditions which can increase risk for getting tuberculosis. Medical students showed better knowledge about poor living conditions and unhealthy diet, smoking and diabetes mellitus as the contributing factors to the incidence of TB (Table 2).

	Number (%) of correct response			
Question	Medical students (n=199)	Dental students (n=101)	p-value	
TB is communicable disease	195 (97.9)	87 (86.1)	0.0001	
Transmission of TB through air	197 (98.9)	81 (82.6)	0.0001	
Close contact with patients with TB infection does not regularly cause the active TB	190 (95.5)	38 (37.6)	0.0001	
Role of immunity in the appearance of TB	195 (98.5)	81 (88.0)	0.0001	
Cough is the most important symptom of TB	190 (95.5)	63 (33.0)	0.0001	
BCG vaccination at birth can not provide 100% protection against TB	166 (83.4)	29 (28.7)	0.0001	

Table 1. Current general knowledge about tuberculosis among medical and dental students

	Number (%) of correct response				
Question	Medical students (n=199)	Dental students (n=101)	p-value		
Risk period of life for getting TB					
Over 65 years	173 (86.9)	74 (73.3)	0.003		
Pregnancy and post pregnant period	37 (18.6)	19 (18.8)	NS		
Puberty	13 (6.5)	36 (35.6	0.001		
Conditions which can increase risk for getting tuberculosis					
Alcoholism	135 (67.8)	69 (68.3)	NS		
Poor living condition and diet	143 (71.9)	47 (46.5)	0.001		
AIDS	166 (83.4)	79 (79.2)	NS		
Smoking	106 (53.3)	29 (28.7)	0.001		
Diabetes mellitus	138 (69.3)	19 (28.7)	0.001		

Table 2. Students` knowledge about risk factors for tuberculosis

Table 3. Students` knowledge about diagnosis and therapy for tuberculosis

	Number (%) of correct response			
Question	Medical students (n=199)	Dental students (n=101)	p-value	
Diagnosis				
Sputum investigation is the fastes way	62 (31.1)	40 (39.6)	NS	
X-ray is not gold standard in diagnosis of TB	84 (42.2)	33 (33.3)	NS	
Therapy				
With three and more medication	192(96.5)	74 (74.0)	0.001	
Duration of treatment is 6-8 months	158 (79.3)	35 (34.6)	0.001	
Medication is necessary every day	183 (91.9)	77 (76.2)	0.001	
Necessity of therapy for pregnant women	184 (92.4)	46 (46.0)	0.001	
TB is deadfull disease	196 (98.5)	80 (79.2)	0.001	

Seven questions referred to diagnosis and therapy of TB. Only one third of students (34%) had the correct opinion that laboratory sputum investigation is the fastest way to detect disease, whereas 66.0% said that those were chest x-ray or laboratory bacterial culture. One of the questions was about test for proving diagnosis of tuberculosis. Two thirds of tested students did not know the correct answer and thought that chest x-ray is the gold standard for proving diagnosis. Medical students have better knowledge about therapy of TB, but there were no differences concerning questions about diagnosis. Among dental students only one third knew the duration of treatment and 46.0% that it is necessary to treat pregnant women with TB (Table 3).

Discussion

One essential step for adequate containment of TB is to ascertain the understanding in society of the risk factors, modes of transmission and diagnosis. Education may be one of the principal means for reducing TB (3). Health care professionals play a vital role in it and their negative opinions may affect the personal consequences of infections, prevention, care and management of the disease (4). Our study investigated knowledge and awareness of medical and dental students about TB, first and foremost because they will be the future practitioners in health care. In general, students had good general knowledge about TB as communicable disease, its mode of transmission, and role of immunity in the appearance of TB. But, there were differences in knowledge between medical and dental students. The general knowledge level of medical students was similar with knowledge of medical students in Oman

(4) and China (5). In the study conducted among final-year medical students in Canada, India and Uganda (6) authors had hypotheses that students in endemic areas would have increased awareness and knowledge about TB. After adjusting for number of curricular hours, the basic level of knowledge was similar at each site. Students' education is one of the most important factors for their further work. It can help them not only in providing appropriate and comprehensive care for TB patients but also in protecting themselves from TB. Besides the prevalence of TB in the community, the effectiveness of TB infection control interventions and area of health care facility, the education level is important factor to diminish the risk for transmission of TB to all health care workers (HCW). Comparing with medical students who almost all had correct answers, about two third of dental students in our study did not know that every person will not get active TB after contact with TB patients. Dental students had a great fear of TB patients for getting the disease. Additionally, the lack of knowledge about most important symptom of TB among dental students was noted. But, they overestimated the effect of BCG vaccination. It may be explained by the less time spent on tuberculosis education. Nevertheless, they showed lower knowledge about TB symptoms than rural Vietnamese adults with cough in Vietnam (7) and patients in Karachi (8). The transmission of tuberculosis in the dental setting was reported (9). Dental aerosols (liquid and solid) contain microorganisms (including M. tuberculosis), dental materials, and tooth particles. Aerosolized bacteria may remain suspended in the air for long periods of time and inhaled into the lungs of oral health workers. Although cough inducing procedures have been identified as carrying the highest risk for TB transmission, infection control practices call for measures to control generated aerosols as well (10). Our dental students need more training about symptoms of TB infections, mechanisms of transmission and current infection control recommendations.

Another part of our investigation was assessing knowledge about risk factors for TB. Students were informed that age above 65 is the risk period of life for getting TB. It was unexpected that about 80% students did not know that pregnancy and post pregnant period could be also one of the possible risk factors. It was especially important

for medical students as possible future gynecologists and pediatricians. Another misunderstanding was about risk of getting TB at the age of puberty. Medical students had lower degree of information than dental students. Our study showed great gaps in students' knowledge about period of life when there is high risk possibility for getting disease. The majority of interviewed students knew that AIDS is condition which can increase risk for getting TB. Among all other questions about conditions, information about AIDS was the best. Contrary to the western countries, AIDS incidence in Serbia remained low (1051 new cases during the period 1990-2006), and TB was not frequent among AIDS cases. For example, among 54 AIDS cases reported in 2004, only 7 (12.3%) had TB (11). Nevertheless, a lot of publications and information about AIDS available in our country in the last decade increased students' knowledge. Among all conditions, which can increase risk for getting TB, the most frequent neglected were smoking and diabetes mellitus, especially in the group of dental students. Limited teaching in internal medicine can explain the lack of knowledge about diabetes mellitus among dental students. Therefore, it was most disturbing that high proportion of students neglected smoking as one of the factors responsible for appearance of TB. Several studies have evaluated the effect of smoking on TB (12, 13). Although possible confounding factors, such as alcohol and socioeconomic status should be examined, there is now considerable evidence that tobacco smoking is associated with TB. Our students need more education about this issue, especially taking into account the fact that among out TB patients majority are smokers. Moreover, patient smokers more often suffer from smear-positive TB, as pointed by Skodric et al (14). In spite of reduction of the smoking rate by 6.9% in adult population in Serbia during the last six years, the prevalence of smoking was 33.6% in 2006 (15).

We separately assessed knowledge about diagnosis and therapy for TB. The knowledge about diagnostic of TB was poor in both groups. Similar low level of knowledge among medical students was seen in other studies (5). This lack of knowledge about standards in TB diagnostics is a disadvantage for medical students as future doctors which can lead to delayed diagnosis and treatment. High proportion of medical students was informed about therapy of TB, its duration and frequency. As it seems that knowledge regarding treatment is adequate, special attention in education of medical students should be paid to diagnostic procedures. Taking into account socioeconomic crisis in Serbia since 1990s, migrations that increase the spread of disease, increasing number of immunocompromised patients, as well as the incidence rate above 30 per 100 000 population (2), it is our opinion that TB should not be seen as history in education for medical and dental students.

In conclusion, in spite of valid basic awareness of TB, there were some gaps in the knowledge of TB, more frequently among dental then medical students. This study suggests that students need more training and more practice.

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Health care-associated infections: repeated prevalence surveys, 2003-2010

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Abstract

Introduction: Health care-associated infections (HAIs) are an important worldwide problem, especially in country with limited resources.

Aims of the research: The aim of the study was to estimate the baseline epidemiological characteristics of health care-associated infections at the University Hospital in Kragujevac, Serbia.

Patients and methods: Four prevalence surveys were conducted in 2003, 2005, 2009, and 2010. All surveys were performed according to the same study protocol.

Results: Urinary tract infections, followed by surgical site infections and pneumonia and lower respiratory tract HAIs were the most prevalent. The prevalence of the urinary tract HAIs continues to rise, and there has been an increase in pneumonia and lower tract HAIs from 2003 to 2010. However, the rate of surgical site infections prevalence has decreased. Antibiotic usage showed a small decrease over time. But, the antibiotic usage without clear reason has increased. The Gram-negative bacteria (*Pseudomonas spp, Escherichia coli* and *Klebsiella spp*) were the most frequently isolated microorganisms.

Conclusion: The results of these prevalence surveys have reflected the sustained efforts at combating HAIs over the past decade in Kragujevac teaching hospital and have provided an incentive for a better definition of infection control priorities in high-risk healthcare settings.

Key words: *health care-associated infection, repeated survey, prevalence, causes, Serbia*

Introduction

Health care-associated infections (HAIs) are defined as infections that are not present and have

no evidence of incubation at the time of admission to a healthcare setting. The health care-associated infections are an important worldwide concern in the medical field, resulting in excess length of stay, mortality and healthcare costs (1, 2).

The frequency of hospital infections varies among different healthcare settings. In developed countries, incidence of nosocomial infections ranges from 5-10%, yet it gets as high as 25% in underdeveloped countries (3). The prevalence of nosocomial infections may be as low as, for example, in Germany (3.5%) and Hong Kong (4.0%), but also very high, as noted in prevalence studies in Russia (17.0%) and Albania (19.1%) (4-7). A prevalence survey conducted under the auspices of the World Health Organization (WHO) in 55 hospitals throughout 14 countries representing four WHO Regions (Europe, the Eastern Mediterranean, the South-East Asia and the Western Pacific) showed that an average of 8.7% of hospital patients had nosocomial infections (8). The highest frequencies of nosocomial infections were reported at hospitals in the Eastern Mediterranean and the South-East Asia Regions (11.8 and 10.0%, respectively), with a prevalence of 7.7 and 9.0%, respectively, in the European and Western Pacific Regions.

The exact prevalence of HAIs is hard to determine, primarily due to insufficient detection and reporting of such infections. In addition, difficulties arise from the heterogeneity of data collected using different methods and over different time periods (9). Prevalence studies are a quick, easy and relatively inexpensive way of collecting data on nosocomial infections. Repeated prevalence studies allow assessment of nosocomial infections trends, while simultaneously providing incentive to health workers who monitor these infections (10, 11).

According to their localization, the most important HAIs are: urinary tract infections (approx.

35-40% BI), surgical site infections and pneumonia, with minor variations in their sequence only (12-15). The WHO survey noted that the most frequent nosocomial infections were infections of surgical wounds, urinary tract infections and lower respiratory tract infections (8).

The microbiological confirmation of HAIs is varied. In a prevalence study in Germany, 56.6% of these infections were microbiologically confirmed, and 55.8% in a prevalence study in Slovenia (4, 12).

The health care-associated infections are most commonly caused by bacterial agents. The top 3 pathogens for urinary tract infections were *Escherichia coli*, *Enterococcus*, and *Pseudomonas aeruginosa* (16). The top pathogens for surgical site infections were *Staphylococcus aureus*, coagulasenegative staphylococci and *Enterococcus*. The top pathogens for pneumonia were *Staphylococcus aureus*, *Pseudominas aeruginosa* and *Enterococcus*.

Recent studies have demonstrated that patients with HAIs received antibiotics more frequently than those without HAIs, and that the inadequate choice of treatment was independently associated with a twofold increase in mortality among the infected patients (17).

The health care-associated infections remain a major health care problem, not only in countries with limited resources but in the developed world, as well (9-11). In recognition for the need to control nosocomial infections, each hospital in Serbia has been required to set up a nosocomial infection control committee; however, there have been only few surveys of health care-associated infections, more information is still needed.

The aim of the study was to estimate the baseline epidemiological characteristics of the healthcare-associated infections at the University Hospital in Kragujevac.

Material and methods

Setting

Four prevalence surveys were performed in a tertiary-care, 1240-bed teaching hospital in Kragujevac, affiliated with the Medical Faculty, University of Kragujevac, Serbia. Each surgical department (general, thoracic, urological, vascular, neurosurgery, plastic and maxillofacial surgery, orthopedic and traumatology, obstetrics-gynecology, otorhinolaryngology, ophthalmology), internal medicine department (internal, infectious, pediatric, dermatology, rehabilitation, neurology, psychiatry, oncology, nephrology, neonatology) and intensive care unit (deals with patients from all departments in the hospital) were included in the study. The University Clinical Hospital Centre Kragujevac is a regional referral centre, where highly specialised or highrisk medical interventions are required. The hospital provides all acute hospital care to the residents of the city of Kragujevac and several large adjacent regions (population about 1.5 million), with about 50.000 admissions annually, and approximately 340.000 patient-days. The hospital had no antibiotics use policy prior to year 2000. The guidelines on preventive measures for surgical site infections were established as of 2005, while guidelines on hand hygiene came into force in 2009. As of 2009, the hospital has a health care-associated infections prevention and control epidemiologist.

Method

A point prevalence study design was used. Four prevalence surveys were conducted in 2003, 2005, 2009, and 2010. All surveys were conducted according to the same study protocol and the same team of investigators. Each survey period lasted for one week for the entire hospital. All patients who had been hospitalized for more than 24 hours on the day of the study were included. Patients were visited daily to collect all pertinent data, which were then recorded in a standardized data collection form.

Cases

Health care-associated infections were diagnosed according to the criteria established by the Centers for Disease Control and Prevention criteria (18). Only the health care-associated infections that were active on the day of the study were taken into account, i.e. the infections for which the prescribed antibiotics therapy was yet to start or currently in progress. If a patient had multiple site infections, each infection was considered as a separate infection. All health care-associated infections were classified according to anatomic localization of the appropriate group, from I to XIII (i.e., urinary tract, surgical site, pneumonia, bloodstream, skin or soft-tissue infections, etc).

Questionnaire

Trained infection control doctors collected data from clinical records, temperature charts, laboratory reports, and information provided by physicians and nurses in each ward using detailed, uniformly made questionnaires. Study variables included patient demographics, primary diagnosis, comorbidities, exposure to medical and surgical risk factors, and the use of antibiotics. Prior to surgery it was recorded if it had occurred during a 30-day period before the survey day or the onset of infection. We recorded antibiotic usage and indication (prophylaxis of the surgical site infections, therapy - either community-acquired or hospital-acquired, and without clear reason). We collected specific information on microbiological characteristics of HAIs (confirmation, report, isolates).

Statistical analysis

All statistical analyses were carried out using SPSS for Windows, Version 10.0 (SPSS). The prevalence of all HAIs and prevalence of HAIs by site are given as a percentage of total number of patients surveyed, except for surgical site infections where an additional prevalence is given using the number of patients undergoing a surgical procedure as the denominator. Corresponding tests (χ^2 test and Fisher's exact test) were used to indicate statistical significance of the differences in infected and non-infected patients.

Results

A total of 3,256 patients, 43.9% of whom were male, were included in the 4 prevalence surveys; 246 hospital-acquired infections were recorded for 227 patients (Table 1). Urinary tract infections, followed by surgical site infections, and pneumonia and lower respiratory tract HAIs were the most prevalent nosocomial infections. Microbiological examination in nearly 70% of the patients with HAIs yielded positive results. Monomicrobial infections were found in almost all patients. HAIs with microbiological reports were decreased. The increase in overall prevalence of HAIs was noted. The prevalence of urinary tract HAIs continues to rise, and there has been an increase in pneumonia and lower tract HAIs from 2003 to 2010. However, the rate of surgical site infections prevalence has decreased.

Antibiotic usage showed a small decrease over time (Table 2). But, antibiotic usage without clear reason has increased.

Gram-negative bacteria (*Pseudomonas spp, Escherichia coli* and *Klebsiella spp*) were the most frequently isolated microorganisms (Figure 1). Due to insufficient number of isolates, the prevalence trends of certain agents according to HAIs by site could not be assessed.

Variables	Survey I	Survey II	Survey III	Survey IV
Surray pariod	December	May	June	November
Survey period	2003	2005	2009	2010
Number of patients	764	866	865	761
Overall prevalence of HAIs (%)	7.1	4.6	8.7	10.1
Prevalence of the most frequent sites of infections				
- Prevalence of urinary tract infections (%)	1.3	2.1	2.9	4.3
- Prevalence of surgical site infections ^a (%)	14.1	4.2	8.8	8.5
- Prevalence of pneumonia and lower tract HAIs (%)	0.8	0.6	2.2	2.5
- Prevalence of skin and soft tissue HAIs (%)	1.4	0.7	1.0	0.8
HAI withouth a microbiology report (%)	13.0	37.5	30.7	41.6
- Culture not done	7.4	32.5	21.4	36.4
- No growth	5.6	5.0	9.3	5.2
HAI with a microbiology report (%)	87.0	62.5	69.3	58.4
Number of isolates	54	25	55	48
- 1	40	25	49	42
$ -\geq 2$	7	0	3	3

Table 1. Prevalence (%) of health care-associated infections (HAIs) in four surveys (2003-2010)

^a Only patients undergoing a surgical procedure.

	Survey I	Survey II	Survey III	Survey IV
Antibiotics	Patients (N=764) No (%)	Patients (N=866) No (%)	Patients (N=865) No (%)	Patients (N=761) No (%)
Yes	389 (51.0) ^a	268 (30.9) ^a	324 (37.5) ^a	302 (39.7) ^a
Indication				
Prophylaxis of the infectionhospital acquiredsurgical site infection^b	50 (12.9) 50/128=39.1	23 (8.5) 23/167=13.8	104 (32.1) 104/147=70.7	74 (24.5) 74/164=45.1
Therapy of the infection - community acquired - hospital acquired	275 (70.7) 44 (11.3)	182 (67.9) 39 (14.6)	149 (46.0) 55 (17.0)	134 (44.4) 69 (22.8)
No clear reason	20 (5.1)	24 (9.0)	16 (4.9)	25 (8.3)

Table 2. Antibiotic usage and indication

^{*a*} P – probability value (χ^2 test and Fisher's exact test, 2-tailed) indicates statistical significance of the differences in infected and noninfected patients (P<0.001).

^b Only patients undergoing a surgical procedure.



Figure 1. Four Surveys of health care – associated infections prevalence (2003-2010) in Clinical Centre in Kragujevac: frequency of the isolated microbial agents

Discussion

Nosocomial infections occur worldwide and affect both developed and resource-poor countries. The overall prevalence of HAIs observed at the Kragujevac teaching hospital appears to be of the higher than the rates reported in hospitals in Germany - 3.5%, Slovenia - 4.6%, and the same magnitude as that reported in Cyprus and Greece - 7.0%, Finland – 7.2% (4, 12, 19, 20). The rate reported here appears to be lower than those reported in surveys in some other European countries, like Russia – 17.0% (6) or Albania – 19.1% (7). These discrepancies may represent real differences in infection controled practices, emphasis on different sites of infection, and/or surveys that involved different patient populations (21). Larger hospitals tend to have more severe cases and use invasive procedures more often, practices that represent risk factors for the HAI development (19, 22). It is possible that HAIs, as some other diseases do, show cyclical, or seasonal variations (primarily related to the frequency and length of hospitalization due to underlying disease) (23). Of course, low prevalence can often be the result of inadequate diagnosis and registration of HAIs, a phenomenon typical for communities which are yet to introduce HAI monitoring. In countries that conducted studies repeatedly, either every year or several-year intervals, each subsequent study showed HAI prevalence similar to or lesser than the previous one, like Norway, and Switzerland (24, 25).

The three most common HAI localizations (urinary tract infections, surgical site infections and respiratory tract infections) observed in our study were found in the prevalence studies in other countries, as well, with minor variations in their sequences (7, 26). After the introduction of the antibiotic use policy at the Clinical Centre Kragujevac, the prevalence of surgical site infections decreased from 14.1% in the first to 8.5% in the latest survey. Consequently, a growing incidence of urinary tract HAIs, and pneumonia and lower respiratory tract HAIs most likely stems from the exposure to numerous invasive procedures (27), correct application of which is yet to be codified in the appropriate Serbian national protocols.

One of the major problems in Serbia is diagnosing HAIs without isolating the causative agent. Our paper observed that more than half of HAIs had laboratory confirmation, which is consistent with the findings of nosocomial infections studies conducted in Slovenia, Finland, and Greece (12, 20, 26). Microbiological infection diagnosis can be present in a significantly higher percentage (7), but it is not uncommon that only a small percentage of nosocomial infections get a laboratory confirmation (28). Study conducted by Medina et al (29) found that almost a third of cases (29.0%) lacked a microbiological confirmation of causative agents, while the pathogen agents could not be proved in 14.8% cases. Certain HAIs, such as surgical site infections, may be diagnosed based solely on the clinical findings (e.g. redness or pus on the incision site), but in other cases only a laboratory report may be used for diagnosis.

Approximately 40% of patients received antibiotics. This finding is consistent with the results from other authors (11). In hospitals in Cyprus and Greece (19), 58.4% patients were receiving antibiotics, where 49.1% received empirical treatment, 32.8% received antibiotics for surgical prophylaxis and 11.5% for bacteriologically documented infection, while in 6.6% no justification for the antibiotic use was provided. Most authors are unanimous in their opinion that rational use of the antibiotics immediately before surgery leads to lower incidence of surgical site infections (30). Reduced incidence of surgical site infections in our study is most likely associated with the implementation of national recommendations for prevention of surgical site infections since 2009. However, numerous studies indicated the use of antibiotics was a risk factor for development of HAIs (22, 27). The use of antibiotics was also an independent risk factor for development of HAIs (27), certainly contributed to by the high antibiotics use without clear reason at the Clinical Centre Kragujevac.

The infecting organisms vary among different patient populations, different health care settings, different facilities, and different countries. In our surveys gram-negative bacteria were the most frequently isolated microorganisms, similar to other countries (12, 20, 26, 28). Due to insufficient number of isolates, the prevalence trends of certain agents according to HAIs by site could not be assessed.

The point-prevalence surveys of HAIs are simple, fast, and relatively inexpensive. Moreover, all our surveys were performed by experienced and well-trained infection control professionals, which warranted for reliability, reproducibility, and quality of data. Repeated prevalence surveys are useful for monitoring trends by comparing rates over time. Studies of HAI incidence would certainly give more accurate data on the frequency-by-type and frequency of certain HAI agents. Finally, our surveys have had certain limitations that should be acknowledged. The research was performed in a single institution and the number of patients with HAIs by sites was relatively small. Despite their limitations, prevalence surveys are usually preferred in determining the magnitude of HAIs when resources are limited. This study clearly showed which HAIs were more prevalent in our hospital. Our study also identified problems related to the use of antibiotics. We identified which HAIs by site should be targeted by infection control measures and provided a baseline for future studies which will enable monitoring of trends over time.

Conclusion

This study suggests that it is necessary to maintain continuous surveillance of health care-associated infections. It is important to emphasize the need for implementation the measures in order to prevent health care-associated infections, esspecialy the preventive measures urinary tract infections as well as pneumonia and lower respiratory tract infections.

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Pathophysiologic aspects of negative Appendectomy in pediatric patients

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Abstract

This review assesses the current state of knowledge regarding the cecal appendix, its apparent function, and its evolution. The association of the cecal appendix with substantial amounts of immune tissue has long been taken as an indicator that the appendix may have some immune function. The appendix is traditionally considered as an evolutionary misfit, a vestigial organ comprised of non-essential lymphoid tissue, a redundant part that serves little purpose in human beings. The decision to remove a normal appearing appendix whether or not another cause of infection or pain is present is not always straightforward. The fact that about 40% of the removed appendices are without signs of inflammation indicates a relatively easy decision for surgical treatment. Removal of the appendix is currently generally not thought to have any functional consequence. The lack of measurable functional, physiologic or immunologic sequels from appendectomy doesn't mean they do not exist, particularly in relation to immune function. That may be due to the sheer redundancy of the lymphoid tissue in the gut, which, if anything, reveals its adaptive value. The cecal appendix may thus be viewed as a part of the immune system that, like those that cause immune compartments allergy, is vital to life in a "natural" environment, but which is poorly suited to post-industrialized societies. The potential role of the appendix as a sensory organ in immune intelligence network requires review of preemptive, incidental appendectomy during abdominal surgery.

Key words: Negative appendectomy, Pathophysiology, Appendicitis, Diagnosis.

Review article

The incidence of acute appendicitis increased rapidly in the last decade of 19th and in the beginning of the 20th century, but later performed a dramatic decline. The exact reasons for this phenomenon are unclear, probably due to important factors such as changes in diet, improved hygiene and better infections treatment in early childhood. Acute appendicitis occurs in all age groups and several studies confirmed the peak of incidence in the second decade of life (23, 3 per 10,000 populations per year); in later years the incidence decreased [1,2]. Males had higher rates of acute appendicitis than females in all age groups (overall ratio 1,4:1) [3]. A life table model suggests that the lifetime risk of appendicitis is 8,6% for males and 6,7% for females; the lifetime risk of appendectomy is 12% for males and 23,1% for females [4]. The main causes for high negative appendectomy rate in females in the adolescent and reproductive age are due to different physiological and pathological gynecological conditions [5].

Despite the use of modern diagnostic tools (ultrasound, computed tomography, laboratory) and advanced scoring systems, diagnosis of acute appendicitis still remains a challenge [6, 7]. Surgical exploration for suspected appendicitis resulting in a disappointingly normal looking appendix is defined as a negative appendectomy and remains a therapeutic dilemma [8]. Indeed, the decision to remove a normal appearing appendix whether or not another cause of infection or pain is present is not always straightforward [9]. The fact that about 40% of the removed appendices are without signs of inflammation indicates a relatively easy decision for surgical treatment [10]. Removal of the appendix is currently generally not thought to have any functional consequence. The lack of measurable functional, physiologic or immunologic sequels from appendectomy doesn't mean they do not exist, particularly in relation to immune function. That may be due to the sheer redundancy of the lymphoid tissue in the gut, which, if anything, reveals its adaptive value. The potential role of the appendix as a sensory organ in immune intelligence network requires review of preemptive, incidental appendectomy during abdominal surgery [11].

An apparent function of the human vermiform appendix

The appendix is traditionally considered as an evolutionary misfit, a vestigial organ comprised of non-essential lymphoid tissue, a redundant part that serves little, if any, purpose in human beings. The teleologic origins of the appendix, however, remain unexplained. It is thought to have descended in our distant herbivorous ancestors from the caecum where it housed the bacteria that digest cellulose. Though it retained this function in modern herbivores, the human appendix contains no significant number of these bacteria and cellulose is indigestible of human being. It seems likely the appendix lost this function before our ancestors became recognizably human.

The human vermiform ("worm-like") appendix is a 5-10cm long and 0.5-1cm wide pouch that extends from the cecum of the large bowel. The architecture of the human appendix is unique among mammals, and few mammals other than humans have an appendix at all. The function of the human appendix has long been a matter of debate. Recent data suggest that the appendix may play an important role in gut-brain communication via a number of immunological pathways [12].

For years, the appendix was credited with very little physiological function. We now know, however, that the appendix serves an important role in the fetus and in young adults [13]. Endocrine cells appear in the appendix of the human fetus at around the 11th week of development. Endocrine cells of the fetal appendix have been shown to produce various biogenic amines and peptide hormones, compounds that assist with various biological control (homeostatic) mechanisms. There had been little prior evidence of this or any other role of the appendix in animal research, because the appendix does not exist in domestic mammals. Among adult humans, the appendix is now thought to be involved primarily in immune functions. Lymphoid tissue begins to accumulate in the appendix shortly after birth and reaches a peak between the second and third decades of life, decreasing rapidly thereafter and practically disappearing after the age of 60th. During the early years of development, however, the appendix has been shown to function as a lymphoid organ, assisting with the maturation of B lymphocytes and in the production of the class of antibodies known as immunoglobulin A (IgA) antibodies. Appendix is involved in the production of molecules that help to direct the movement of lymphocytes to various other locations in the body.

In this context, the function of the appendix appears to be to expose white blood cells to the wide variety of antigens, or foreign substances, present in the gastrointestinal tract. Thus, the appendix probably helps to suppress potentially destructive humoral (blood-and lymph-borne) antibody responses while promoting local immunity. The appendix - like tiny structures called Payers' patches in other areas of the gastrointestinal tract takes up antigens from the intestinal contents and reacts to them. This local immune system plays a vital role in the physiological immune response and in the control of food, drug, microbial or viral antigens. The connection between these local immune reactions and inflammatory bowel diseases, as well as autoimmune reactions in which the individual's own tissues are attacked by the immune system, is currently under investigation. The phenotype of the appendiceal immunological competent cell population is unique in its composition of B-cells. Compared to peripheral blood, the appendix contains a significantly higher number of the CD19 and B1 subsets [14]. Bazar therefore hypothesized that the appendix may serve as a sentinel or an "eye" in the gut conveying immunological signals to the brain [11]. Several functional gastroenterological disorders have been attributed to a dysfunction of this gut-brain axis [15].

Appendix as a primitive sensory-perception organ

Many authors proposed the appendix is a primitive sensory-perception organ, part of a larger immune intelligence network. Modern sensory organs of the visual, olfactory, and auditory systems enable the host to sample the surrounding environment at great distances by perceiving its physical and chemical properties. Such sensory data elements presented to the brain form the basis of modern intelligence by creating a representative map of the environment. Prior to the modern emergence of complex sensory systems, primitive organisms may have relied more heavily on a cruder method of sampling their surroundings:

digesting the environment. A previously unrecognized role of the appendix is emergent in this framework [11]. We propose that the immune system is a parallel system of intelligence in which the gut, including the appendix, plays a prominent role in data acquisition. The immune system is essentially a virtual unwired network of interacting cells that acquires, processes, and responds to environmental data. The imune system extracts antigenic information from the internal and external environment of the host in order to produce anadaptive response, and has capabilities for memory: the humoral immune system. Through crossreactivity, the immune system also has the ability to generalize from specific information. Immune intelligence is not based on a fixed geometry of interconnected cells (nodes), but rather relies on random interactions of its immune constituents in a fluid environment. Furthermore, whereas the neuronal network architecture is centralized, the immune network is decentralized [16].

The immune system is basically a virtual network of interactive cells that acquire process and respond to stimuli in their environment. The gut performs functions similar to antigen presenting cell system (APCS), albeit on a much larger scale. Like its counterpart APCS, deconstructs the gut environmental content by physical and chemical digestion. Even after components of known and potential biologic value are taken up by the host for its use, the remaining components may contain enormous informational value regarding the environment that could provide Darwinian advantage. This information is sampled in the gut through a dense network of lymphoid tissues, beginning with the tonsils and ending in the colon. Once thought to be defense against microbial invasion bunkers, we propose that these lymphoid tissues also deserve recognition as data collection centers for the immune intelligence network. Essentially, the cells lining the lymphoid tissue are sampling the environment in a form fragmentized. These data packets are then delivered to the rest of the immune system to enrich the overall content value of the immune intelligence network [17]. In this framework, the appendix may be a sentinel organ sampling. Its position immediately after the ileocecal valve appears hardly accidental. The colon is mostly involved in maintaining ionic and water balance for the host. Where better to put

a large data collection center than after completion of digestion and absorption of biologically relevant macromolecules, the last of which are typically absorbed in the terminal ileum? The post-digestive detritus still holds enormous informational value that may confer adaptive advantage to the host. Whereas the upstream lymphoid organs such as the tonsils are reading large blocks of data, the appendix is reading the same data after filtering and substantial fragmentation. Data from all pockets of lymphoid tissues are delivered to the immune intelligence network and become part of the host "knowledge". For unicellular organisms, digestion of food is the primary form of recognition of the environment. Before the development of complex sensory organs - the eye and ear, even multicellular organisms get nutrition information from the environment. Although the relative value of immune intelligence limited the development of neural intelligence, organisms still use information from both systems in the integration of responses to a number of environmental features and changes. The appendix, in this setting, may represent an organ in transition. Perhaps in the era before complex sensory systems, the appendix was a key organ for sampling the environment. Its continued existence may simply reflect its value in the by gone days. The notion that the appendix is value less may ignore its ongoing contribution to host intelligence. While the relative value of immune intelligence has diminished since the modern emergence of neural intelligence, organisms may still use information from both systems in an integrated fashion to respond appropriately to ecologic opportunities and challenges.

Appendicitis may represent a momentary maladaptation during the evolutionary transition of sensory leadership from the gut to the eye. Perhaps the diminishing Darwinian value of the appendix in the era of complex sensory organs has led to reduction of its size. The smaller size of the modern appendix may leave it susceptible to obstruction at the base, occasionally causing the familiar condition of appendicitis. However, given the potential role of the appendix as a sensory organ in the immune intelligence network, the practice of pre-emptive removal of a normal appendix during an unrelated abdominal surgery may need to be revisited. Removal of the appendix is currently generally not thought to have any functional consequence. The lack of measurable functional, physiologic, or immunologic sequelae from appendectomy may be due to the sheer redundancy of the lymphoid tissue in the gut, which if anything, reveals its adaptive value. However, removing a larger fraction of gut lymphoid tissue may affect proper immune sampling of the environment If it can be shown that removing the appendix alters immune function, then such knowledge may need to be factored into the decision for elective appendectomy for low-grade appendicitis that might otherwise be amenable to medical therapy.

Intestinal epithelium serves as a physical barrier that separates and maintains the particularity and specificity intraluminal and subepithelial compartment. They realized that intestinal epithelium plays a crucial role in the immune process by creating a series of pro-inflammatory mediators [14, 18]. Intestinal mucosa plays a key role in the first line defense against pathogenic intraluminal microorganisms or chemical agents [19]. Due to these findings, the function of the appendix is the subject of discussion. Since the organ is rich in lymphoid tissue, many investigators believe that there is an immune function. In recent studies, there has been increased interest for the appendix after the report that may contribute to understanding the etiology of ulcerative colitis. The appearance of ulcerative colitis in patients who had appendectomy is less frequent compared with the general population. Later studies have confirmed this fact, but have suggested that the inflammatory process of the appendix rather than as an appendectomy surgery, type of patronage of developing ulcerative colitis [20,21]. These studies also showed that in patients who underwent appendectomy for acute appendicitis inflammation symptoms and clinical course of ulcerative colitis were significantly milder than in the control group [22,23].

It has recently emerged (Bollinger et al, 2007) that the appendix is, in fact, a pocket for safe keeping some of the 'good' gut bacteria, in the form of biofilms, so they're not all flushed away if the dose amoebic dysentery of (for instance) comes through The appendix is thought to have some immune function based on its association with substantial lymphatic tissue, al though the specific nature of that putative function is unknown. Based (a) on a recently acquired un d erstanding of immune-mediated biofilm formation by commensally bacteria in the mammalian gut, (b) on biofilm distribution in the large bowel, (c) the association of lymphoid tissue with the appendix, (d) the potential for biofilms to protect and support colonization by commensal bacteria, and (e) on the architecture of the human bowel, we propose that the human appendix is well suited as a "safe house" for commensal bacteria, providing support for bacterial growth and potentially facilitating re-inoculation of the colon in the event that the contents of the intestinal tract are purged following exposure to a pathogen [24].

An immune function of the human vermiform appendix

Since the processus vermiform is rich in lymphoid tissue, many researchers believe that is due to different immune functions [25, 26]. Phenotype of the immune competent cells of the appendix is unique in composition and content of B-cells. In comparison to peripheral blood, appendix contains a significantly higher number of CD 19 and B-cell subtypes [14]. Recently, there has been increased interest in the physiology of appendix after a report that may contribute to understanding the etiology of ulcerative colitis. Basic and epidemiological studies have confirmed the link between the appendicitis and inflammatory bowel disease. The nature of this relationship is different in ulcerative colitis and Crohn's disease. The incidence of ulcerative colitis in patients who had appendectomy is less frequent compared with the general population. Later studies have confirmed this phenomenon, but have suggested that changes during the inflammatory process in appendix, and not as an appendectomy surgery, have influence of developing ulcerative colitis. In patients who underwent appendectomy for acute appendicitis inflammation, symptoms and clinical course of ulcerative colitis were significantly milder than in the control group. Data of previous appendectomy is considered protective in ulcerative colitis. A meta-analysis of studies performed seventeen types of case-control confirmed that the mucosal immune response that leads to appendicitis and appendectomy has consequential impacts on the pathogenic mechanism for ul cerative colitis [27]. Large epidemiological studies have confirmed that the previous statement of appendectomy increases the risk of Crohn's disease [28]. Patients with ulcerative colitis (UC) have a less frequent history of prior appendectomy than

the general population. The appendix is a site of involvement in UC, where mononuclear cells are presumed to be at a state of basal activation [29, 30]. There is no direct information about the function of enteric nervous system of appendix, but believes he has a role in intestinal immune functions. There is evidence for mutual interaction between intestinal nerves and immune system in modulation of intestinal inflammation. The increase neuropeptides in the appendix is involved in the pathophysiology of acute pain in the right lower quadrant (RLQ) of the abdomen, without signs of acute appendicitis (Di Sebastiano, 1999). It is proved that appendiceal enteric nervous system induced inflammatory reaction. Based on this information as well as the controversial structure appendiceal enteric nervous system, the testing authority shall be deemed appropriate. The potential role of the appendix as a sensory organ of immune intelligence network requires review preemptive, incidental appendectomy during a b dominal surgery. Due to the different diagnos t ic and prognostic approach, the risk of diagnostic failure in appendiceal disease leads in unnecessary surgery (negative appendectomy). Otherwise, the risk is underestimated, leading to delayed treatment and increased morbidity. The goal of modern surgical treatment is focused on the balance between the number of negative appendectomy rate and the perforation rate at the time of surgical treatment. Indication for surgery depends to a large extent, the subjective impression of the surgeon. Surgical and histopathological finding does not reveal clearly appendiceal disorder. Sometimes, macroscopic morphological changes in the appendix like sharp bends and the presence of lymphoid hyperplasia, appendicolith and increased resistance in the middle luminal water perfusion may explain the origin of the patient's problems. The obstruction of the appendix, especially caused by appendicolith, is responsible for the clinical sings of acute inflammation. In neurogenic appendicopathy, processus vermiform looked normal macroscopically. However, there is always ultra structural close relationship between the enterochromitofine cells and nerve fibers of Auerbach's plexus. They form a complex morphological and functional unit surrounded by a common basal membrane.

In the past, the appendix was often routinely removed and discarded during other abdominal surgeries to prevent any possibility of a later attack of appendicitis [31]. The appendix is now spared in case it is needed later for reconstructive surgery if the urinary bladder is removed. In such surgery, a section of the intestine is formed into a replacement bladder, and the appendix is used to re-create a 'sphincter muscle' so that the patient remains continent (able to retain urine). As a result, the appendix, once regarded as a nonfunctional tissue, is now regarded as an important 'back-up' that can be used in a variety of reconstructive surgical techniques. It is no longer routinely removed and discarded if it is healthy. Morbidity after negative appendectomy is lower than after appendectomy for appendicitis [32]. Finally, the risks and costs associated with the negative appendectomy were determined: morbidity 6%, reoperation 2% and a significant increase in outpatient costs. In patients operated on minimally invasive approach, however, the morbidity rate was 0,3%. These findings suggest that morbidity and increased costs after negative appendectomy, although usually minimal, can have significant value [33-35].

Abbreviations

RLQ – right low quadrant APCS - antigen presenting cell system UC - ulcerative colitis IFN- interferone

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Environment and quality of life of older people

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Abstract

Introduction: Quality of life (QoL) is an individual's perception of his or her position in life in the context of the culture and value system where they live, and in relation to their goals, expectations, standards and concerns. World health organization (WHO) identified four broad domains as being universally relevant to quality of life, namely physical health, psychological well-being, social relationships, and environment.

Aim: The aims of this study were to investigate the relationship between environmental domain of QoL and socio-demographic characteristics of older people and to determine the association between environmental domain and self-reported QoL and health satisfaction.

Material and Methods: The World Health Organization Quality of Life BREF questionnaire (WHOQOL-BREF), developed by WHO was used to assess quality of life on random sample of 200 people aged 60 years and over who live in Retirement Home in Novi Sad. Items within the questionnaire were organized into four domains: Physical, Psychological, Social Relationships and Environment.

Results: The majority of the participants were females (69.8%). The mean age was 79.2 years (SD=6.6 years). The mean value of the Environmental domain score (EDS) was 67.8 (on scale 0-100). Information (Q13) and home environment (Q23) were the two highest scoring items. There were no statistically significant differences between the mean EDS of the participants with regard to socio-demographic characteristics. Mean EDS of the participants who had some kind of disease were significantly lower than those who had not (p<0.05). Participants who had higher mean of EDS statistically significant better rated their quality of life (F=17.7; p<0.001) and those who had the highest value of EDS were very satisfied with their health (F=15.1; p<0.001).

Conclusion: Elderly people who have a chronic disease have a significantly lower average value of EDS. Older people who better assess the environment are more satisfied with their health and have a better quality of life.

Key words: WHOQOL-BREF, Quality of life, old people, environment

Introduction

In 2000, approximately 10% of the world's people were 60 years old or older. According to the United Nations Medium Variant population projection, falling fertility and mortality rates will cause this figure to rise to over 20% by 2050. This means that 400 million older people will be living in the developed countries-and over one and half billion in the less-developed world! (1).

Eighteen out of the 20 countries in the world with the highest percentages of older people are in the European Region of World Health Organization (WHO): in those countries, between 13.2% and 17.9% of the population are over 65 years old. Within the next 20 years, there will be a highly significant increase in the proportion of people in this age group, with the fastest growing population in most countries being those are very old (i.e. aged 80 years and above). In the next 30 years, the proportion of people aged over 80 years (as share of the over-65 population) will increase, in Europe as a whole, from 22% to over 30% (2).

Population of Vojvodina (north part of Republic of Serbia with 1968356 inhabitants) is classified as very old, since more than 16% of population is 65 and older. It has been estimated that average age of population in Vojvodina increased for 9.1 years in period 1953-2007, and in 2009 reached 40.8 years. Ageing index (calculated as the proportion of persons 60 years old or over and persons under age 19) has been tripled since the

middle of the 20th century and in 2009 in Vojvodina was 1.03 (value higher than 0.4 point to an ageing of the population). Life expectancy at birth has risen and for males is 71.1 whereas for females 76.4 years (3).

All these facts indicate that the ageing of population in Vojvodina, as well as the whole world population, is the problem which we have to face with. Therefore, the interests of the elderly and improving quality of life (QoL) in this age including their health concerns are poised to take on greater prominence in coming years.

QoL is a uniquely personal issue, it is the subjective perception of how an individual feels about their health status and/or the non-medical aspects of their lives (4).

There are a lot of definitions and explanations concerning QoL. WHO defines QoL as "the perception of the individuals or groups that their needs are being satisfied and that they are not being denied opportunities to achieve happiness and fulfillment" (2). Moreover, QoL is an individual's perception of his or her position in life in the context of the culture and value system where they live, and in relation to their goals, expectations, standards and concerns. It is a broad ranging concept, incorporating in a complex way a person's beliefs and relationship to salient features in the environment (5).

Following the definition of QoL the World Health Organization Quality of Life Group (WHOQOL Group) began creating questionnaires, as the most suitable instruments for its measurement. Two main generic instruments are the WHOQOL-100, which consists of 24 facets grouped into six domains, and the WHOQOL-BREF, which is reduced 26-item version with four domains: physical, psychological, social and environment. Although the WHOQOL-100 appears to be a suitable instrument for a comprehensive assessment of QoL in research and in many clinical studies, its length imposes some limitations on its use in longitudinal studies involving repeated administration (5, 6).

The development of these instruments included a multidimensional and multicultural approach that suggested the assessment of physical, psychological, social relations, environmental and overall QoL and health satisfaction domains (7). There are two broad approaches to measuring health status from the perspective of the older person; instruments that are generic and instruments that are specific to the concerns of older people. Generic instruments aim to include aspects of health status and QoL of relevance to the general population, and hence are applicable across different population groups, irrespective of age or co-morbidity (8).

The subjectivity and complexity of QoL presents a challenge not only to design of QoL measurement scales, and their composition, but also their scoring and/or weighting (9).

Each area of quality of life can also have knock-on effects on the others. For example, having access to transport may promote independence and social participation, promote life and enhance perceived quality of life, but the former are partly dependent on having health and adequate finances (10).

QoL is in many cases defined by quality of the environment. Residents with poor air quality, poor water quality, poor housing, or poor regional economies have, by definition, low QoL indicators (11).

Only a few existing generic QoL measures explicitly include the environment as a dimension of health-related QoL. However, the importance of the environment for the QoL in older people has been identified and recognized for a long time. For instance, the environment is strongly associated with life quality among older people with respect to fall prevention, social interaction, activity involvement, independence, safety and security, and psychological well-being (12, 13).

In contrast to the extensive literature on physical, psychological and social components of QoL, there has been a paucity of studies addressing the relationships between environmental factors and QoL. Identification of differences in QoL in relation to environmental domain is necessary for a better understanding of the subjective health of older people and to identify subgroups with lower QoL.

The aims of this study were to investigate the relationship between environmental domain of QoL and socio-demographic characteristics of older people and to determine the association between environmental domain and self-reported QoL and health satisfaction.

Methods

Sample

Random sample of 200 people who live in Retirement Home in Novi Sad were included in this study. Inclusion criteria were aged 60 years and over, oriented in time, place and to other people and not situated in stationary part of the institution. Ethical approval was obtained from the Medical faculty of Novi Sad. A letter of introduction describing the study was given and written informed consent was obtained from all participants before interviewed questioning with WHOQOL-BREF questionnaire.

Instrument

The WHOQOL-BREF contains a total of 26 questions and it is based on four domain structure (Physical health, Psychological, Social relationships and Environment). Each domain includes three to eight items. Moreover, two questions yields information on global QoL, and heath satisfaction. Each item is based upon self report and scored on 5-point Likert scale. The time frame for responses is the previous two weeks. An additional 6 questions were included concerning sociodemographic characteristics such as age, gender, marital status and educational level, as well as present health status. Bosnian-Croatian-Serbian version of WHOQOL-BREF was used in this study. This language version was obtained from The WHOQOL Group. The WHOQOL-BREF shows good psychometric properties of internal consistency reliability, content validity, and discriminant validity (6,7).

Statistical analysis

Statistical analysis was performed using the statistical package SPSS 14.0 for Windows. Results are given as mean \pm standard deviation (SD), confidence interval (CI) and proportion. Differences in sample means were tested by Student's t-test and ANOVA. The level of statistical significance was set at p<0.05.

Results

Out of sample of 199 people aged 60 and over (one case was deleted with more than 20% missing data) 69.8% were female. Mean age was 79.2 years (SD=6.6, Max=97, Min=63). With regard to education level, 40.6% indicated no education or primary school, 15.6% junior high school, 24.6% senior high school and 18.6% college degree and above. The majority of participants were widowed (73.4%), 10.6% divorced, 8% married, 6.5% single and only 1.5% lived separately. More than two thirds of participants (68.8%) reported that they were ill at that moment and almost half of them (48.8%) had cardiovascular disease, 18.5% musculoskeletal, 9.6% endocrine and 5.9% neurological disease. The most frequently reported diagnosis was angina pectoris (15.6%). The average length of the used time for filling this questionnaire was 12 minutes.

Descriptive data of the items of Environment domain are shown in Table 1. Satisfaction with transport services (Q25) had the lowest response rate. Physical environment (Q9) scored lowest among the 8 items. On the other hand, information (Q13) and home environment (Q23) were the two highest scoring items.

Table 1. Item scores of Environmental domain of WHOOOL-BREF

WHOQOL-BREF – Environment domain-Item		N	Ā	SD
Q8	Physical safety	199	3.58	1.09
Q9	Physical environment	198	3.29	1.15
Q12	Finances	198	3.54	1.39
Q13	Information	199	4.07	1.05
Q14	Leisure	199	3.72	1.27
Q23	Home environment	197	4.07	0.85
Q24	Health services	198	3.87	0.86
Q25	Transport	191	3.58	0.99
	Environment domain	199	67.8	16.1

The results showed no statistically significant differences between the mean Environment domain scores of the participants with regard to socio-demographic characteristics. The results also showed that the mean Environment domain scores of the participants who had some kind of disease were significantly lower than those who had not (t=2.2; p=0.029) (Table 2).

Participants who had higher mean of Environment domain score statistically significant better rated their quality of life (F=17.7; p<0.001) (Figure 1). Those who had the highest value of Environment domain score were very satisfied with their health (F=15.1; p<0.001) (Figure 2).

Table 2.	Mean Environment	domain assessmen	t and socio-a	lemographic c	characteristics (of the stud	y group

Socio-demographic characteristics	N (%)	Environment domain \overline{X} (SD)	р		
Gender					
Male	60 (30.2)	71.2 (16.5)			
Female	139 (69.8)	66.4 (15.8)	ns		
Age					
60-69	20 (10.1)	66.7 (20.0)			
70-79	71 (35.7)	68.0 (15.5)	ns		
80-	108 (54.3)	67.9 (15.9)			
Education			-		
No school, primary school	80 (40.6)	65.5 (14.9)			
Junior high school	31 (15.8)	70.4 (15.4)			
Senior high school	49 (24.6)	69.6 (14.4)	115		
College degree and above	37 (18.7)	68.2 (21.1)			
Marital status	<u>`</u>	·			
Separated, divorced	34 (17.1)	68.2 (19.0)			
With partner	19 (9.5)	70.4 (14.8)	ns		
Widowed	146 (73.4)	67.4 (15.7)			
Presence of disease					
Yes	137 (32.2)	66.2 (15.7)	n=0.020		
No	62 (68.8)	71.6 (16.5)	p=0.029		

ns =non significant



Figure 1. Environmental domain and Qol assessment (Q1)



Figure 2. Environmental domain and health satisfaction (Q2)

Discussion

We live in an ageing world. The increasing presence of older persons in the world is making people of all ages more aware that we live in a diverse and multigenerational society. It is no longer possible to ignore ageing, regardless to whether one views it positively or negatively (14).

WHOQOL-BREF is multidimensional generic instrument to assess QoL and has been developed by WHOQOL Group. Very few QoL instruments were demonstrated to be suitable for use with elderly people living in institutions especially for crosscultural comparisons (15, 16). Other studies showed acceptable reliability and validity of WHOQOL-BREF, and demonstrated that this instrument is a suitable for QoL assessment in older people (17, 18, 19, 20). Unusual among other health-related QoL assessments the WHOQOL-BREF includes an environmental domain assessing subjective evaluations of material resources and conditions (21).

The present study investigated the relationship between environmental domain of QoL and sociodemographic characteristics of older people and association between environmental domain and self-reported QoL and health satisfaction.

Quality of environment relates to a feeling of physical safety and security, physical environment, financial resources, getting a new information and knowledge, participation in leisure, home environment, health services and adequate transport.

Environmental domain is represented by the largest number of items compared to other domains (8 items). Comparing the mean value across domains of The WHOQOL-BREF environmental domain had the highest value (67.8). Information (Q13) and home environment (Q23) were the two highest scoring items. Physical environment (pollution, noise, traffic and climate) scored lowest among the 8 items.

Environment with its characteristics for sure has the influence on QoL of all people regardless of age. In the spirit of Pearson description of ideal nursing home, it can be concluded that the ideal residential home can be described as a place where people live their lives with dignity, a good quality of life and with as little physical and psychological discomfort as possible (22).

The health of elderly requires greater attention to their multidimensional needs including physical, psychological and social aspects all of which are influenced by environmental concerns (17).

In this study, results showed that mean value of Environmental domain is higher in males, but this difference was not found to be statistically significant. This result correlates with previous studies (23, 24). On the other hand, in research of Arslantas D. et al. males had statistically significant higher value of this domain (25).

Age did not have significant influence on the Environmental domain. Other studies also reported that this factor did not affect this domain (23, 25).

Research showed that variables such as educational level and marital status did not substantially affect the Environmental domain. Mean values of Environmental domain were higher in participants with junior high school and who live with partner, but this was not statistically significant. Literature also showed that educational level did not have influence on this domain (23), whereas a study performed in Turkey informed us that participants with higher educational level had statistically higher values of Environmental domain and in widows the average score for Environmental domain was the lowest (25). In study performed in India, it was observed that the mean scores of the two groups of single (unmarried and widowed) and married differed significantly in the domain of environment (23).

Participants who had some kind of disease scored Environment domain significantly lower than those who had not. Similarly, in other study older people who had a chronic co-morbid condition had scores in all four domains significantly lower than those who did not (19).

One of the possible explanations for non existing difference in Environment domain between groups concerning socio-demographic characteristics is a fact that all participants live in Retirement home, therefore they probably have a same living condition, equal financial resources, have same opportunity for leisure, similar means of transportation and health services.

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Legal Framework for Support Services for Persons with Disabilities in Serbia

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Abstract

The new Law on Social Protection which Parliament of Serbia adopted in March 2011 prescribes for setting up of support services for independent living, including personal assistance, supported housing and provision of training for independent living for persons with disabilities in their respective communities by the local authorities. The authors analysed documents of international law, national legislation and examples of good practices in the field of support services in Serbia: Personal assistant service organized by Center for Independent Living of Serbia, supported housing organized by Association for Promotion of Inclusion in Serbia and day- care centers. Analysis shows that users of the abovementioned Services were satisfied with those services and maintained that such programs should become part of the system of social security of Serbia.

Key words: support services, national legislation, disability

Introduction

Like any other human being, a person with disability has a right to full and dignified life. He/ she has the right to independence and individual autonomy. Even if the person with disability cannot perform the basic lively functions on his/ her own, and needs assistance to get out of the bed, to dress, feed, maintain personal hygiene, that person can be independent if he/ she can make decisions about her/ his life, enjoy the right to choice, and assume responsibility for the choices made. Like other humans, persons with disabilities also have the right to make mistakes and to learn from the wrong choices they may have made. With appropriate support services and staff that will assist person with disability in performance of his/ her daily activities in a way that suits that person most, at the time and in a way which person chooses, that person can be an equal and productive member of society that can lead a full life. Support services aren't limmited exclusively to the basic daily activities. Classroom assistants assist children with learning difficulties to attend schools, students with disabilities to enjoy the right to education on an equal basis with their non- disabled peers. Workplace assistants assist persons with disabilities at their work, thus enabling them to be employed. The existence of appropriate support services, accessible environment, transport, information and communication enables persons with disabilities to participate in various segments of social life-political, economic, cultural, religious. It constitutes the key component of equalization of opportunities for persons with disabilities and significant precondition for full and equal participation of those persons in society.

Documents of International Public Law on Support Services for Persons with Disabilities

UN Standard Rules on Equalization of Opportunities for Persons with Disabilities

United Nations General Assembly adopted Standard Rules for Equalization of Opportunities for Persons with Disabilities in December 1993. Adoption of this act was the crowning moment of the UN Decade for Persons with Disabilities (1983- 1992) and it represents a significant step forward in the struggle for rights of persons with

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disabilities. The purpose of the Standard Rules (1) is to ensure that persons with disabilities have the same rights and duties as all other citizens in their respective societies. UN Standard Rules brought about the changes of legislation in more than 40 countries all over world and promoted introduction of the new support services for persons with disabilities, such as personal assistance (2).

Convention on the Rights of Persons with Disabilities

United Nations' General Assembly unanimously adopted Convention on the Rights of Persons with Disabilities and the Optional Protocol to it on December 13th 2006. The Convention and Optional Protocol (3) to it were opened for signature and ratification on March 30th 2007. Both instruments entered in force on May 3rd 2008. Until June 13 th 2011, there were 101 ratification and 149 signatures of the Convention. Serbia ratified the Convention and Optional Protocol to it on May 29 2009 and both instruments became legally binding between Serbia and the other parties to the treaties on July 31st 2009.

The purpose of the Convention is to promote, protect and ensure the full and equal enjoyment of all human rights and fundamental freedoms by all persons with disabilities, and to promote respect for their inherent dignity (article 1). States Parties to the Convention recognize the equal right of all persons with disabilities to live in the community, with choices equal to others, and shall take effective and appropriate measures to facilitate full enjoyment by persons with disabilities of this right and their full inclusion and participation in the community (article 19). This includes the right of persons with disabilities to choose with whom they and where shall they live, and the access to a range of support services in their respective local communities, including personal assistance. Nevertheless, as above- mentioned rights are economic- social, one should bear in mind that such rights are to be realized progressively, i. e. gradually and with the maximal use of the available resources.

Revised European Social Charter

Council of Europe adopted the revised European Social Charter in 1996, the Charter entered in force in 1999. Serbia ratified the Charter in May 2009. Article 15 of the Charter (4) prescribes for state parties obligation to take measures in order to ensure effective realization of right of persons with disabilities to independence, social integration and participation in their respective communities, regardless of persons age, nature and origin of disability.

Recommendation Rec. (2006)5 of the Committee of Ministers to member states on the Council of Europe Action Plan to promote the rights and full participation of people with disabilities in society: improving the quality of life of people with disabilities in Europe 2006-2015

Council of Ministers of member states of Council of Europe adopted Recommendation on Action Plan for persons with disabilities for 2006- 2015. It recommended to governments of member states to incorporate principles put forth in the Action Plan in their respective national legislations and policies, to implement them in practice in order to promote the rights and full participation of persons with disabilities in all areas of social life, and enhance the quality of life of those persons.

The Council of Europe Disability Action Plan 2006-2015 (5) seeks to translate the aims of the Council of Europe with regard to human rights, non-discrimination, equal opportunities, full citizenship and participation of people with disabilities into a European policy framework on disability. This Action Plan aims to provide a comprehensive framework that is both flexible and adaptable in order to meet country-specific conditions (1.1.2). The Action Plan aims to encompass number of areas, as disability is a cross- cutting phenomenon. The Plan defines the measures that member states have to take in 15 key areas of activities. Community living for persons with disabilities is one of those areas. Action plan provides for measures that would enhance community living of persons with disabilities (Action line No. 8) that would enable those persons to live independently. The above- mentioned measures range from independent living arrangements to sheltered, supportive living in small-scale settings. It also implies a coordinated approach in the provision of user-driven, community-based services and person-centered support structures.

Serbias Legal Framework for Support Services for Persons with Disabilities Constitution of Republic of Serbia

Constitution of Serbia prohibits any discrimination on grounds of physical and intellectual disability (6). Article 69 of Serbias Constitution prescribes that each citizen in need of social assistance to overcome social calamities and create conditions for satisfaction of basic needs is entitled to social assistance and support. Such support is also extended to that persons family if necessary. Persons with disabilities, war veterans and civilian survivors of armed conflicts are entitled to special protection in accordance with the law (article 69, clause 4).

Law on Social Protection

Parliament of Serbia adopted new Law on Social Protection on March 31st 2011. For the first time the law explicitly provides for services for independent living: Personal assistant service, supported housing and training for independent living. One of the aims of the Law (7) is to promote independence and inclusion in local community; this provision clearly reflects the contents and spirit of article 19 of Convention on the Rights of Persons with Disabilities (3) and article 15 of the revised European Social Charter (5).

Persons with physical impairments are envisaged as main users of personal assistant service, while persons with intellectual disabilities are envisaged as main users of supported housing. Local authorities are obliged to finance personal assistant service, while Serbias is financing supported housing. Services may be provided both by authorities, and entities from civil and private sector, under the condition of meeting quality standards for provision of a particular service.

Law on Prevention of Discrimination against Persons with Disabilities

Law on Prevention of Discrimination against Persons with Disabilities of Serbia prescribes that local authorities should promote setting up of support services for persons with disabilities in order to enhance independence of above- mentioned persons and realization of their rights (8). This provision entered in force on January 1st 2007 (article 53).

Strategy for Improving the Position of Persons with Disabilities in Serbia 2007- 2015

Government of Republic of Serbia adopted the Strategy for Improving the Position of Persons with Disabilities in Serbia 2007- 2015 on December 28th 2006. The Strategy (9) is based on the biopsychosocial model of approach to disability and the respect for the human rights of persons with disabilities. The overall aim of the Strategy is improvement of position of persons with disabilities in society to the position of equal citizens with all rights and responsibilities. The purpose of the Strategy and the action plans for its implementation is to define goals, measures and activities that will contribute to incorporation of social model and human rights based approach in the measures defining the position of persons with disabilities in Serbia.

The Strategy defines 6 main goals. Each of those goals is further developed and implemented through specific objectives. The Strategy also defines measures for realization of each of the specific objectives. The third main goal is making social, health care and other services accessible to users, primarily persons with disabilities, but their families as well. The above- mentioned services should be based on the rights and needs of users. The needs should be determined in accordance with the modern internationally adopted methods. In order to ensure the implementation of the above- mentioned goal 3, the Strategy prescribes for the following specific objectives:

Specific objective 5: To enhance the system of support and services focused on the user in accordance with his/ her needs;

Specific objective 6: To strengthen the families of persons with disabilities through support system for the provision of specific services and facilities aimed at assisting the integration of persons with disabilities into community;

Specific objective 7: To enhance the quality of work of the service providers.

Examples of good practice in Serbia

Personal Assistance Service

Personal Assistance Service in organization of the Center for Independent Living of PWDs Serbia is one of the forms of social support for people with disabilities; it enables their social inclusion and enjoyment of human rights and dignity. This service as a pilot project successfully realized in Belgrade, Smederevo, Jagodina, Leskovac and Sombor. In different stages the project was supported by the Development Agency of the Republic of Ireland, Catholic Relief Services CRS, Ministry of Labour and Social Policy of the Republic of Serbia, Serbia's Social Innovation Fund, United Nations Development Programme UNDP, Balkan Community Initiatives Fund, Oxfam and municipalities of Zvezdara, Smederevo, Jagodina, Novi Sad and Sombor. The project included more than 70 users - persons with disabilities and more than 100 personal assistants.

The philosophy of independent living simply implies that persons with disabilities have equal rights and that their freedoms, choices and opportunities manage all aspects of their lives. Independent living is a concept that supports the efforts of persons with disabilities to achieve equal opportunities and full participation in society as well as other citizens. For many people with disabilities personal assistance is the first most important help in independent living that provides the freedom and solution to many problems. This is often a major prerequisite for consideration of the existence of equal opportunities, self-determination and ultimately - the independent living. Provision of these types of social care services for people with disabilities would reduce their dependence on family and other people; it would increase independence and allow them greater social and work engagement; it would provide them better quality of life. At the same time, it would reduce unemployment, both consumers and people who will work as personal assistants. It is important that people with disabilities do not depend on good or bad will of the parents, family, friends...

The employees are interviewed by the users and chosen according to their needs. This is one on one support, which means that one personal assistant helps one person with disabilities. Personal assistant is the person who provides the service, ie. works for only one specific user with disability. This guarantees the best quality service, because services are provided according to the specific and individual needs of every user, defined by the user himself. User trains his personal assistant, so that he could help him in the best possible way while assisting him in satisfying these needs. This also implies that the user can specify the time and place where he will enjoy these services. Personal assistant has a fund of working hours carried out in consultation with the user. Unfortunately, only a minority experiences an independent living with choice, control and support of personal assistance. These services for people with disabilities currently are not available by authorities, they are implemented by NGOs. One of the goals of Personal Assistance Service is to merge with the system, or become institutionalized form of support for disabled persons, because it is clear that this is a life-changing service which enables these persons to work, travel, and live like others. Without a personal assistant they would be deprived of this possibility. The first step towards the implementation of Personal Assistance Service within the system was made in late 2008 when the Working group of the Ministry of Labour and Social Policy in collaboration with the Center for Independent Living of PWDs Serbia has defined a draft of standards for this service.

Supported housing for people with disabilities

Supported housing for people with disabilities within the Serbian Association for Promoting Inclusion and day care, accommodates users not only with intellectual disabilities, but also with other types of disabilities. Starting from 2004, the program of supported housing included 23 people with disabilities, of different sex, age, type and degree of disability. All users are deinstitutionalized from the Home for children and young people with learning disabilities in Sremcica. The main objective of the project is to increase the capacity of persons with disabilities by raising the level of competence of the users, as well as their integration in an open environment. Basic support team consists of different profiled experts, according to the user needs, but also of a number of educated non-professionals/assistants who provide direct, all inclusive or periodic, customer support. Judging by the content of activities and adequate choice of users, assistants and staff, all benefits and values of the project are being confirmed: diversity, flexibility, efficiency, education, and the ability to predict valid results. The quality of service has been the subject of many reports, indicated by numerous factors (10, 11, 12).

Supported housing is a form of social service for persons with disabilities which include accommodation in apartments in the community with provided support, in accordance with individual needs of users in order to help them live as independently as possible. Supported housing is as a service based on the following principles: it is situated in homes in the community, according to the choice of users and with the support in accordance with individual needs of users; involves support provision and encouragement in daily activities and situations, and improvement of competence level for performance of daily activities; encouragement of the development of user skills through active involvement in community life, as well as supporting the vocational training and working engagement of the users in an open community. In accordance with Social Security Reform strategies, Minimum standards for supported housing services for persons with disabilities as a provider of housing with support have been defined and piloted by the Ministry of Labour and Social Policy and the Republic Institute for Social Protection, with the active participation of the Serbian Association for Promoting Inclusion from Belgrade and the Home for persons with mental disabilities "In the heart of Apple from Pancevo. Implementation of supported housing implies the compliance with the Minimum Standards by the service providers. One of the most important standards is education of Supported housing service in accordance with the program "Supported housing a program of support services staff training," which was developed by the Serbian Association for Promoting Inclusion, accredited by the Republic Institute for Social Protection. The key factor for quality life of persons with disabilities is actually considered to be the quality of provided services, ie. alignment with the requirements and support environment with individual characteristics and abilities of each person (12).

Day care

There are seven day care centers for children with disabilities in Belgrade, which service about 400 people, although the city has 2,000 children in need for these services. Day care centers for persons with various forms of disability exist in other cities and municipalities in Serbia. In accordance with the ability, structure, degree of disability and the interests of the users, suggestions and objective preferences of parents and local community offer, a daily schedule and program in day care center have been established. The proposal of daily activities: arrival and reception children preparation for breakfast and breakfast-personal hygiene identification day, communication individual assessment of the ability of functioning, educational work brunch work engagement prepare for lunch and dinner leisure activities recreational workshops preparation for leaving and leaving This daily rhythm depends on the working time of the Day care center, number of groups and number of children in groups, the number and types of workshops and the number of skilled staff. With these programs it is necessary to predict all the activities provided by local community: swimming, cultural and artistic societies, hiking society, etc. Professional staff:

- special education teachers
- nurses
- occupational therapists
- health caregiver

The right to housing is ensured by directing users at the appropriate social welfare institution that provides day care services or upbringing and educational institution that provides such services as well. The right to housing has a:

- child with physical or mental disabilities
- child suffering from autism
- child with disabilities in social behavior
- adult, if this type of care is most appropriate

Age structure is up to 27 years, but having in mind that the problem of What after 27 years? Has not been resolved day care centers accommodate the elderly people as well. Day care center for intellectually disabled children and youth located in Shakespeare Street in Dedinje is one of the seven day care centers for children with disabilities in Belgrade. It is designed for the living accommodation of children and youth with intellectual disabilities with the capacity of 100 users, although it currently accommodates 128 users. The day care center includes a population of 15-51 years, moderate, heavy and multiple disabled. Working hours are from 6 to 18 hours. Transport of users is provided. Users of the center have food, health care and professional staff consisted of special

education teachers, occupational therapists, health caregivers, physical education teachers, nurses, psychologist, social worker, dentist, and physiotherapist. The Center organizes recreation room for all users once a year, for which the finance is provided by the City of Belgrade. Working content with users is very rich and conducted according to the individual programs - from educational work, occupational activities carried out in workshops for art and crafts, weaving, textile, manufacture of plastic bags, making aromatic candles, theater workshops, working with clay, carpentry workshops, and other. Users have access to the Cabinet for a household, computer workshop and custom hall for physical education, as well as the training ground and a playground. One of the plans for implementation in the future is the establishment of mobile teams for help in the home and extended temporary care. In accordance with Social Security Reform strategies, Minimum standards for supported housing services have been established. In late 2008, Working group of the Ministry of Labour and Social Policy in collaboration with organizations of persons with disabilities and their legal representatives, with the support of the Department for International Development (DFID) of United Kingdom prepared a draft standard for using services in day care centers.

Instead of conclusion

The main goal of any support services is to improve the quality of life of users. We believe that such important projects, which are, as we have seen, primarily related to the quality of life and equality in the community, therefore, the projects of support for persons with disabilities, have proved to be extremely important for users. For their originality and complexity, these programs may constitute an excellent basis for the systematization of experiences in the future. Acceptance of the preliminary solution and planned implementation of its content opens more defined and greater range of action for all interested parties for a comprehensive approach to the persons in need for specific support in meeting daily living needs, as well as for the wider community, without whose help this population would remain deprived of basic rights in the domain of independent living and action in a real social environment. It is indicated that the more dominant

problem which endangers the sustainability of service is the lack of appropriate legislation that would regulate these services more accurate and introduce them into the system – which greatly makes the financing difficulty and threatens the quality and sustainability of the service itself in Belgrade but also in other cities across Serbia.

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Validation of macromolecules as an early marker in glomerular and tubulointerstitial diseases – current proteomics and computational approach

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Abstract

Renal diseases represent one of the biggest health problems. The prevalence of the chronic renal failure in adult population in Europe represents over 10% of all kidney diseases. The efficiency of the current diagnostic procedures is often too low to diagnose disease at an earlier stage and to prevent the development of complications. This limitation underlines the need for further research and the search for new molecular parameters that have the possibility of effective application in early diagnosis and prevention. Macromolecular complexes are commonly addressed to large groups of molecular assemblies which are present in different part of intra and extracellular spaces. They are essential for cellular signal transduction, development, cell grown, structural integrity and play important role in many other biochemical and biological pathways. A large number of experimental designs was used for integrative structure determination of macromolecular assemblies and had required a multidisciplinary approach. Application of proteomic technologies enabled more detailed analysis of the functions of proteins and examined their importance in various physiological states, in sickness and during the application of appropriate therapy. This review is focused on technological innovations in fields of biochemistry, molecular biology, informatics and proteomic studies that allow identification of potential diagnostic biomarkers, better understanding of patho-mechanisms of diseases and effective therapy.

Key words: glomerular diseases, tubulointerstitial diseases, macromolecules, mass spectrometry, peptide mass fingerprinting, computational modeling

Introduction

Renal diseases represent one of the major health problems nowadays. The prevalence of the chronic renal failure in adult population in Europe represents over 10% of all kidney diseases, as a result of a rising number of patients with diabetes mellitus and high blood pressure.^[1] The efficiency of the current diagnostic procedures is often too low to diagnose disease at an earlier stage and to prevent the development of complications. This limitation underlines the need for further research and the search for new molecular parameters that have the possibility of effective application in early diagnosis and prevention.

Macromolecular complexes are commonly addressed to large groups of molecular assemblies which are present in different part of extra and intracellular spaces. They are consisted of at least two (usually ten or even hundreds) noncovanlently interacting macromolecular components, such as proteins, lipids, oligo- and polysaccharides and nucleic acids, in variable sizes, shapes and frequently dynamic structures. Most of them are essential for cellular signal transduction, development, cell grown, structural integrity and many other biochemical and biological pathways.^[2-4]

Technological innovations in fields of biochemistry, molecular biology and computational biology have been implemented with proteomic studies allowing identification of potential diagnostic markers, better understanding of diseases pathway and providing more effective therapeutic principles. Some of these methods indentify and characterize unique components from the complexes, but fail to give more information about their position and quantity in macromolecular assemblies. Other methods are good tool to give the answers to these requirements. Current matter of choice in macromolecular research accepts integration of data from different experimental methods. The ability of mass spectrometry to identify and to quantify thousands of proteins from complex samples can be expected to impact broadly on biology and medicine.^[2, 5, 6] Dynamic nature of protein complexes which consider constant structural changes presents a critical point during definition of their elementary structure. Human proteome presents the most complicated interacting network in comparison to other species. Therefore, there may be thousands of biologically relevant macromolecular complexes whose structures are yet to be characterized.^[5, 6]

Glomerular kidney disease

Glomerular damage disrupts a basic renal function – blood filtration and the removal of the harmful substances from the body (elimination of toxins and their metabolites, end products of carbohydrates metabolism, fats and proteins from the blood flow and their excretion in the urine) while preserving a normal cellular composition of the blood and vital proteins. Various diseases can contribute to the development of glomerular damage: either by directly damaging the renal tissue (infection, intoxication, local toxic effects of drugs, immune system dysfunction, genetic dysfunction, idiopathic disease) or as a part of a systemic disease (diabetes mellitus, cardiovascular diseases, liver diseases and digestive tract diseases).^[7, 8]

Diabetic nephropathy

Diabetes (diabetes mellitus, DM) is the most common cause of chronic renal failure worldwide.^[1, 9] The most important complication of diabetes is diabetic nephropathy (DN), which is, from a clinical point, defined as the presence of persistent proteinuria (more than 0.5 g/24h) in diabetic patients with severe retinopathy and high blood pressure, and in the absence of urinary tract infection or heart failure. About 10 - 50% of all patients with DM type 2 develop kidney damage in 15 - 30 years from the onset of disease.^[10]

During physiological state, filtration of the macromolecules is prevented by intact glomerular structures^[11, 12]. A charge-selective filtration barrier for anionic macromolecules at glomerular basement membrane (GBM) level is represented by heparansulphate proteoglycans (HSPGs) and sialoproteins. Glomerular epithelial cells play a central role in proteoglycan synthesis which can be impaired by hyperglycemia, inflammation and oxidative stress. ^[13-15] Prolonged high blood glucose concentration may lead to the micro-and macro vascular lesions that cause the development of DM complications in the target organs (retina, heart, kidney). The direct impact of the increased concentrations of glucose and its entry into the cell are reported on the metabolism of polyols,^[16] a disturbance in the activity of intracellular metabolic pathways, the activation of protein kinase C,^[17] the formation of reactive oxygen species and the development of oxidative stress,^[18] increased production of glycation end products (AGEs),^[19] impaired calcium methabolism^[20] and abnormal expression of numerous pro-fibrotic growth factors.^[21, 22] There is a significant accumulation of extracellular matrix (ECM) provoking a disturbance of the basal membrane in the glomerulus and tubules, as well as the proliferation of mesangial matrix, which inevitably leads to the development of glomerulosclerosis and tubulointestitial fibrosis.^[23] Damage of the glomerular barrier results in an increased macromolecular filtration and their direct effects on tubular cells in acute (induction of lysosomal damage, energy depletion, activation of transcriptional factors such as AP-1 and NKkB, up regulation of various proinflammatory and profibrotic genes, ephithelial-to-mesenchymal transformation, and tubular injury) and chronic form (hypoxia, loss of peritubular capillaries and development of interstitial fibrosis) of kidney injury.^[24, 25]

The most reliable method of monitoring the development of diabetic nephropathy is detection of microalbuminuria.^[26] Taken into consideration that impaired macromolecular pathway is emphasized at the beginnig of the disease, following investigations should be addressed to early molecular changes at the cellular level. Recent data has underlined the potential of IgG, IgM and alpha-1-macroglobulin as markers of early changes of the macromolecular metabolism in the kidney, existing before first detectable morphological changes.^[27]

Tubulointerstitial kidney disease

Tubular disorders are divided according to the origin into primary (congenital) defects and secondary kidney disease. Secondary tubulopathy occurs more frequently than the primary. These states include tubulointestitiopathies, glomerulonephritis with the clinical presentation of severe nephrotic syndrome, kidney disease in renal transplant rejection, amyloidosis, multiple myeloma and other pathological conditions. Consequently, tubules may be damaged by the effects of nephrotoxic drugs and nephrotoxins.^[28]

Tubulointestitial diseases produce damage to kidney intestitium and surrounding tubules. They can occur in the acute and chronic form, leading to the progressive development of chronic renal insufficiency. The most common causes are local (bacterial pyelonephritis) or systemic infectious disease, kidney toxic reactions to the effect of certain medications (analgesics, antibiotics), allergic reaction (to drugs such as penicillin, cephalexin, and non-steroidal anti-inflammatory drugs) and other disorders of the immune system, the effects of toxins (aristolochic acid, ochratoxin A). The signs and symptoms depend primarily on the underlying disease that leads to this condition. In general, there is a tubular type of proteinuria (proteins of low molecular weight, the general markers of tubular damage are considered to be beta-2-microglobulin (B2M) and alpha-1-microglobulin (AMBP) in the urine).^[28, 29]

Nephrolithiasis

The majority of renal stones are formed of calcium oxalate, and less in the form of hydroxyapatite (HA). Some of the urine macromolecules are defined as crystallization inhibitors (osteopontin (OPN), Tamm-Horsfall protein (THP), chondroitin sulfate (CS), human serum albumin (HSA)), and have a significant impact on HA secondary nucleation, growth, and aggregation, but involving different sites of crystal-macromolecule interaction.^[30] Acidic macromolecules inhibit calcium oxalate nucleation, growth, aggregation and attachment to cells in vitro. They can be considered as potential effective therapy for kidney stones.^[31]

Experimental methods for determination of components of macromolecular assembly

A variety of proteomics methods produce spatial information at different resolution levels. The stoichiometry and composition of protein components in a macromolecular assembly can be defined by quantitative immunoblotting^[32] and mass spectrometry (MS).^[5, 6, 33] The positions of unique components in complexes can be determined by cryo-EM and labelling technique. The existence of protein-protein interaction and intensity of this interaction are well measured by the yeast twohybrid system and affinity purification.^[6] Relative orientations of components and information about interacting residues can be inferred from cryo-EM and OH radical footprinting. Information about the atomic structures of components and their interactions can be determined by X-ray crystallography and NMR spectroscopy.^[6, 33]

Peptide mass fingerprinting (PMF) and mass spectrometry coupled with affinity purification experiments (AP-MS/MS)

A large number of proteomic experiments considering detection of macromolecular complexes was conducted: some of them were defining a components of different organelles and membranes (lysosomes,^[34] membrane proteins,^[35] chromatin-associated protein network,^[36] inter-organelle communication between mitochondria and peroxisomes^[37]), extracellular structures, organs and body liquids (peritoneal dialysate fluids,^[38, 39]) or diseases associated protein markers (diabetic nephropathy^[40], endemic nephropathy^[41]).

Identification and quantification of the proteins from specific proteome could provide efficient information about vital biological pathways. Shotgun, tandem mass spectrometry-based strategy is widely used in biological and biomedical research. Identification of proteins from different samples (tissue samples, body fluids, cell extracts and others) usually considers following steps:^[39-41] precipitation of the proteins from the samples, separation of the proteins with 2-DE, protein digestion and peptides analysis by MS or MS/MS.

Proteomic data alone have an inability to define unique macromolecular complex structure. From the list of identified proteins, it is hard to form an exact combination equivalent to natural assembly due to possibility of various protein-protein interactions which are not specific for one assembly only, existence of the protein which is not a real member of complexes, or missing data. Three dimensional interpretations of different assemblies demands coupling of proteomics with other techniques that provides spatial information.^[42]

Affinity purification techniques are used to study protein components and protein-protein

interactions within protein complexes. The identification of individual components is performed by MS.^[43] This method has found different implementations: determination of viral interactions during infections,^[44] identification of novel ryanodine receptor 1 protein interaction with calcium homeostasis endoplasmic reticulum protein,^[45] definition of endothelial-specific membrane protein, cadherin^[46] and others.

Disadvantages of AP-MS/MS consider high rates of false positive data sets. Although this approach determines all components of targeted complexes, it is hard to provide any information about structure and spatial construction of the assemblies.^[47, 48]

Protein footprinting

As well defined by Guan,^[49] the term 'footprinting' refers to assays that examine macromolecular structural changes by determining the solvent accessibility of the backbone, bases or side chains of macromolecules using their sensitivity to chemical or enzymatic cleavage or modification reactions. To identify and characterize proteins which are interacting to the DNA binding sites, protein footprinting coupled with MS is especially powerful technique. Structures of some individual proteins are reached,^[50] but, despite that knowledge, protein interaction maps and their potential to build different complexes are mater of further research.

Hydroxyl radicals (OH) is frequently used in footprinting to provide high-resolution probes for examining the structure and conformational changes of both DNA and RNA.^[51] This approach in investigation could be used for many protein research, such as mapping the G-actin binding surface of cofilin,^[52] quantifying galectin-1 footprinting,^[53] or examination of unfolding of apomyoglobin.^[54] The basic principle involved exposition of the proteins to the OH radicals resulting in oxidative modification of the sites from the side-chain of the macromolecular assembly. Further analysis are performed by MS/MS sequencing of the oxidized peptides. The oxidation events might be expected to induce protein unfolding.^[55]

Proteolysis is another method used in protein footprinting experiments. This method uses site-specific proteases to generate specific peptide mixture. Obtained peptide mixture provides identification of the proteins using different MS analysis.^[56] For example, DNAse I was used in investigation of DNA binding domain of interferon regulatory factor-2 protein and DNA protein interactions.^[57] Tubulin and drug-treated tubulin were alkylated separately and analysed by MS/MS. The level of alkylation was markedly decreased after treatment.^[58]

The size of the macromolecules and complexity of the assemblies are not limiting factor for protein footprinting investigation.^[59] This approach is still not efficient to provide information for three dimensional pictures of macromolecular assemblies.

Different visualisation techniques in determination proteins structure as a part of complex molecular systems

Cryo-electron microscopy (cryo-EM), as a form of transmission electron microscopy where the sample is studied at cryogenic temperatures, is a matter of choice in determination of spatial relationships of macromolecular complexes. However, these methods had shown low resolution in presentation of unique assemblies. Information about assemblies structures and their localization within the cell structure provided by cryo-EM could be gathered into system called cellular atlas.^[60] This system is complex of networking maps made trough multi-step processes from the creation of collection of the elementary data from each components to the acquisition of three dimensional cellular tomograms and their interpretation. This methods of constructing a three dimensional interpretations of macromolecular complexes requires a new approach to every unique biological systems due to their dynamical nature and perplexity. Also, the original experimental methods used for samples analysis which provide a collection of primary data (precipitation methods, affinity purification or affinity chromatography) have a significant impact on final interpretation. The resolution of the final results can be improved if the collection of the primary data was provided from multidisciplinary approach (for example, macromolecular map of T. acidophilum was created with use of data from LC-MS/MS combined with two different purifications methods).^[61]

Electron tomography studies large pleomorphic macromolecular structures, mostly used for obtaining three dimensional models of subcellular macromolecular entities and their spatial relation-
ships in natural density within nanomolar resolution, from simple protein-protein complexes to advanced structures such as organelles, or entire cell molecular architecture.^[84] Cryo-EM is primary imaging methods for tomography. Cellular tomograms contain a vast amount of information which can be processed with image analysis for further data interpretation. Tomograms maps provide insights into statical cellular components, but also could give further explanation of dynamical changes in these complex systems. Further development of data analysis and statistical interpretation are required for using this promising but costly imaging method.^[62]

Proteomics techniques can facilitate the characterization of the structure of macromolecular assemblies trough integrative modelling. One of the challenge for integrating proteomics in future represent a visualisation and definition of dynamic nature of macromolecular assemblies depending of functional or intrarmolecular relations, but also on extramolecular interactions. Since the amount of experimental data about macromolecular assemblies grows, integrative structure determination will be vital for characterization of these molecules and the corresponding cellular processes.^[63]

Computer modelling of macromolecular complexes

Comparative modelling technique builds a macromolecular complex model by using a structure of a similar well defined complex as a template. ^[64] Protein docking is the computational modelling and relies on searching through possible three dimensional structures of macromolecular complexes. It can be applied when no structure of a similar assembly is known. Comparative patch analysis is a combination of protein docking and comparative modelling techniques. Its principle is to use docking technique for analyzing only those interaction modes suggested by structurally defined interactions between each of the complex components, or their homolog's, with any other protein.^[65] Most protein docking methods treat components as rigid bodies.[66] When substantial conformational change occurs within the components at the time of complex formation, further analysis required flexible docking procedures.^[67] Although the second group of docking methods are more 'natural', the number of possible combination for macromolecular structure prediction is significantly increased, which make computational modelling extremely complicated and time consuming. Continuously improvement of precise definition of similarity and difference between components of one assembly, as well as side-chain reactivity, surface accessibility and distance constraints is underlined.^[68] Docking methods are systematically assessed every two years through blind trials in the Critical Assessment of Prediction of Interactions (CAPRI).^[68]

Computational docking is a good research tool in order to define final structure of macromolecular assemblies. Taken on molecular level, this final structure is often at the very end of reaction chain consisted of many different intermedial and transient complex forms. Therefore, continuously improvement of docking procedures is emphasized. One of the mostly recommended tool server is The ClusPro docking server^[69] which includes modelling of multidomain proteins and oligomers, frequently in combination with additional data from experimental or other computational techniques. Different important macromolecular assemblies were conducted: the configuration of the histone assembly^[70], enzymatic reactions,^[71] cancer development^[72] and many others.

Conclusion

Despite a fast development of proteomics and molecular biology research techniques, the determination of final three dimensional structures of macromolecular assemblies and characterization of their interaction pathway are still depended on computer modelling and creation of different statistically based approximations.

Future perspectives are raising a significant importance to proteomics providing insights into macromolecular evolution and architectural principles.

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Cigarette Smoking-Induced Acute Eosinophilic Pneumonia

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Abstract

Introduction: Acute eosinophilic pneumonia (AEP) is idiopathic disease characterized by acute febrile illness, progressive respiratory failure, diffuse pulmonary infiltrates, and pulmonary eosinophilia. The aetiology of AEP is unknown, although several studies have proposed that cigarette smoke is potentially related to the onset of AEP. Herein is a report of a rare case showing the causal association between short-term period of excessive smoking and AEP

Case report: A 25-year-old patient was admitted to the ICU (during on-duty hours) as an emergency case due to acute disease occurred a day prior to hospitalisation. His symptoms were febricity, dry cough, excessive fatigue and general weakness. The patient was a non-smoker who had smoked 30 cigarettes a day prior to the onset of the symptoms. At the time of admission, he was voluntary, but somnolent, orientated, febrile, dyspneic, cyanotic, adynamic, and without peripheral lymphadenopathy. Due to both poor oxygenation and the life-threatening condition, the corticosteroid therapy, in addition to the antibiotic therapy were immediately administered to the patient. The eosinophilia was diagnosed based on control tests, such as Le 22.0×10^9 , with dominating eosinophilic leucocytes of 12.59 (0-7% reference value) and neutrophils of 86.26 (44-72% reference range), Se 58mm/h, CRP 115, fibrinogen 6.5, while other parametres ranged within the reference scales. Afterwards, eosinophil chamber count of 2300 was found (<350mm³ reference value). The specific protein value amounted to IgE 255.0 IU/ml (0-100 reference value). The MSCT of the thorax revealed: pneumonic infiltrates of sub-segment type, including associated pleural thickening, observed

in the subhilar and bibasal parts, both sides. Moreover, pleural effusion was observed in a minor incisure on the right and in the upper part of a major incisure on the left.

Conclusion: The majority of reported cigarette smoking-induced AEP cases are young adults who were first-time smokers. In light of such reports and considering the increase of early cigarette smoking in young adults, it is important that physicians are aware of the possibility of this potentially life-threatening, but fully reversible disease.

Key words: eosinophilic pneumonia, smoke, case report

Introduction

Acute eosinophilic pneumonia (AEP) was first described by Allen et al (1) as idiopathic disease characterized by acute febrile illness, progressive respiratory failure, diffuse pulmonary infiltrates, and pulmonary eosinophilia. AEP is a rare condition that is clinically distinct from chronic eosinophilic pneumonia (2). Patients with AEP often develop severe respiratory failure, but the response to steroid treatment is excellent. The aetiology of AEP is unknown, although several studies have proposed that cigarette smoke is potentially related to the onset of AEP (2). Epidemiologic study of this disease identified 18 patients with AEP among 183,000 US military personnel deployed in or near Iraq, indicating that all of the patients were smokers, with 78% of them recently beginning to smoke (3). These data suggest a possible association between new-onset smoking and AEP (3).

Herein is a report of a rare case showing the causal association between short-term period of excessive smoking and AEP.

Case report

A 25-year-old patient was admitted to the ICU (during on-duty hours) as an emergency case due to acute disease occurred a day prior to hospitalisation. His symptoms were febricity (maximally measured value to 39°C), dry cough, excessive fatigue and general weakness. Previous medical history clear; he denied any significant disorders relevant to the heredity and any drug administration as well. The patient was a non-smoker who had smoked 30 cigarettes (at a party in a closed room full of smoke) a day prior to the onset of the symptoms.

At the time of admission, he was voluntary, but somnolent, orientated, febrile, dyspneic, cyanotic, adynamic, and without peripheral lymphadenopathy. Late bilateral inspiration gaps were registered basally by auscultation. The coronary action was rhythmic, tachycardiac, with clear cardiac sounds and no murmurs; TA 130 /80mmHg, Fr 120/min. The abdomen and extremities findings were negative. Gas analyses on admission indicated partial respiratory insuficiency (pO2 - 6.7kPa, pCO2 -4.8kPa, O2 saturation – 86% of). The chest X-ray revealed bilaterally underlined interstitium, paracardially on the right and, to a minor extent, spotlike bronchopneumonic changes on the left-hand side (Fig. 1). Initial laboratory tests: Le 31.2, Ne% 91.5, Eo% 1.5, Er 4.94 Tr 314, Se 28; other parameters ranged within reference values. Due to both poor oxygenation and the life-threatening condition, the corticosteroid therapy (Lemod Solu 80mg), in addition to the antibiotic therapy (Cephalosporin III generation and macrolids) were immediately administered to the patient. Since the satisfactory oxygenation (pO2 - 12.2, pCO2-4.0, satO2 - 97%, pH - 7.41) was achieved quickly, mechanical ventilation was not considered. His condition improved the following day, and in 3 days, the respiratory insufficiency entirely normalized, together with the chest X-ray improvement. After getting significant chest X-ray regression and the general condition promotion, the eosinophilia was diagnosed based on control tests, such as Le 22.0x10⁹, with dominating eosinophilic leucocytes of 12.59 (0-7% reference value) and neutrophils of 86.26 (44-72% reference range), Se 58mm/h, CRP 115, fibrinogen 6.5, while other parametres ranged within the reference scales. Afterwards, eosinophil chamber count of 2300 was found (<350mm³ reference value). The specific protein value amounted to IgE 255.0 IU/ml (0-100 reference value). Additional tests also done, such as (immunoglobulin, immunity complexes and antinuclear antibodies: ANCA, and ANA, rheumatoid factor, cryoglobulin and antibodies to hepatitis B and C, HIV) were within reference values. Haemoculture remained sterile, the serology to type A and type B influenza virus was negative, and the serology to adenovirus, mycoplasma (Mycoplasma pneumoniae), Chlamydia psittaci and Coxiella burnetii were also negative. No acidalcoholic resistant bacillii were isolated in sputum. During admission, lung functional tests and diffusion ranged within reference values (FVC 99%, FEV1 103%, FEV1%, FVC 87.61). Faeces parasite test was negative. The MSCT of the thorax (Sept 01, 2010) revealed: pneumonic infiltrates of sub-segment type, including associated pleural thickening, observed in the subhilar and bibasal parts, both sides. Moreover, pleural effusion was observed in a minor incisure on the right and in the upper part of a major incisure on the left. (Fig. 2). Considering the prompt chest X-ray regression, bronchial examination and BAL were not made.



Figure 1.

Despite no confirmation of the eosinophilic infiltrates presence in the lung tissue we, however, assented that clinical indications were firm enough to diagnose the acute idiopathic interstitial eosinophilic pneumonia provoked by nicotine, but with good clinical and chest X-ray regression to the administered therapy. Control tests indicated an eosinophils drop off in a count chambre to 300 (ref. value<350) and therefore, the patient was discharged. One-month Pronison-20mg therapy was advised, including the follow-up of total CBC (cell blood count).





Discussion

Several studies have highlighted a link between new-onset smoking and AEP (4, 5, 10). One day prior to the onset of the disease, our patient had attended a party and he smoked 30 cigarettes during few hours. He had never smoked before that day. So far, little data are available about initial numbers of cigarettes smoked by new-onset smoking AEP patients. In study conducted by Uchiyama et al. on 33 consecutive patients with AEP, authors concluded that recent alterations in smoking habits, not only beginning to smoke, but also restarting to smoke and increasing daily smoking doses, are associated with the AEP development (2). The same study showed that 71% of patients who had begun smoking, smoked ≥10 cigarettes per day, indicating that they generally started smoking at relatively high quantity of daily cigarettes (2).

Most of the clinical characteristics of our AEP patient were similar to those previously reported in the literature. He was admitted in our department with acute febrile illness, severe hypoxemia, bilateral diffuse infiltrates with interstitial pattern on chest X-ray, characteristic MSCT findings and rapidly improvement after administration of intravenous Methylprednisolon. Somewhat unusual was the finding of pronounced neutrophilia in the blood at initial presentation, suggesting bacterial pneumonia. Other investigators also reported an increase in neutrophils circulating in the blood occurs in the early phase of cigarette smoke-induced AEP, followed by an increase in oesinophils (12, 13). This fact may mislead practitioner in obtaining the diagnosis and also delay administration of corticosteroids.

The exact mechanism how cigarette smoke induces AEP is unknown. Cigarette smoke has been shown to be a strong inflammatory stimulus that induces proinflammatory cytokines and chemokines, such as interleukin-6, tumor necrosis factor, and interleukin-8, and recruits activated macrophages and neutrophils to lung tissue (7). On the other hand, interleukin-5, interleukin-3, and granulocyte-macrophage colony stimulating factor, produced mainly by the T-helper-2 lymphocytes, regulate eosinophil development in the bone marrow and increase their survival by inhibiting apoptosis (14,15). The respiratory system appears to be most vulnerable to eosinophils as the effector cell-mediating tissue injury. However, the role of the eosinophil in present disorder has not been fully elucidated. In one study (2) and one case-report (15) a cigarette smoke provocation test was performed and all patients had positive results. Importantly, recent evidence has revealed that 1h of passive smoke exposure at levels observed in bars or restaurants increases inflammatory cytokine levels, particularly in men (6). The smoke-induced inflammation persisted at elevated levels for at least 3h after short-term exposure to passive smoke (6). However, there is no concrete evidence that cigarette smoke itself directly induces eosinophilic inflammation in the lung. Further studies will be required to elucidate the precise pathogenesis of cigarette smoking-induced AEP.

The majority of reported cigarette smoking-induced AEP cases are young adults who were firsttime smokers. In light of such reports and considering the increase of early cigarette smoking in young adults, it is important that physicians are aware of the possibility of this potentially lifethreatening, but fully reversible disease.

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Clinical features of scleritis associated with systemic immune-mediated diseases

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Abstract

Purpose: The purpose of this study is to compare clinical features of patients with scleritis associated with rheumatoid arthritis (RA), patients with scleritis associated with other systemic immune-mediated diseases and patients with scleritis without associated immune mediated diseases ("idiopathic scleritis").

Material and methods: During the period from 2000-2010 we examined 105 patients with scleritis, divided into three groups: first group - 35 patients with "idiopatic "scleritis, second group - 40 patients with scleritis associated with rheumatoid arthritis, and third group - 30 patients suffering from scleritis associated with systemic vasculitis diseases. Patient data, including age and sex, recurrence, bilaterality of scleritis, and follow-up period were analyzed.

Results: The number of recurrences was not significantly different regarding the type of scleritis; however, the overall number of recurrences was larger in patients with scleritis associated with RA (p<0.05). Bilateralism and the shortest period of recovery were prominent in scleritis of unknown etiology and scleritis associated with systemic diseases, while the necrotizing form with pain was most frequent in scleritis associated with RA (p<0.05). The accompanying diseases of the eye were equally present in all the groups of patients, except for a considerable difference in the occurrence of keratoconjuncivitis sicca, which was significantly prominent in scleritis associated with RA (p<0.05).

Conclusion: Scleritis associated with rheumatoid arthritis is a more severe ocular condition than scleritis without associated diseases, while it is as severe as scleritis associated with other immunemediated diseases.

Key words: scleritis, clinical features, immune-mediated diseases

Introduction

Scleritis is a chronic inflammation of deep layers of sclera, which is characterized by edema and the cellular infiltration of the sclera and episcleral tissues. The pain is severe and it is intensified by the eye movement and reading, thus making work impossible (1-4). Watson and Hayreh classified scleritis into two categories: anterior and posterior (5,6). Anterior scleritis can be diffuse, nodular, necrotizing with inflammation (necrotizing) and necrotizing without inflammation (scleromalatia perforans). The most common clinical forms are diffuse scleritis and nodular scleritis. Scleritis may occur isolated ("idiopathic scleritis") or in association with systemic diseases of connective tissue (rheumatoid arthritis - RA, systemic lupus erythematosus - SLE, polyartheritis nodosa - PAN, scleroderma, Wegener's granolumatosis - WG) (5,6,7).

RA is the most frequent systemic disease associated with scleritis. The detection of immune-mediated diseases in patients with scleritis is a sign of poor general and ocular prognosis because it indicates serious systemic and ocular complications (8-11). Scleritis associated with rheumatoid arthritis can have ocular complications such as: peripheral ulcerative keratitis - PUK, keratoconjunctivitis sicca - KKS, cataract - CAT, anterior uveitis – APU (4).

The purpose of this study is to compare clinical features of patients with scleritis associated with rheumatoid arthritis (RA), patients with scleritis associated with other systemic immune-mediated diseases and patients with scleritis without associated immune mediated diseases ("idiopathic scleritis").

Material and Methods

During the period from 2000-2010 we examined 105 patients with scleritis. All examined pati-

ents were divided into three groups: first group - 35 patients with "idiopatic scleritis", second group -40 patients with scleritis associated with rheumatoid arthritis, and third group - 30 patients suffering from scleritis associated with systemic diseases (SLE, PAN, scleroderma, WG, giant cells arthritis). Ophthalmological examination included: the best corrected visual acuity (BCVA) by Snellen signs, the biomicroscopy of anterior segment, applanation tonometry and indirect ophthalmoscopy. Patient data, including age and sex, the bilaterality of scleritis, and the follow-up period were analyzed. Scleritis was characterized according to the classification of Watson and Hayreh (5, 6). All patients with RA had a definitive diagnosis, according to the criteria of the American College of Rheumatology (11). Systemic immune-mediated diseases other than RA associated with scleritis included connective tissue diseases and other inflammatory conditions. Diagnosis criteria for these systemic immunemediated diseases have been published elsewhere (3, 9). The timing between the onset of scleritis and onset of RA, as well as prior ocular surgeries, were recorded. The severity of the joint disease, extent of extra-articular systemic manifestations, and mortality incidence were analyzed.

Patients with infectious scleritis and scleritis associated with miscellaneous conditions (derma-

tologic or metabolic conditions, foreign bodies, chemical injuries) were excluded.

Statistical analysis

The one-way analysis of variance (One–Way ANOVA) and Post Hoc (Tukey HSD) analyses were used to test the mean age and gender differences between the examined groups.

The comparison of certain attributive and discontinued numerical characteristics was done by Chi Square Test (c^2 – test) or Kruskal Wallis Test.

For the statistical analysis of the data, SPSS Windows (Ver. 8.0) was used.

Results

The clinical characteristics of patients with scleritis in the examined groups are given in Table 1.

There is equal representation of both sexes regardless of the scleritis type; however, patients with scleritis of unknown etiology are considerably younger than patients with scleritis associated with either RA or systemic diseases. There was no significant difference in recurrence regarding the scleritis type, but the total number of recidives was greatest in patients with scleritis associated with RA (p<0.05). Bilateral occurrence and the shortest period of recovery are the characteristics of scleritis of

Variable	Scleritis of unknown etiology (n=35)	Scleritis associated with RA (n=40)	Scleritis associated with ot- her systemic diseases (n=30)
Men	13 (37.1%)	12 (30%)	16 (53.3%)
Women	22 (62.9%)	28 (70%)	14 (46.7%)
Age	36.71±14.23	46.25±11.6 [#]	46.3±13.7 [#]
Number of recidives	2.77±1.896 ^b	4.6±5.03	2.53±2.22 ^b
Recovering time	2.7±3.61 ^b	7.58±9.24	6.23±7.57
uni/bilateral	10/25	28/12ª	25/5ª
Nodular	10 (28.5%)	17 (42.5%)	8 (26.5%)
Diffuse	25 (71.5%)*	16 (40.0%)	20 (66.5%)
Necrotizing	0 (0.0%)	7 (17.5%)**	2 (7.0%)
PUK	4 (11.4%)	3 (7.5%)	5 (16.6%)
CAT	8 (22.8%)	8 (20.0%)	2 (6.6%)
KKS	4 (11.4%)	15 (37.5%)	5 (16.6%)
APU	6 (17.1%)	3 (7.5%)	5 (16.6%)
Without disease	13 (37.1%)	11 (27.5%)	13 (43.3%)

Table 1. Clinical characteristis of patients with scleritis in examined groups

p < 0.05; # p < 0.05 vs scleritis without associated diseases

 ^{a}p <0.05 vs. scleritis without associated diseases, ^{b}p <0.05 vs. SC associated with RA

p < 0.05 vs.scleritis associated with RA and other immune-mediated diseases

**p<0.05 vs. scleritis idiopathic and scleritis associated with other immune-mediated

unknown etiology compared with the other types of scleritis (p<0.05). There is a considerable difference in the occurrence of diffuse and necrotizing forms between the examined groups of patients, which was not found in the case of the nodular form of scleritis. The diffuse form was mostly characteristic of scleritis of unknown etiology and scleritis associated with systemic diseases, while the necrotizing form of pain was most frequent in scleritis associated with RA (p<0.05). Accompanying eye diseases are equally present in all the examined groups of patients, except for a considerable difference in the occurrence of KKS, which was significantly more present in scleritis associated with RA (p<0.05).

In order to prove the correlation of the type of scleritis with associated diseases as well as the severity of the disease judging from: the number of recidives, unilateralism/ bilateralism and the disease duration, we did the linear regression Table 2.

In the linear regression model the older age of patients, bilateral occurrence of changes, nodular and necrotizing types of changes and longer recovery time showed a significant association with the occurrence of scleritis associated with RA and other systemic diseases in comparison with patients with primary scleritis of unknown etiology.

Disscusion

Scleritis is an inflammation of deep layers of sclera. It can occur as isolated ("idiopathic«) or

associated with systemic diseases of connective tissue (RA, SLE, Wegner's granulomatosis, PAN). RA is the most frequent systemic disease of connective tissue associated with scleritis (11,12,13).

In our series of 105 patients with scleritis, 75 were discovered to have a causative systemic immune-mediated diseases, rheumatoid arthritis being the most common - in 40 patients (53.3%), followed by SLE in 14 patients (18,6%), followed by Wegener granulomatosis (5.3%). A surprisingly wide scale of values ranging from 0.67% to 57% for scleritis associated with systemic diseases has been found in literature. Sainz de la Maza found in their study that 47.6% of patients with scleritis had associated systemic diseases of connective tissue, 39.02% of which occurred in patients with RA, while 17.7% of patients had Wegener granulomatosis (3,4). It has also been found in literature that a third of patients with the necrotizing form of scleritis has systemic vasculitis diseases, one of the most prominent being RA. The same authors state that these forms take a very unfavorable course and can lead to spontaneous perforation of the bulbus and even result in death due to the presence of the vasculitis disease.

In our study women made 62.9% of patients with idiopathic scleritis, 70% of patients with scleritis with RA, and 46.7% of patients with scleritis with associated diseases. The reason for the greater presence of women in relation to men in patients with scleritis with associated diseases was

Table 2. Association of demographic and clinical findings with scleritis associated with RA and other systemic diseases

	Unstandardized Coefficients		Standardized Coefficients	4	C' -	95% Confidence Interval for B	
	В	Std. Error	Beta		51g.	Lower Bound	Upper Bound
(Constant)	0.626	0.237		2.641	0.010	0.155	1.097
sex	0.009	0.084	0.010	0.112	0.911	-0.158	0.176
age	0.008	0.003	0.246	2.750	0.007	0.002	0.015
only one attack	0.086	0.097	0.085	0.885	0.379	-0.107	0.278
number of recidives	-0.013	0.015	-0.099	-0.845	0.400	-0.044	0.018
unilateral	-0.328	0.089	-0.341	-3.677	0.000	-0.505	-0.151
nodular	-0.248	0.180	-0.248	-1.381	0.171	-0.604	0.109
diffuse	-0.341	0.175	-0.359	-1.947	0.055	-0.690	0.007
necrotizing	-0.185	0.228	-0.110	812	0.419	-0.636	0.267
recovering time	0.020	0.007	0.311	2.644	0.010	0.005	0.034

Linear regression, Enter Model, 95% CI for B>0 favorable SC with RA and other systemic diseases

given by Sainz de la Maza M., who says that such results are to be expected since the most common systemic diseases in the examined groups are RA and SLE – typically women's diseases (3,4).

Patients with scleritis associated with RA were older than patients with idiopathic scleritis, but not older than patients with scleritis associated with other systemic diseases.

Watson and Hayreh divided scleritis into anterior and posterior types according to the anatomic distribution of the disease (5,6). Anterior scleritis is further subdivided into: diffuse, nodular, necrotizing with and without inflammation (scleromalatia perforans). These authors emphasize that the posterior type of scleritis (diffuse, nodular and necrotizing with or without inflammation) appears in 95% of cases, while the posterior type is considerably rare. Diffuse scleritis is the most frequent type of scleritis, while nodular scleritis is the second cause of anterior scleritis, representing 20% of all types of scleritis, and is associated with severe systemic immune-mediated diseases.

Sainz de la Maza point out that the diffuse type is more present in patients with scleritis of unknown etiology, while the necrotizing type is more common in patients with systemic diseases of connective tissue, in which case it takes an unfavorable course (3,4). The same authors found that different types of scleritis in patients with scleritis associated with rheumatoid arthritis did not differ significantly when compared with patients with scleritis associated with systemic immunemediate diseases other than rheumatoid arthritis.

In our study a significant difference between diffuse and necrotizing types in the examined groups of patients was found; the difference, however, was not found in the nodular type of scleritis. The diffuse type of scleritis was significantly more present in the group of patients with scleritis of unknown etiology, while the necrotizing type was most frequent in patients with RA. The nodular type was more frequently found in patients with RA, but the difference was not statistically significant. In our study 8.6% of patients had necrotizing scleritis and all of the patients had associated systemic diseases, but a majority had associated RA, one patient had SLE and one had WG.

Several important things have recently become clear about treatment of patients with scleritis.

Topical non steroidal anti-inflammatory drugs are routinely insufficient treatment for scleral inflammation. Systemic non steroidal anti-inflammatory drugs (NSAIDs) are efficacious in many cases of diffuse and nodular scleritis, if there is no response to these drugs, short-rterm treatment with oral, intramuscular, intravenous, steroidal anti-inflammatory drugs is recommended. However, no clear quidelines exist regarding the most appropriate subsequent therapeutic choices in case of systemic steroidal anti-inflammatory drugs unresponsiveness or side effects. High dose systemic steroidal anti-inflammatory drugs alone may be efficacious in controlling scleral inflammation in same cases of necrotizing sclertis. Systemic immunosupresive drugs (cyclophoshamid, metotrexate, azathioprine, cyclospotine) have been shown to be efficacious in halting necrotizing scleritis and scleromlatia perforans. Recently, some case reports revealed that infliximab and rituximab can be used for the treatment of active necrotizing scleritis (12-15). It was also recently reported that adalimumab could be a good alternative in patients with severe nodular scleritis. Adalimumab is a fully human monoclonal antibody against the soluble and membrane TNF; it has been used in moderate to severe RA refractory to traditional DMARDS with good outcomes in terms of symptoms control, preventing radiological progression and functional disability (17).

In our study there was a small number of the necrotizing type of scleritis, while scleromalatia perforans and posterior scleritis were not found. The reason for a small number of the seriously destructive form of scleritis probably lies in the fact that in our series the majority of patients had a less destructive form of scleritis. All of our patients with RA as well as patients with other systemic diseases of the connective tissue took non steroidal inflammatory drugs and corticosteroids. A number of patients also used immunomodulatory drugs or cytotoxic drugs which are a basic therapy in auto-immune disorders and which can affect the course of the disease and can either reduce or stop the progression of the disease (15-18).

A special characteristic of scleritis is its recurrence. Recurrence does not have to involve the same part of sclera nor does it have to occur on the eye - subject to the first attack. The diffuse form is described in literature as more frequently bilateral than the nodular one, which is more frequently unilateral. In the literature it can be found that nodular scleritis is more frequent in patients with rheumatoid arthritis than in patients with other systemic immune-mediated diseases (3-6).

The average of recidives in our study in the group of patients with scleritis associated with RA was considerably higher than in the group with scleritis associated with other systemic diseases and scleritis of unknown etiology respectively (p<0.05).

Unilateral recidives were more common in the group of patients with RA, as well as the group with scleritis associated with systemic diseases, while bilateral recidives were a characteristic of scleritis of unknown etiology (2-5).

In the group of patients with scleritis associated with RA, as well as the group with scleritis associated with other systemic diseases, recovery time was significantly longer than in the group with scleritis of unknown etiology (p<0.05). On the other hand, there was no significant difference in recovery time between the groups with scleritis which had associated diseases (p >0.05).

In our study there was a significant correlation between the diffuse type of scleritis and the bilateral manifestation of the disease in patients with scleritis of unknown etiology, while its correlation with the number of recidives was not found. In this group bilateral manifestation was connected with the younger age of patients. In the group with scleritis associated with RA the correlations between the number of recidives and the necrotizing form of scleritis with the recovery time were established, while in the group with scleritis with systemic diseases only the correlation between the number of recidives and the duration of the disease was found.

Several studies have demonstrated that patients with rheumatoid arthritis associated with scleritis usually have an advanced joint disease and extraarticular manifestations, many of which reflect underlying systemic vasculitis. In a similar way, our study showed that the presence of scleritis in patients with rheumatoid arthritis not only was associated with severe and disabling arthritis but was also a sign of a widespread systemic disease. A few of our patients had advanced arthritis and most of them, especially the ones with necrotizing scleritis, had extra-articular manifestations. The most common extra-articular manifestations were subcutaneous nodules (50%) and skin vasculitis ulcers (31.25%). Other extra-articular manifestations included: pulmonary disorders, cardiac abnormalities, neurological involvement, amyloidosis. Life-threatening vasculitis lesions may develop elsewhere. Several studies have shown that the prognosis for life is poorer in patients with rheumatoid arthritis complicated by scleritis than in those without. McGavin found a 3-year mortality rate of 45.5% for patients with rheumatoid arthritis and scleritis versus 18.2% for patients but without scleritis (20). Foster and coworkers report that in a series of 20 patients with rheumatoid arthritis and necrotizing scleritis, 7 patients died of vascular-related events within a 10year period (21). Other patients were treated with immunosuppressive drugs, suggesting that the use of immunosuppressive drugs may improve prognosis in patients with necrotizing scleritis associated with rheumatoid arthritis.

Other eye diseases were equally distributed in all the examined groups of patients, except for a significant difference in the occurrence of KKS, which was much more common in patients with scleritis associated with RA. The reported incidence of keratitis in patients with scleritis associated with rheumatoid arthritis ranges from 36% to 43.3%. The incidence of KKS is between 11.6% and 50% in literature (11, 12, 13). The KKS in RA is classically described as an aqueous tear deficiency (1).

Conclusion

Scleritis associated with rheumatoid arthritis is a more severe ocular condition than scleritis without associated diseases, while it is as severe as scleritis associated with other immune-mediated diseases.

Abbreviations

Rheumatoid arthritis – RA Systemic lupus erythematosus – SLE Polyartheritis nodosa – PAN Wegener's granolumatosis – WG Keratoconjunctivitis Sicca- KKS Best corrected visual acuity- BCVA Ulcerative keratitis – PUK Cataract - CAT Anterior uveitis – APU

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Acute Bowel Obstruction: Risk Factors of Adverse Outcomes Following Surgery

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Abstract

Objective: To identify the risk factors of the adverse outcomes following surgery for the acute bowel obstruction (ABO).

Methods: Annual cross-section included patients undergoing surgery for the acute bowel obstruction, at the Clinic for Emergency Surgery, from December 2009 to December 2010. Patients had non-resection procedures or bowel resection with the intestinal anastomosis or temporary intestinal diversion. Demographic and perioperative data as well as outcome results were collected. Stepwise logistic regression was used to build models predicting 30-day morbidity and mortality and derive risk index values.

Results: Out of 272 patients, 145 underwent non-resection surgical procedures and 127 underwent bowel resection. The median ICU stay and median hospital stay was significantly higher among patients who underwent bowel resection (p=0,001 and p<0.0001,respectively). Morbidity was 37.1%. In multivariate analysis, the variables with the highest risk values included age over 65 years and ASA class 4-5, for 30-day morbidity. The overall 30-day mortality was 10.3%. For 30-day mortality, age over 65 years, comorbidity conditions, ASA class 4-5 and malignant etiology of ABO were the variables with the highest risk values.

Conclusions: Advanced age and ASA score with delayed operation were the risk factors significantly associated with the increased complication rate, while the advanced age and ASA score, comorbidity and malignant etiology were the risk factors significantly associated with the increased death rate. Surgery type was not a predictor of the adverse outcomes. Identification of risk factors is useful to predict outcomes and pro-

vide supportive care to high-risk patients undergoing surgery for ABO.

Key words: Acute bowel obstruction; Surgery; Risk factors; Outcome.

Introduction

Acute bowel obstruction (ABO) is well known clinical entity, which even today presents a major cause of admission to emergency surgery departments and still represents a challenge for surgeons, in the third millennium as well. (1) There is a large number of etiology factors which involve the mechanical bowel obstruction. The most common cause of small bowel obstruction (SBO) is adhesions. (2) Approximately 60% of the mechanical large bowel obstructions (LBO) are caused by malignancies, 20% are caused by diverticular disease complications, and 5% are the result of the colonic volvulus. (3,4)

Acute bowel obstruction is associated with the significant morbidity and mortality. (2) Generally, mortality for acute bowel obstruction has decreased during the past 50 years from 50% to 2%-19%. (5-7) A critical factor in managing these patient is to make decision whether they have to be subjected to emergency surgery. One of the keys to immediate surgical management of the intestinal obstruction is an early recognition of the bowel strangulation or perforation, because mortality increases 2 to 10 folds in such cases. (1) However, despite the significant improvement in diagnostic procedures and imaging studies (Plain radiograph X-rays, Abdominal Ultrasound, Computed Tomography scan) during the last few decades, there are no specific signs of the bowel strangulation. Careful clinical evaluation, in conjunction with the radiologic studies, is essential for the decision of proper management of patients with the acute mechanical bowel obstruction; if any uncertainty existed, prompt operative intervention would be indicated. The potential risks of delayed surgery for ABO include bowel strangulation, necrosis, and subsequent peritonitis and systemic sepsis. Therefore, the primary goal in patients presenting with ABO is to diagnose whether strangulation is definitely present or when its presence cannot be reliably excluded.

Despite overall progress in diagnostic and therapeutic approach, the acute bowel obstruction has presented highly severe conditions, with the significant morbidity and high mortality. All potential responsible preoperative and intraoperative risk factors are still discussed. Studies have shown that death is influenced by patient-related factors such as age, comorbidity, bowel gangrene and delay in treatment.(8) The assessment of the potential risks of peri-operative mortality and morbidity is increasingly important for the clinicians. Interrelations between the individual factors can be studied only by multifactorial statistical methods.

The authors designed the study to identify and analyze the risk factors influencing the complications and death for the acute bowel obstruction (ABO) that includes both entities: small bowel and large bowel obstruction. Multifactorial statistical methods were used to determine individual factors influencing the major outcome variables.

Patients and methods

The authors retrospectively studied **272** adult patients who underwent surgery due to ABO, within 12h-24h, at the Clinic for Emergency Surgery, from December 2009 to December 2010.

Surgical intervention is therefore mandatory for patients with the complete bowel obstruction, signs or symptoms of strangulation and/or perforation. Emergency operations are defined as those performed as soon as possible and no later than 12 hours after the patient has been admitted to hospital. Patients with paralytic ileus were excluded from this study, as well as patients who were managed safely with nonsurgical treatment. The American Society of Anesthesiologists Score (ASA) was used to categorize pre-operative risk by assessing the physical status of patients before surgery. (9) The ASA score was used for this purpose due its simplicity, universal use and evaluation of the individual patient parameters. The patients were selected into five ASA categories (1-5) (sixth category was excluded because it represents a brain dead patient). Comorbidity is defined as presentation of two or more coexisting medical conditions or disease processes that are additional to the initial diagnosis of ABO. Comorbidity conditions included cardiovascular diseases, congestive heart failure, diabetes mellitus, chronic obstructive lung disease, hypertension, renal disease, obesity, liver cirrhosis, preoperative use of chemotherapy and/ or radiation therapy.

After admission, the vital signs and a serial of clinical examinations were measured individually every 3 h and every 6 h, respectively, in all patients to evaluate their symptoms and signs of ABO by the same attending surgical team who performed surgery. All patients underwent plain abdominal X-ray on admission and after 12 h. Abdominal ultrasound (US) was also performed in all patients on admission, while the abdominal computed tomography (CT) scan was performed in a portion of the patients based on the clinical judgment of the attending surgical team.

Following symptoms and sings of ABO indicated laparotomy:

- Clinical diagnosis included symptoms such as abdominal pain, absence of flatus or stool, nausea or vomiting, dehydration, abdominal distension, tachycardia, NGT >500 ml more than 24h.
- Plain abdominal X-rays revealed dilatation of the small bowel and air-fluid levels.
- Abdominal ultrasound (US) showed dilatation of the proximal bowel and free intraperitoneal fluid.
- Computed tomography (CT) scan as a positive sign showed dilatation of the proximal bowel, free intraperitoneal fluid volume of at least 500 ml, mesenteric edema and lack of the ''small bowel feces sign."

Depending upon the intraoperative findings, two surgical approaches were applied to treat patients with ABO: non-resection procedure (non resection procedure GROUP, n=145) and bowel resection procedure (resection procedure GRO-UP, n=127). Non-resection procedures included the following operations: adhesiolysis, simple reposition for hernia incarceration and temporary loop enterostomy or colostomy. In resection group, bowel resection was completed in one of two ways: as temporary intestinal diversion or end-enterostomy, or end-colostomy; either bowel resection with the intestinal anastomosis was applied to restore the continuity of the gut. Resection with primary anastomosis was our procedure of choice in patients with the necrotic bowel. However, in generalized peritonitis in high-risk patients with poor general condition, resection and stoma were the treatment of choice. The extension of the intestinal resection depends on the bowel vitality. The important signs were presence or absence of the mesenteric arterial pulsation, normal motility, and coloration of viable intestine or discoloration of necrotic bowel. When ischemic damage is more spread, an adhesiolysis is sufficient followed by 10-15 minute period of observation to allow for possible improvement in the gross appearance of the involved segment.

The following information was obtained: patient demographics; previous abdominal surgery; comorbidity; ASA score; etiology of obstruction; type of operation; length of postoperative Intensive Care (ICU) and hospital stay; number and type of complications (30 days morbidity rate defined as one or more complications) and death (30 days mortality rate). To define and grade postoperative complications, a classification of complications by Clavien and Dindo was used, based on the type of therapy needed to correct the complication. (10,11) Atelectasis (grade 1) required physiotherapy, while tachyarrhythmia and pneumonia (grade 2) required conservative medicamentous therapy. Simple wound infection (grade 1) was treated by opening of the wound at the bedside. In case of postoperative pelvic abscess formation, percutaneous drainage was performed in hemodynamically stable nonseptic patient. The clinical signs of free anastomotic leakage (grade 3) in the abdominal cavity confirmed by CT scan, as well as dehiscent wound leading to eventration of the small bowel (grade 3), were indications for re-laparotomy and surgical repair. Life-threatening complications (grade 4) including the single organ dysfunction such as Acute Respiratory Distress Syndrome (ARDS) and multiorgan dysfunction (Multiple Organ Dysfunction Syndrome, MODS) required ICU management supported by mechanical ventilation.

Statistical analysis

Data are expressed as mean values with standard deviations or as medians with interquartile ranges. Categorical data are presented by absolute numbers with percentages and analyzed using a chi-square test. For continuous variables, Student's t test or the Mann-Whitney U-test was used. The bivariate relationship between morbidity and mortality and each of the variables that were significant in previous tests were then entered into a stepwise logistic regression procedure. A univariate and multivariate logistic regression was used to assess the model of predictors for outcome. In all tests, p value<0.05 was considered to be statistically significant.

Results

Patient demographic and perioperative characteristics

A total of 272 patients underwent surgery because of ABO, during one-year period. The demographic and perioperative characteristics are shown in **Table 1**.

Fifty-three percent of patients (145) underwent non-resection procedures: adhesiolysis was performed in 65.5% (95), simple reposition for hernia incarceration in 17.9% (26) and 16.6% (n=24) patients had temporary loop enterostomy or colostomy. In resection group, 29.0% (79) patients had temporary intestinal diversion or end enterostomy, or end colostomy, while 17,6% (48) of patients had bowel resection with the intestinal anastomosis.

Fifty-eight percent of patients (159) had no previous laparotomy. Out of 113 (41,5%) patients who had undergone previous abdominal operation, 28 (10.3%) had appendectomies, 27 (9.9%) gynecologic operations, 24 (8.8%) operations of the small or large bowel, 18 (6.6%) cholecystectomy, 18 (6.6%) operations of the small or large bowel, 17 (6.2%) surgery of the stomach, and 16 (5.9%) other interventions (including the operations of the urinary and vascular systems, the liver, spleen and pancreas). There were significantly more previous laparotomies in patients undergoing non-resection surgery (p=0.004).

Characteristics	Non-resection procedure n (145)	Resection procedure n (127)	Total n (272)	р
Age (year)°	64.24±16.52	67.72±14.03	65.86±15.48	p>0.05
Sex	66	55	121	n>0.05
Male*	45.5%	43.3%	44.5%	p=0.03
Previous laparotomy*	72 49.7%	41 32.3%	113 41.5%	p=0.004
Comorbidity conditions*	59 40.7%	53 41.7%	112 41.2%	p>0.05
ASA class 4-5†	43 30.1%	50 40.0%	93 34.7%	p>0.05
Emergency operation within ≤ 12h*	134 93.1%	112 89.6%	246 91.4%	p>0.05
Small bowel obstruction*	110 75.9%	57 44.9%	167 61.40%	p<0.0001
Malignant etiology *	21 14.5%	56 44.1%	77 28.3%	p<0.0001

Table 1. Demographic and perioperative characteristics.

°Values are expressed as mean \pm SD.

*Values are expressed as number of patients and percentage.

⁺*ASA, American Society of Anesthesiologists

There were no significant differences between the 2 groups (resection/non resection) in relation to any comorbid conditions. The coexistence of two or more comorbid conditions was recorded in 34.8% (39) of patients, the most common was the coexistence of heart diseases and diabetes mellitus. Cardiovascular diseases (congestive heart failure, atrial fibrillation, ischemic heart disease) were present in 39.3% (44) of patients, arterial hypertension in 25.0% (28), diabetes mellitus in 15.2% (17), chronic obstructive lung disease in 10.7% (12), preoperative use of other therapies (chemotherapy and radiation therapy) in 3.6% (4), chronic renal disease in 2.7%(3), obesity and hypercholesterolemia in 1.8% (2), and liver cirrhosis in 1.8% (2) of them.

Sixty-one percent of patients (167) had small bowel obstruction and they had significantly more non-resection operations, out of which 75.4% (83) were adhesiolysis (p<0,0001). Adhesions were considered the cause of obstruction in 125 patients (45.9%). The second most common cause of obstruction was a large bowel malignancy, in 73 patients (26.8%), out of which 74.0% (54) were recorded in patients with the bowel resection. There were significant differences between these 2 groups in relation to malignant etiology (p<0.0001). Moreover, adhesions were the most prevalent etiology of obstruction in the small bowel obstruction (n= 117; 90.5%), while neoplasia was the most common etiology in the large bowel obstruction (n= 67; 64%). In 47 (17.3%) patients, the cause of obstruction was an incarceration of the bowel in hernias, dominated by inguinal hernias. Other factors were volvulus in 9 (3.3%) patients, Crohn's disease in 5 (1.84%), retroperitoneal tumors in 4 (1.45%), small bowel tumors in 2 (0.73%), retroperitoneal tumors in 4 (1.45%), radiation injury in 3 (1.10%), foreign body in 3 (1.10%) and one (0.36%) gallstone ileus.

Outcome

The median ICU stay and hospital stay were significantly higher among patients who underwent bowel resection (p=0.001 and p<0.0001) (**Table 2**).

During postoperative period, 72 (26.5%) patients had one complication, while 29 (10,7%) had two or more complications. Respiratory complications were most frequent, developed in 38 (14.3%) patients (atelectasis, pleural effusion, pneumonia, ARDS), followed by cardiovascular complications in 30 (11.0%) (tachyarrhythmia, hart failure, acute

Value	Non-resection procedure n(145)	Resection procedure n(127)	Total n(272)	р
Complication *	50 34.5%	51 40.2%	101 37.1%	p>0.05
ICU length of stay (days)°	0(1)	1 (2)	1 (1)	p=0.001
Hospital length of stay (days)°	6 (2)	7 (2)	6 (3)	p<0.0001
Mortality *	13 9.0%	15 11.8%	28 10.3%	p>0.05

Table 2.	Postoperative	values
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*Values are expressed as number of patients and percentage.

°Values are expressed as median with interquartile range.

myocardial infarction, thrombosis/embolism). Metabolic disorders were manifested in 12 (4,4%) patients, septic complications in 6 (2.2%) and MODS in 4 (1.5%). Superficial wound infection was observed in 17 (6.3%) patients and wound dehiscence in 4 (1.5%). Clinically significant anastomotic leakage was reported in 2 (0.7%) patients. The pelvic abscess formation was diagnosed in one (0.4%) patient Among patients with specific surgery complications, 4(1.4%) required re-laparotomy: the application of secondary sutures of the abdominal wall in 2 cases and surgical repair of the anastomotic leakage in another 2 patients.

Twenty-eight patients died (10.3%). Thirty-day mortality rate was similar for the bowel resection and non-resection groups. Five patients (1.8%)

developed cardiac arrest and died after congestive heart failure. Two deaths (0.7%) occurred in the immediate postoperative period as a result of the acute myocardial infarction. In two (0.7%) patients the cause of death was a massive pulmonary embolism due to deep venous thrombosis. Four patients (1.5%) who developed multi-organ failure in the postoperative period died because of Multiple Organ Dysfunction Syndrome (MODS). Five patients (1.8%) died following the Adult Respiratory Distress Syndrome (ARDS).

Mortality and morbidity risk factors

Risk factors frequency in postoperative complications and mortality are shown in **Table 3.** Significantly highest complication rate was observed in pa-

Variable	No complications (n=171)	With Complications (n=101)	р	Survived patients (n=244)	Deaths (n=28)	р
Age >65	72	95	p<0.0001	141	26	p<0.0001
	42.1%	94.1%		57.8%	92.9%	P
Comorbidity	69	43	p>0.05	87	25	n<0.0001
conditions	40.4%	42.6%		35.7%	89.3%	p<0.0001
Previous	67	46	n>0.05	101	12	m>0.05
laparotomy	39.2%	45.5%	p~0.03	41.4%	42.9%	p>0.05
ASA class	31	62	n~0.0001	68	25	n~0.0001
4-5 †	18.3%	62.6%	p<0.0001	28.3%	89.3%	h~0.0001
Desection	76	51	n>0.05	112	15	m>0.05
Resection	44.4%	50.5%	p~0.03	45.9%	53.6%	p-0.03
Anastomosis	29	19	n>0.05	45	3	m>0.05
Allastolliosis	17.0%	18.8%	p~0.03	18.4%	10.7%	p>0.05
Malignant	45	32	n>0.05	63	14	n=0.007
ethiology	26.3%	31.7%	p-0.03	25.8%	50.0%	p=0.007
Dolonorotomy	0	6	n=0.001	4	2	m>0.05
Relaparotomy	0%	6.3%	p-0.001	1.7%	7.4%	p≥0.03

Table 3. Risk factors frequency in postoperative complications and mortality

†ASA, American Society of Anesthesiologists

tients older than 65 years (p<0.0001). Similarly, the complication rate was higher among patients who had ASA class 4-5 (p<0.0001), and who underwent re-laparotomy during the same hospitalization due to specific surgical complications (p=0.001). Surgery type, previous laparotomy and malignant pathology were not a significant predictor of morbidity.

The death rate was significantly higher among older patients (p<0.0001), in those with comorbidity (p<0.0001), ASA class 4-5 (p<0.0001) and malignant cause of the ABO (p=0.007). Mortality rate did not depend on surgery type, previous laparotomy and re-laparotomy.

Logistic regression analysis was carried out to determine the individual effect of each risk factor of postoperative mortality and morbidity (Table 4). Age over 65 years, ASA class 4-5 and delayed operation for more than 12 hours were associated with the increased 30-day morbidity. The age over 65 years, comorbidity conditions, ASA class 4-5 and malignant etiology were predictive of 30-day mortality in the logistic regression analysis. Surgery type, previous laparotomy and relaparotomy did not influence the risk of complications and the risk of death. For 30-day morbidity, the variables with the highest risk values included age over 65 years and ASA class 4-5. For 30-day mortality, age over 65 years, comorbidity conditions, ASA class 4-5 and malignant etiology of ABO were the variables with the highest risk values.

Discussion

Our study investigated the risk factors that contribute to morbidity and mortality of patients requiring surgery for ABO. Advanced age and ASA score with delayed operation were the risk factors significantly associated with the increased complications rate, while the advanced age and ASA score, comorbidity and malignant etiology were the risk factors significantly associated with the increased death rate.

Acute bowel obstruction is one of the most common causes of emergency surgical admission worldwide, and 20% of admissions due to acute abdominal pain are because of the intestinal obstruction (12,13,14,15) Out of these, approximately 80% have small intestinal obstruction. (14) This study also showed that the majority of patients had small bowel obstruction. The causes of obstruction reported here correspond well with those found in earlier studies.(14,15,16) In this study, the etiology of bowel obstruction is most commonly attributed to adhesions following previous abdominal surgery. Adhesions might occur in more than three-fourths of patients following laparotomy; they are a leading cause of the small intestinal obstruction, developed after the injury of normal peritoneal tissue due to unique inflammatory process of fibrin formation and fibrinolysis. (17) There are no available serum markers or imaging studies considered to be predictive of the incidence, severity or extent of adhesions. Ellis noted that 1% of patients developed small bowel obstruction due to postoperative adhesions within one year of operation. (18) In clinical practice, the type of surgery is discussed as an important factor that influences the development and extent of postoperative adhesions, and the time interval to bowel obstruction seems to be longer after appendectomy and herniorrhaphy than after colorectal and gynecologic procedures. (2) In our study,

Variable	Univariate		Multivariate			
Morbidity risk factors	р	RR	95% C.I.	р	RR	95% C.I.
Age >65	<0,0001	21,771	9,038-52,441	<0,0001	21,257	8,807-51,308
ASA class 4-5†	<0,0001	7,459	4,246-13,105	<0,0001	8,674	4,289-17,543
Delayed operation > 12h	0,002	4,329	1,715-10,932	/	/	/
Mortality risk factors						
Age >65	<0,003	9,496	2,204-40,911	0,007	9,824	1,856-51,985
Comorbidity conditions	<0,0001	15,038	4,414-51,238	<0,0001	21,778	5,494-86,336
ASA class 4-5†	<0,0001	21,078	6,161-72,116	<0,0001	23,326	5,979-91,007
Malignant etiology	0,009	2,873	1,298-6,358	0,022	3,676	1,210-11,165

Table 4. Mortality and morbidity risk factors: Logistic Regression Analysis Results

†ASA, American Society of Anesthesiologists

the appendectomies, cholecystectomies and large bowel resections were more prevalent earlier operations in patients who required adhesiolysis. This is in accordance with the literature data. (12,19)

Large bowel neoplasia and hernias were the next most common causes. A significant number of colorectal malignancies present with the obstruction and large bowel cancer, particularly sigmoid cancer, is the most common etiology of large intestinal obstruction with the prevalence of 40%-90%. (14) Emergency presentations of colorectal cancers are common in the elderly and carry high perioperative mortality risk.

The abdominal hernias continue to account for 8%-25% of all cases of the intestinal obstruction (16,20). Moreover, in a few series, the abdominal hernias represent the most common cause of intestinal obstruction accounting for 30%-55% and still remain the most common cause of the bowel strangulation. (14,20,21) Similar distribution of etiologic factors have been observed in other studies, with smaller contributions from inflammatory bowel diseases, volvulus, radiation injury, foreign body and gallstone ileus. (14)

Appropriate treatment of the acute bowel obstruction is still controversial. It is very important to pay attention and be very cautious in treatment of patients with the acute mechanical bowel obstruction because of the high risk of strangulation and significantly high incidence of bowel ischemia, necrosis, and perforation. (22) It is well known that early recognition of the strangulated obstruction is often life-saving and requires emergency surgery. Numerous studies have shown that bowel strangulation is an independent predictor of complications and delay in surgery treatment is an independent predictive factor of death, with mortality rates 2 to 10 times higher than in those patients with non-strangulated obstruction. (20,23) A total of 272 patients undergoing surgery due to acute mechanical bowel obstruction were analyzed in our study. Ninety one percent (246) of patients were operated within the first 12 hours of admission. Bowel resection with temporary diversion or primary intestinal anastomosis was performed in 46.7% (n=127) and non-resection operation in 53.3% (n=145) of patients. Although ICU and total hospital stay was significantly longer in resection group (p=0.001 and p<0.0001, respectively), the morbidity and mortality rates were similar for the bowel resection and non-resection groups.

A morbidity rate was similar for the bowel resection (40.2%) and non-resection (34,5%) groups and comparable with the literature. (2,6,12) High incidence of cardiopulmonary complications is likely secondary to the patient's age and resulted from complications of the coexisting cardiovascular or respiratory comorbidity. As well known, comorbidity is associated with worse outcomes, more complex clinical management, and increased health care costs (6,7).

Although mortality from the acute bowel obstruction has dramatically fallen by 50% over the past decades, the current literature reports wide variations ranging from 2% to 19%. (2,6,7,12,20,24) Thirty-day mortality rate following surgery in our study was 10.3%, however, it was similar between groups. High mortality rate was most probably recorded due to the fact that our study population consisted of older adults (mean age 65.86±15.48 years) who were more likely to suffer from medical comorbidities. Previous studies have showed that expected mortality rates in elderly patients who underwent emergency operation consistently ranged from 6% to 24%, while expected morbidity rates varied between 40% and 56%.(2) Despite advances in perioperative care, emergency operations due to acute bowel obstruction in elderly patients are still challenging problems for surgeons because of the high morbidity and mortality risk. (2,6,7,13)

Limitation in this study was that patient population consisted predominantly of older adults who generally have multiple comorbidities and higher ASA scores. Nevertheless, our study reflects an annual cross-section of patients with the acute bowel obstruction who required emergency surgery. General increase of human population over 65 years of age has been tripled in the world during the last five decades, and as a consequence, the demand for surgery of older and sicker patients has been growing. (27) However, these patients were more likely to have emergency surgery, which typically results in higher mortality and morbidity. Another limitation of this study is that the data cannot account the impact of non-operative approaches to ABO. The study was designed to collect only data on surgically treated patients and it did not include alternative nonsurgical therapy.

The logistic regression analysis provides information of significant risk factors on 30-day morbidity and mortality measured by the relevant relative risks. The relative risks estimate the increased risk of 30-day morbidity and mortality for each individual preoperative and intraoperative variable. Risk factors of postoperative morbidity included age over 65 years, advancing ASA score and delayed surgery. Several studies have described the association between ASA score and postoperative mortality in elderly patients undergoing emergency gastrointestinal surgery. (25, 26) It is important to emphasize that the type of surgery does not affect the outcome, and more demanding procedures such as bowel resection and primary anastomosis, compared to adhesiolysis, do not increase the morbidity. However, Margenthaler et al. analyzed the outcomes following the surgery for small bowel obstruction and showed that morbidity rate, but not the mortality rate, was significantly higher in patients requiring small bowel resection compared with those requiring adhesiolysis only.(2) The risk factors that clearly influence the observed mortality rate include age over 65 years, comorbidity, advancing ASA classification and malignant etiology of ABO.

Risk factors should be recognized prior to surgery in order to reduce complications and initialize individualized treatment as soon as possible. However, some risk factors such as age and gender can not be obviously modified before surgery. Nevertheless, many of preoperative and intraoperative factors may be altered. Patients who undergo surgery may be at risk for cardiovascular and pulmonary morbidity and mortality, not only intraoperatively but also during their recovery period. This risk applies particularly to those patients with known cardiac or cerebrovascular disease; however, it may also apply to asymptomatic persons who are older than 50 years and have the potential to develop atherosclerotic cardiovascular disease. Learning about risk factors is important to clinicians for preoperative evaluation and supportive care provided to high risk patients undergoing surgery of the acute bowel obstruction.

In conclusion, it was found that the advanced age and ASA score with delayed operation were the risk factors significantly associated with the increased complication rate, while the advanced age and ASA score, comorbidity and malignant etiology were the risk factors significantly associated with the increased death rate. Although older patients are at high risk, they often require emergency surgery. To reduce morbidity and mortality of these patients, it is necessary to insist on timely management of comorbidity conditions and elective operations for clinical entity which are common in this age, such as, elective surgery repair of the abdominal hernia, or early detection and treatment of the colon cancer. Future analysis of risk factors may constitute the basis for designing the treatment strategies and standardization of care to minimize the risk of adverse outcomes following the surgery of the acute bowel obstruction.

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Abbreviations

American Society of Anesthesiologists (ASA); Computed Tomography (CT); Ultrasound (US); Intensive Care Unit (ICU); Acute Respiratory Distress Syndrome (ARDS); Multiple Organ Dysfunction Syndrome (MODS).

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A case of spinal extradural angiolipoma

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Abstract

Angiolipoma is a benign tumor composed of mature adipocytes admixed with vascular elements. This article presents a case of spinal extradural angiolipoma in 52-year-old man, who underwent surgical treatment with preoperational diagnosis of schwannoma. This rare clinical entity must be considered in the differential diagnosis for any spinal epidural lesion.

Key words: Angiolipoma; spinal tumor; extradural lesion, spine, epidural tumor

Introduction

Spinal angiolipomas are rare benign tumors, containing vascular and mature adipose elements. They account for 0.14-1.2% of all spinal axis tumors (1-3). They are usually localized within the thoracic extradural space of the spinal canal and their common clinical presentation is myelopathy, mainly in the way of a slowly progressive paraparesis and sometimes in an acute form (1-3). Two subtypes of spinal angiolipoma exist: non-infiltrating and infiltrating, most cases occur in the extradural compartment, and are of the non-infiltrating subtype (1-3). The infiltrating type of spinal angiolipoma is encapsulated and contains areas with a dominant vascular component. The infiltrating form tends to arise in ventral locations within the thoracic and lumbar portion of the spinal column, and these lesions typically invade vertebral bodies and pedicles (2). In most cases complete removal is possible; however, prognosis is good even for infiltrating lesions (1,3).

Clinical summary

A 52-year-old man presented with a a six-month history of progressive bilateral lower extremity weakness and pain. Magnetic resonance imaging showed posterior extradural mass at the level of T3-T4 vertebrates. The mass was markedly hypointense to fat tissue on T1 weighted images and was slightly hypointense to fat tissue on T2 weighted images (Figure 1). He underwent surgical treatment with preoperational diagnosis of schwannoma and T3-T4 laminectomy was performed, and the extradural tumor was totally excised.



Figure 1. MRI of thoracic spine: T1-weighted (A) and T2-weighted (B) sagittal image without contrast demonstrating extradural lesion at T3–T4 level. T1-weighted axial image showing marked hypointens (C), T2-weighted axial image showing slightly hypointens (D) extradural mass.

Pathological Findings

The yellowish-brown lesion appeared moderately vascular and displayed no evidence of dural invasion. The tumor consisted of a brown hemorrhagic mass measuring 2.5 cm x 1.5 cm x 1 cm. On histological examination, the tumor was shown to be mainly composed of dilated vascular channels by a single layer of unremarkable endothelial cells admixed with capillary channels and of mature adipocytes (Figure 2). Ki-67 proliferation index was found to be 4-5%.



Figure 2. The lesion composed of dilated vascular channels admixed with capillary channels and of mature adipocytes (.H&E; X40) (A). Mix of mature adipocytes and large, branching, blood-filled cavernous vascular channels (H&E; X100) (B, C).

Discussion

Spinal angiolipomas are rare lesions with the first reported case described by Berenbruch in 1890. In 1945, Ehni and Love characterized the pathology of the neoplasm as benign and composed of admixed fat and blood vessels. The histopathological picture is characterized by the presence of two types of tissue: fatty and vascular. The fatty tissue is of the adult type and shows no remarkable findings. The blood channels have been variably described as sinusoids, thin-walled vessels, and thick-walled vessels exhibiting proliferation of the smooth muscle layer many of the vascular channels contained microthrombi1. These lesions are considered a subgroup of lipomas. Spinal angiolipomas differ from spinal lipomas in several ways. The former usually appear in adults, are almost always located in the epidural space, and are not associated with congenital myelovertebral malformations. In contrast, the latter typically arise in childhood and are usually located in epi- and intradural spaces; most are associated with congenital myelovertebral malformations (2).

There is no consensus on the pathogenesis of spinal angiolipoma. Several theories have been proposed on the histogenesis of angiolipomas. Since they harbour features common for both lipomas and hemangiomas, Ehni and Love postulated angiolipomas arise from pluripotential mesenchymal stem cells that undergo differentiation along both adipose and angiod lineages. The ratio of fat to vessels ranges from 1:3 to 2:3. Others consider them to be congenital malformations or benign hamartomas (1,2).

It is concluded that spinal angiolipomas predominantly affect women. Their preponderance in older, peri-, or postmenopausal women, and their clinical exacerbation in pregnant women support a role for hormonal influence (3). Magnetic resonance imaging is the most valuable radiological modality for diagnosing spinal angiolipomas. These tumors are typically hyperintense on non-contrast T1-weighted images owing to their fatty content (2,3). Large hypointense foci observed within spinal angiolipomas on non-contrast T1-weighted images are correlated with increased vascularity. Our patient's lesion appeared hypointense on non-contrast T1-weighted images, and the pathological specimen was indeed mainly composed of dilated vascular channels.

Angiography is another radiological modality that is used to diagnose and treat spinal angiolipomas. When hypointense foci are detected on noncontrast T1-weighted images, angiography can be done to investigate further and embolization can be performed. Embolization of a highly vascularized angiolipoma can facilitate surgical removal².

The treatment of spinal angiolipomas is surgical removal with an excellent prognosis regardless of degree of infiltration. Thus adjutant radiotherapy is not recommended even for subtotal resection. Most tumors are not adherent to the dura enabling gross total removal (1,2). This rare clinical entity must be considered in the differential diagnosis for any spinal epidural lesion including nerve sheath tumor, metastasis, chronic extradural haematoma, lymphoma, and meningioma.

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Cesarean Section in a Patient with Triflusulfuron Poisoning at Term: A Case Report and Review

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Abstract

A 29 year old woman, G9P1, at 38th week of gestation, was admitted to emergency department by nausea and vomiting after a suicide attempt by a herbicide named Arrat containing of Triflusulfuron. There was not any clinical abnormality which can be a finding of herbicide poisoning in mother and fetus. Blood tests and serum cholinesterases of mother were normal. Fetal Non-Stress Test was normal. We have successfully delivered the patient by cesarean section due to absence of the spontaneous labor findings at 4th hour of the herbicide poisoning for shaving the fetus for possible fetal injury. Herbicide poisoning in pregnancy is a rare condition. After stabilization of the mother, management of delivery and removal of the fetus is important decision for the protection of fetus from poisoning.

Key words: Pregnancy, suicide, herbicide, Triflusulfuron, Cesarean, delivery.

Introduction

Main mechanisms of Herbicides are to inhibit or to interrupt normal plant growth and development¹. They are widely used in agriculture, industry and urban areas for weed management¹⁻³. However, improper herbicide use may be associated with unwanted plant and human health risks¹⁻³. In this article we have discussed a patient who has a suicide attempt by triflusulfuron and delivery choices as well as pregnancy outcome.

Case Report

A 29 year old woman, G9P1, at 38th week of gestation, was admitted to emergency department by nausea and vomiting. She had attempted suicide by an herbicide nearby named Arrat containing of triflusulfuron(BASF Türk Kimya San. Ltd. Şti, 34752 İçerenköy-Ataşehir/İstanbul, Turkey) figure1.



Figure 1. The figure shows the herbicide drug, Arrat with Turkish usage guidelines.

She had drunk two cups of tea Triflusulfuron (about 40 mg and 25% containing drug powder) following a profound anxiety attack. She had brought the nearest emergency department after 20 minutes with the drug. In the first emergency department, gastric lavage has been made, active coal was given by nasogastric tube, and hydration and forced diuresis was made after calling of poison control center (PCC). She had been sent to our clinic for further management of the suicide attempt and herbicide poisoning, management of pregnancy and saving the fetus.

In the first examination, she was awake, heart rate was 90 bpm regular and blood pressure was 130/80 mm Hg. Cardiac and pulmonary examination was normal. Laboratory analysis showed normal hemogram levels with white blood count was 12.500 and serum biochemical tests were within normal limits including serum choline esterase. She was in 38th week of gestation according to the last menstrual date and 36th week by ultrasound. Fetal Non-Stress Test (NST) was normal and there was not any significant change by follow-up evaluation. Poison Control Center has advised to terminate the pregnancy within 6 hours. There was not any symptom for birth labor. Because she had a Cesarean section history before, we did not choose the induction of labor. The cesarean section was per-

formed through a low midline incision and a 2.2 kg male infant was delivered 5 minutes after anesthetic induction. The APGAR scores were 8 at 1 min, and 6 at 5 min, and apnea was developed suddenly. Urgent cardiopulmonary resuscitation was started for the severely asphyxia infant for the establishment of satisfactory heart rate and respiration in the delivery room. Massive secretions from the Lung by naso-tracheal tube were aspirated and the fetus was transported to the neonatal intensive care unit. 30 minutes later, general health conditions were normalized and there was not mechanical ventilation need. Serum cholinesterase evaluation of newborn and mother was yielded normal findings. A psychiatry consultation was made and diazepam and sertralin was initiated. Mother and newborn discharged after two days and 30th day follow-up for neurological development and serum test for kidney-liver functions were normal.

Discussion

This article summarizes a suicide by an herbicide containing of Triflusulfuron which was not a common poisoning in daily practice in a pregnant woman. Although the toxicity of Triflusulfuron is low, the amount here is above the vital limits for a human⁴⁻⁷. If she did not tell that she had drunk a Triflusulfuron containing drug Arrat and if the medical aid had delayed she and her baby would be died. Suicide attempt here with Triflusulfuron, an herbicide is an acute poisoning. Herbicide poisoning generally occurs by the ingestion, inhalation, or absorption of a substance intended for use as a weed killer or defoliant¹⁻⁷. Many of them commonly used agricultural herbicides can produce symptoms ranging from skin irritation to hypotension, liver and kidney damage, and coma or convulsions⁶⁻⁷. Estimated fatal doses may be as small as 1-10 g⁶⁻⁷. Some herbicides such as Paraquat contain extremely toxic substances. Poisoning is characterized by dysphagia, burning stomach pain, throat constriction, diarrhea, or other severe symptoms⁵. In our patient, there was not any above mentioned symptoms in mother and fetus. We have thought that was due to successful treatment of poisoning in the first emergency department. Fifth minute's APGAR of fetus was important but, it is difficult to link this event to the poisoning or poisoning.

Triflusulfuron is an herbicide commonly used in Turkey. After oral administration in rats, triflusulfuron-methyl is rapidly absorbed and excreted in urine and faeces6-7. Triflusulfuron-methyl underwent hydroxylation/demethylation of the triazine ring and cleavage of the Sulphonylurea Bridge. Triflusulfuron poisoning may occur in human when used. Short term and chronic toxicity were decribed⁶⁻⁷. Triflusulfuron has a low order of acute toxicity. The rat oral LD is > 5,000 milligrams/ kilogram (mg/kg), the acute rabbit dermal LD50 is > 2,000 mg/kg and the rat inhalation LC50 is > 5.2 mg/L. Triflusulfuron has irritating property to the eye but not to skin. Triflusulfuron is not mutagenic or clastogenic and does not induce unscheduled DNA synthesis. The developmental and teratogenic potential of triflusulfuron was investigated in rats and rabbits. The results indicate that triflusulfuron was maternally toxic in the rat at doses of > 300 mg/kg/day. No evidence of teratogenicity was observed at the HDT in either the rat or rabbit. The sub-chronic toxicity of triflusulfuron was evaluated in the rat and dog at high doses. Triflusulfuron was poorly tolerated in the rat at doses of > 516 mg/kg/day as indicated by increased mortality, decreased body weight gain and kidney damage due to the presence of triflusulfuron-containing calculi present in the urogenital tract. The chronic toxicity of triflusulfuron was investigated in long term studies in the rat, mouse and dog. Target organs included the liver, kidney and blood. NOELs were established at dose levels of 32.1, 1.2, and 129 mg/kg/day, respectively. The mouse is the most sensitive species with a NOEL=1.2 mg/kg/day. The carcinogenicity studies on triflusulfuron showed no evidence of an oncogenic response in either mouse or rat. The chemical is classified in category E. The metabolism of triflusulfuron has been well characterized in standard FIFRA rat, goat and poultry metabolism studies. Parent triflusulfuron accounts for the majority of the excreted dose in these species. Cleavage of the sulfonylurea bridge occurs at a low rate but it is more prevalent in goats and hens than in rats. Hydroxylation of the phenyl ring, which constitutes the major metabolic pathway elucidated in wheat, also was found in the rat. None of the metabolites identified in these studies are considered to be toxicologically different than parent. There is not any serum marker of poisoning. But, liver, kidney functions and arterial blood gas analysis can be advised for suspected patients⁶⁻⁷.

Main limitation of this case is the absence of blood or urine analysis of Triflusulfuron in mother and fetus.

In conclusion, to the best of our knowledge, this is the first case of poisoning by Triflusulfuron in pregnancy. Proper history taking, evaluation and consulting with PCC may be life saving for both mother and fetus. Emergency delivery can be advised if pregnancy was at term of fetal pulmonary maturation was complete.

Acknowledgement

Written informed consent of patient was obtained.

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An Iatrogenic Postoperative Complication of Closed Thoracic Drainage - Gastric Perforation: Report of a Case

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Abstract

A 64-year-old male patient was admitted to the hospital with multiple abdominal and pelvic injuries after a car accident. During hospitalization, the patient developed peritonitis symptoms again after unilateral thoracic drainage at sixth intercostal space axillary midline on the left side. The intra-operative examination for peritonitis showed an iatrogenic penetration of the thoracic drainage tube into the gastric cavity, which result in a gastric perforation. For multiple trauma patients, the place of thoracic drainage tube might be more complicated because of abnormal abdominal cavity pressure, thus it is necessary to conduct more preoperative sonography or X ray and intra-operative examination, such as finger-exploration of the pleural, to make more detailed evaluation of the surrounding organs before conventional drainage.

Key words: complication; closed thoracic drainage; gastric perforation

Introduction

With conventional thoracic drainage strategy, severe chest trauma-induced hemorrhage and pneumothorax¹ usually turns out to have good prognosis, and rarely needs any further thoracic surgery². In early stage of chest trauma, the use of the closed thoracic drainage can educe complications like intrathoracic pneumatosis and hematocele, to timely prevent atelectasis and pulmonary complications, such as infection and empyema, and help to observe ongoing bleeding and tension pneumothorax. However, the operation procedures may also cause complications, such as damage of peripheral organs. Here we report one case of an iatrogenic postoperative gastric perforation after a closed thoracic drainage, which was misdiagnosed as empyema.

Case Report

A 64-year-old male patient was injured in car accident. A laparotomy was done immediatedly after he was admitted to the local County hospital, in which an intestinal patch and mesentery patch followed by a peritoneal drainage was conducted. Due to decreased oxygen saturation and bilateral pleural effusion indicated by chest CT, the closed thoracic drainage was separately conducted on the right side of the patient after 3 days and at sixth intercostal space axillary midline on the left side after 4 days. 200ml of yellow slightly turbid, foul liquid had been drained out from left side tube. There was no improvement of oxygenation of the patient while the drainage volume kept increasing, and the suppurative abdominal incision was partial dehisced with yellow-green liquid with foreign odor in the dressing. Then the patient was transferred to our hospital for further treatment with a preliminary diagnosed as "multiple trauma; laparotomy, intestinal patch, mesentery patch and peritoneal drainage; incision infection; left side of multiple rib fractures, bilateral closed thoracic drainage, left empyema". After admission, a series of CT showed "1) The left side of multiple rib fractures; 2) Abdominal postoperative changes including a small amount of intra-abdominal gas, intestinal pneumatosis (Fig1);" Orthostatic abdominal plain film after oral contrast agent and the esophagus and stomach opacification with diatrizoate showed stomach cavity leakage of contrast agent, considering for the formation of fistula. (Fig2). Thus secondary laparotomy was taken. The intra-operative examination showed a penetration of the thoracic drainage tube into the gastric cavity, which result in a gastric perforation. Therefore the diagnosis about left empyema was amended as "iatrogenic gastric perforation induced peritonitis"



Figure 1. A series of CT showed that abdominal postoperative changes including a small amount of intra-abdominal gas, intestinal pneumatosis and a tube near stomach



A)



Figure 2. Orthostatic abdominal plain film after oral contrast agent (A) and the esophagus and stomach opacification with diatrizoate (B) showed an intestinal obstruction and stomach cavity leakage of contrast agent, considering for fistula formation.

Discussion

The incidence of technical complications about closed thoracic drainage was nearly one percent³. The complication of drainage tube indwelling includes: 1) The tube dislocates from the chest cavity, and slips into intercostal space or deep lateral muscle. 2) The drainage tube is inserted into abdominal cavity. (3) The drainage tube is inserted either too deep or too shallow. Even it may be too close to the heart and induce arrhythmia. And great vessels erosion may emerge if the tube is inserted to the top thoracic area^{4,5}, and even traumatic chylothorax in certain case report⁶.

The place of thoracic drainage tube in patients with multiple trauma might be more complicated. A case of traumatic diaphragmatic rupture was reported in which herniated stomach mimicked a tension pneumothorax⁷. If diaphragmatic hernia was suspected, the entrance of tube should be higher than the usual right location, and the tube inserted along upper breast to diaphragma, so as to avoid the damage of intraperitoneal internal organs in chest cavity⁸. In multiple trauma cases, even without hernia, the existence of thoraco-abdominal injuries and a long period of bed-ridden often prone to induce gastrointestinal disorders, especial gastrointestinal flatulence, which could become the predisposing factors for unnecessary damage of internal organs induced by closed thoracic drainage.

The volume and quality of the pleural fluid drainage should be dynamically observed, especially at early stage of closed thoracic drainage. Inadequate drainage, or a deteriorated situation may provide us with information about possible solidified hemothorax or diaphragmatic rupture. Obviously, in this case, the patient was misdiagnosed and delayed for proper treatment. It seems doctors failed to be aware of possible iatrogenic complication at early stage, due to the existence of multiple trauma and intestinal injury in a patch in this case. Thus to abdominal character and thoracic drainage fluids traits should be paid attention, and the puncture site should be secondarily confirmed timely.

In summary, for multiple trauma patients, it is necessary to carry out more preoperative sonography or X ray and intra-operative examination, such as finger-exploration of the pleural, to make clear the situation of the surrounding organs and needle positioning before conventional preoperative drainage. Moreover, the alteration of pleural effusion and thoraco-abdominal signs need close observation after puncture.

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Gemcitabine-Cisplatin Induced Acute Pancreatitis: a Case Report

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Abstract

Background: Many drugs can cause acute pancreatitis, also this phenomenon rarely with chemotherapeutic compounds. Several reports of pancreatitis following the use of chemotherapy drugs but pancreatitis has not been reported with gemcitabine and cisplatin

Case: A 68-year-old female diagnosed bone metastatic lung cancer. She was started on chemotherapy with a regimen of gemcitabine and cisplatin (GC). On second day of the 1st dose of GC, patient was admitted to the hospital and subsequent workup revealed acute pancreatitis.

Conclusions: This is the first case report of acute pancreatitis caused by gemcitabine-cisplatin regimen. When a patient experience prolonged nausea and vomiting follwed to the chemothreapy regimen, acute pancreatitis come to mind to prevent fatal complications.

Introduction

Gemcitabine and cisplatin is an active regimen for the treatment of metastatic non-small-cell lung cancer. Its toxic effects are well described, but pancreatitis has not been reported in this regimen. We presented a case in which gemcitabine and cisplatin appears to have caused acute pancreatitis. Many drugs can cause acute pancreatitis, but this phenomenon rarely with chemotherapeutic compounds. Several reports of pancreatitis following the use of chemotherapy drugs, but exact etiology of the causative drug is difficult because many patients will receive concomittant drugs such as steroids and 5-hydroxytryptamine-3 receptor (5-HT₃) antagonists that have been implicated in this complication. Exclusion of the primary disease process as causes can bedifficult in some cases because pancreatic metastases can also cause pancreatitis(1). Drug-induced pancreatitis is not common and overall incidence ranges from 0.1 to 2% of pancreatitis cases (2). Drug-induced pancreatitis is usually a diagnosis of exclusion. Chemotherapeutic agents have been known to be associated with acute pancreatitis. However, gemcitabine and cisplatin associated acute pancreatitis has never been reported.

Case report

A 68-year-old female diagnosed bone metastatic lung cancer on july 2010. A PET /CT scan revealed that primary lesion on upper lobe of right lung and multiple bone metastases. Histopathology examination of biopsies revealed adenocarcinoma of lung. She was started on chemotherapy with a regimen of gemcitabine and cisplatin (GC). Cisplatin (CDDP) 100 mg/m2 iv day 1. Gemcitabine (Gemzar) 1000 mg/2 iv days 1, 8, 15 was planned every 28 days. On second day of the 1st dose of GC, patient had begun to complain of nausea, vomiting, and abdominal pain. The patient was admitted to the hospital and subsequent workup revealed acute pancreatitis with an amylase of 2529 U/L, lipase of 7964 U/L with normal levels of serum trygliserid, calcium and bilirubin. There was no evidence infection such as fever, cough or leukocytosis. Endoscopic ultrasound didn't reveal a galldbladder stone and biliary duct dilatation of the patient. The patient was placed on nil per os (NPO) and treated with intravenous fluids. The patient also required total parenteral nutrition for 3 days. She recovered with normalization of amylase and lipase within 5 days (20 vs 25 U/L respectively). Follow-up CT scan didn't show any abnormality of pancreas for following complications. Patients didn't have abnormal lipid profile, alcohol compsuption, diabetes mellitus, smoking or on treatment any other disease. GC treatment was interrupted immediately and docetaxel for 6 cycles and then Pemetrexete for 6 cycles were given to the patients. No abnormalities of pancreas enzymes were detected during the other regimens.

Discussion

Our patient was started on chemotherapy consisting of gemcitabine and cisplatin. This particular regimen was based on the lung cancer and also GC regimen showed a significant improvement in disease-free survival (DFS) and overall survival (OS) (3). It is well tolerated regimen however; acute pancreatitis associated with this regimen has never been previously reported in a patient with lung cancer.

Acute pancreatitis is an emergency characterized by abdominal pain, nausea, and severe vomiting, with elevated serum amylase and or lipase usually three times the upper limit of normal (4). Our patient had elevated serum amylase and lipase over 20 times. The pathogenesis is related to involve enzymatic autodigestion of the pancreas. Gallstones and alcohol comsumption have account for over 80% of cases. Hypertriglyceridemia, hypercalcemia, drugs, and infection are rarer causes. Drugs have only up to 2% of cases (4,5). Acute pancreatitis has been associated with paclitaxel, ifosfamide, vinorelbine, cisplatin, cytarabine, tretinoin, and L-asparginase (6). L-Asparaginase is associated with acute pancreatitis with an incidence of between 2 and 18%. Cytarabine and cisplatin associated acute pancreatitis is well documented in the literature (3). Kumar et al. have reported paclitaxel associated acute pancreatitis (7). The mechanisms behind pancreatitis secondary to these chemotherapeutics are unknown (3). It is possible that there might be a direct noxious effect secondary to the accumulation of toxic metabolites of these drugs in pancreatic tissue (3). Our patient developed signs of acute pancreatitis after several hours of chemotherapy and resolved in a few days (4-5 days) like the other acute pancreatitis related to the chemoteropatic agents. In conclusion this is the first case report of acute pancreatitis caused by gemcitabine-cisplatin regimen. When a patient experience prolonged nausea and vomiting follwed to the chemothreapy regimen, acute pancreatitis come to mind to prevent fatal complications.

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Socio-demographic and clinical characteristics of persons who had commited a suicide attempt

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Abstract

Introduction: The suicide attempt is a risk factor for completed suicide. The majority of those who commit suicide have made previous attemps. The greatest risk for suicide is the presence of psychiatric disorder.

Aims: The aim of this study was to describe socio-demographic and clinical characteristics of persons who had commited a suicide attempt.

Materials and methods: A retrospective study was conducted in the period from January 2000 to the July 2007 and as a source of data we used medical records. The study included 105 persons who had committed suicide attempt and who were hospitalized at the Department of Psychiatry of Clinical Center University of Sarajevo. We analyzed sociodemographic variables such as: gender, age, occupation, place of residence and clinical variables: the diagnosis, symptoms, the length of stay in hospital, the method of suicide attempts, the number of suicide attempts before the last one and the heredity.

Results: Out of a total number of examinees (n=105), 61/105 (58.1%) were females and 44/105 (41.9%) were males. The highest number of suicide attempts were in males between 30-49 years of age (21/44 or 48.8%) and in females between 40-59 years of age (32/61 or 53.3%). There was statistically significant difference in the frequency of suicide attempts between seasons spring/summer/autumn/winter (36.9% vs. 27.2% vs. 17.5% vs. 18.4%) $(\chi^2(3)=10.126; P=0.017)$. Based on a persons' occupation, the most frequent ones were retired persons 22/105 (22.9%). The most common diagnosis according to International Statistical Classification of Diseases and Related Health Problems ICD-10 was F20-F29 (36/105 or 34.3%). In females, the median of hospitalization time was 28.0 days (IQR=42.0), and 23.5 days (IQR=40) in males (Z=-296, P=0.767).

Conclusion: Clinicians must recognize the risk factors for suicide. Intervention on a person's suicide attempt is imminent.

Key words: suicide attempt, socio-demographic and clinical characteristics

Introduction

A suicide attempt is a risk factor for a completed suicide. The absolute risk in humans followedup for 5-37 years was 7-13% (1,2,3,4,5,6) roughly corresponding with 30-40 times increased suicide death risk in those who had attempted suicide compared with the general population (7). Suicide is the third leading cause of death for adolescents and young adults from 15-24 years. Many mental disorders (such as a schizophrenia or depression) begin or worsen during these ages which all contributes to this statistics. Therefore, individuals with schizophrenia, schizoaffective disorder, depression, alcohol and drug abusers, personality disorders are at a high risk for suicidal behaviour (20% to 40% make suicide attempts) (8,9,10). Some of them have dual diagnoses (mental illness and a supstance abuse disoder). Sometimes adolescence age alone is enought for some teens to attempt suicide. Older man are more likely to use lethal methods. Older individuals, generally, make fewer suicide attempts compared to completed suicide than other age groups. The majority of those who commit suicide have made previous attemps. Attempted suicides result in emergency room visits and are tipically ,,conted" in studies, but researches really don't know how many other people attempt suicide and do not end up in the hospital. It is unclear whether number of respondents is entirely reliable in national statistics concerning numbers of suicide attempts. The rates of suicide attempts do not differ between males and females. The majority of individuals attempt suicide in the first 10 years of their illness. The risk is higher when following acute psychotic episodes and during the first 6 months after hospitalization. Major depression and substance abuse may be related to suicide attempts in schizophrenia. Current depression, feelings of hopelessness, and drug abuse are repeatedly identified risk factors (11, 12, 13).

Suicide risk assessment should be distinguished between an acute and a chronic risk: the acute risk might be raised by recent changes in circumstances of a person's mental state, while the chronic risk is determined by a diagnosis of a mental illness, social and demographic factors. Bryan and Rudd suggest a model in which a risk is categorized into one of four categories: Baseline, Acute, Chronic high risk, and Chronic high risk with acute exacerbation. Risk levels can also be described as Nonexistent, Mild, Moderate, Severe, or Extreme, and the clinical response can be determined accordingly (14).

The greatest risk for suicides is in the presence of a psychiatric disorder. The mental disorders associated with suicide are the mood disorders (depression and bipolar disorders), schizophrenia, borderline and personality disorder, alcoholismus and drug abuse. Mood disorders are the most common psychiatric disorders associated with suicide. In general population' studies, 30% to 64% of persons who commit suicide have primary depressive disorders.

Materials and methods

A retrospective study was conducted in the period from January 2000 to the July 2007 and as a source of data we used medical records. The study included 105 persons who had committed suicide attempt and who were hospitalized at the Department of Psychiatry of Clinical Center University of Sarajevo. We analyzed socio-demographic variables such as: gender, age, occupation, place of residence and clinical variables: the diagnosis, symptoms, the length of stay in hospital, the method of suicide attempts, the number of suicide attempts before the last one and the heredity.

We calculated the specific incidence rate according to the formulas: the number of new suicide attempt cases that occurred during a specified period of time/the total number of psychiatric patients hospitalized during that period of time x 1,000. The Kolmogorov–Smirnov statistic test with a Lilliefors significance level was used for testing normality. Results are expressed as median and interquartile range (IQR) in case of continuous non-normal distributed variables. In case of categorical variables, counts and percentages were reported. Statistical analysis comparing two groups was performed with Mann-Whitney U-test for non-normal distributed continuous variables, and Chi-Square or Fisher's Exact Test for categorical variables. A P-value <0.05 was considered as significant. Statistical analysis was performed by using the Statistical Package for the Social Sciences (SPSS Release 19.0; SPSS Inc., Chicago, Illinois, United States of America) software.

Results

Out of a total number of examinees (n=105), 61/105 (58.1%) were females and 44/105 (41.9%) were males. The median age for females was 45.0 (IQR=18.5), and 40.0 years (IQR=25.0) for males. There was a statistically significant difference between age groups <20 years, 20-39, 40-59 and \geq 60 years (4.9% vs. 38.8% vs. 42.7% vs. 13.7%), (χ^2 (3)=42.903; P<0.001). The highest number of suicide attempts were in males between 30-49 years of age (21/44 or 48.8%) and in females between 40-59 years of age (32/61 or 53.3%). There was a statistically significant difference in age distribution between females and males (χ^2 =42.903; P=0.02) (Fig. 1).



Figure 1. The frequency of suicide attempts according to gender and age distribution (n=105), Department of Psychiatry of Clinical Center University of Sarajevo, January 2000 – July 2007.

Based on a persons' occupation, the most frequent ones were retired persons 22/105 (22.9%), followed by, unemployed persons 17/105 (16.2%), housewifes 10/105 (9.5%), merchants 9/105 (8.6%), workers 7/105 (6.7%), trade workers 6/105 (5.7%), teachers 5/105 (4.8%), officials 5/105 (4.8%), students 4/105 (3.8%), technicians 4/105 (3.8%), military and police's officers 4/105 (3.8%), lawyers

and economists 3/105 (2.9%), health-care workers 3/105 (2.9%), guesthouse workers 2/105 (1.9%) and others 2/105 (1.9%). The majority of patients were admitted from Canton Sarajevo (92/105 or 87.6%), followed by, Srednjo-bosanski Canton and Zenicko-dobojski Canton (4/105 or 3.8%), respectively, followed by the Entity RS (2/105 or 1.9%), Bosansko-podrinjski Canton and Hercegovacko-neretvanski Canton (1/105 or 1.0%), respectively and from other countries (1/105 or 1.0%).

In females, the median of length of stay in hospital was 28.0 days (IQR=42.0), and 23.5 days (IQR=40) in males. There was not statistically significant difference in length of stay in hospital between males and females (Z=-296, P=0.767) (Table1).

There was statistically significant difference in the frequency of suicide attempts between seasons spring/summer/autumn/winter (36.9% vs. 27.2% vs.



Figure 2. The frequency of suicide attempts according to seasons (n=103), Department of Psychiatry of Clinical Center University of Sarajevo, January 2000 – July 2007.

In females, the methods of intoxication with medication was the most common used method of suicide attempt (32/61 or 52.5%), followed by hanging and drowning (15/61 or 24.6%), internal use of corrosives agents (6/61 or 9.8%), stabling or cutting oneself (5/61 or 8.2%) and jumping from height (3/61 or 4.9%). In males, the method of intoxication with medication was the most common used method of a suicide attempt (15/44 or 34.1%),

also, followed by stabling or cutting oneself (14/44 or 31.8%), internal use of corrosives agents (7/44 or 15.9%), hanging and drowning (6/44 or 13.6%), and jumping from height (2/44 or 4.5%). There was a statistically significant difference in a suicide attempt used method between males and females (χ^2 (4)=12.111; P=0.013) (Fig.4).



Figure 3. The specific incidence rate of suicide attempts according to gender (n=103), Department of Psychiatry of Clinical Center University of Sarajevo, January 2000 – July 2007.

The most common diagnosis according to International Statistical Classification of Diseases and Related Health Problems ICD-10 was F20-F29 (36/105 or 34.3%), followed by, F30-F39 (26/105 or 24.8%), F00-F09 (12/105 or 11.4%), F60-F69 (9/105 or 8.6%), X60-X84 (9/105 or 8.6%), F40-F49 (7/105 or 6.7%), F10-F19 (3/105 or 2.9%), and F50-F59, F90-F98, X85-Y09 (1/105 or 1.0%) respectively. Predominant symptoms were: hallucinations (31.0%), suicidal thoughts (24.1%), imperative hallucinations (7.8%), delusions and anxiety (6.9%) respectively, deppressive mood (5.2%), paranoid thoughts and conflict behaviors (3.4%) respectively, homocidal ideas and aggressiveness (2.6%) respectively, tension and unusual thought contents (1.7%) respectively, "baby blues", fear and jealousy (0.9%) respectively.

The heredity of suicidal behavior was determined in females 18/61 (29.5%) and in males 12/44 (27.3%). There was not statistically signif-

Table 1. Comparison of length of stay in hospital by gender

Gender	N	Median	IQR	Min.	Max.	P-value
Female	61	28.0	42.0	1	122	0.767
Male	44	23.5	40.0	1	130	0.707
icant difference in the frequency of the heredity of suicidal behavior between males and females ($\chi^2(1)=0.063$; P=0.802)



Figure 4. The frequency of a suicide attempt used method according to gender (n=105), Department of Psychiatry of Clinical Center University of Sarajevo, January 2000 – July 2007.



Figure 5. The number of suicide attempts before last one according to gender, Department of Psychiatry of Clinical Center University of Sarajevo, January 2000 – July 2007.

The majority of females (32/61 or 52.5%) had not commited suicide attempts before last one, 15/61 (24.6%) made two, 10/61 (16.4%) made one, and 4/61 (6.6%) made three suicide attempts before last one. Two thirds of males (29/44 or 65.9%) had not commited suicide attempts before last one, 6 (13.6%) made one or two suicide attempts, respectively, and 3/44 (6.8%) made three suicide attempts. There was not statistically significant difference in multiple suicide attempts before last one between males and females (Fisher's exact test=2.479; P=0.507) (Fig. 5)

Discussion

A 2008. review of 56 countries based on WHO mortality data, found that hanging was the most common method in most of the countries accounting 53% of the male suicide and 39% of the female suicide (15). Worldwide, 30% of suicides result from pesticides. Other methods of suicide include blunt force trauma (jumping from a building or bridge), self-defenestrating, stepping in front of a train, or car collision,

Women are more likely then men to attempt suicide. In our study 58.1% of the female and 41.9% of the male attempted suicide.

Investigations showed that women, in terms of a suicide attempt method, tend to an overdose or cutting their wrists. In our study, the method of intoxication with medication was the most commonly used suicide attempt method in females (52.5%), followed by, hanging and drowning (24.6%), internal use of corrosives agents (9.8%), stabling or cutting oneself (8.2%) and jumping from height (4.9%). In males, the method of intoxication with medication was the most commonly used suicide attempt method (34.1%), also, followed by, sharp object stabling or cutting oneself (31.8%), internal use of corrosives agents (15.9%), hanging and drowning (13.6%) and jumping from height (4.5%).

In the study Harkavy-Friedman et al., 33% of the study group reported at least one suicide attempt, 60% of those who had attempted suicide reported multiple attempts, 52% of those who had attempted suicide made attempts of moderate to extreme lethality and 37% reported a strong suicidal intent. The most severe suicidal attempts included overdosing (42%), slitting wrists (16%), jumping (8%), hanging (6%), and other methods (i.e., stabling oneself 18%) (16).

The presence of psychotic symptoms is an important risk factor for suicidal behavior. Some patients with psychosis may have persecutory delusions from which they may wish to escape, or they may experience command hallucinations telling them to kill themselves.

Most suicide occurs in the spring time. Our study showed statistically significant data about suicide attempts in spring time (36.9%). A current mental status is the most important in the assessment of every patient with suicidal potential. Specific attention should be given to thought content, mood, affect, and factors that may lead to impulsive behavior.

In our study the most common diagnosis were F20-F29 (34.3%) and F30-F39 (24.8%); the most common symptoms were: hallucinations (31.0%), suicidal thoughts (24.1%), and imperative hallucinations (7.8%). Impulsive behavior is often seen in psychiatric disorders, particularly in bipolar disorder, some personality disorder, and substance use disorder. Impulsive behavior increases the risk for a suicide, and it is especially dangerous when combined with substance abuse or alcohol. In our study we determined conflict behaviors (3.4%), homocidal ideas and aggressiveness (2.6%), respectively.

In our study, somatic diagnoses were present in 11.4% of cases. Patients with medical cause for a mood or psychotic disorder may be at increased risk for self-harm.

Conclusion

Clinicians must recognize the risk factors for suicide. Intervention on a person's suicide attempt is imminent. The evaluation of suicide risk must involve a careful patient history view, including present psychiatric or medical condition, prior suicide attempts, as well as family and social histories. Probably more attention needs to be focused to the importance of gender in assessment of suicide risk and treatment of suicide attempters. The greatest risk factor for suicide is the presence of a psychiatric disorder. Management of patients with risk of suicide might include cognitive therapy aimed at reducing hopelessness. Psychiatric management includes establishing and maintaining a therapeutic alliance, monitoring the patient's safety, psychiatric status and level of functioning. Therefore, in many instances, suicide can be prevented.

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The fractional concentracion of exaled nitric oxide in controlling children's asthma

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Abstract

In last few years, increased incidence of asthma in pediatric patients caused appearing of new trends in diagnostics, treatment and controlling asthma. In accordance to updated GINA guidelines in 2011 asthma is classificated to controlled, partly controlled and uncontrolled.

Aim of study: Show the position and role of ciclesonide – inhaled corticosteroid in asthma control and eosinophilic inflammation of airway in which we used level (fractional concentracion) of exhaled nitric oxide (FENO) as a marker of eosinophilic inflammation.

In retrospective - prospective study we assigned 44 patients with asthma 12 to 17 years old who had been receiving treatment with ciclesonide and who had been controlled in Pulmonary counsel of Pediatric Clinic in second half of the 2008.

Each patient had received ciclesonide for 5 months and we determined level of asthma control in accordance to the updated GINA guidelines 2011 and level of exhaled NO as marker of eosinofilic inflammation before end after treatment with ciclesonide for each patient. In this study we excluded patient with infection airway, complicated asthma and patient with weight more then 95 percentiles because of unreproducibly results of FENO. Thirty six of 44 patients received inhaled corticosterois - ciclesonide as monotherapy (88,82%). Before the treatment 5 of 44 patients (11,36%) had uncontrolled asthma, 36/44 (81,82)had partly controlled asthma and 3/44 (6,82%) had controlled asthma. After 5 months of treatment by ciclesonide 34/44 (77,27%) had controlled asthma, 10/44 (22,73%) had partly controlled asthma, mild eosinophilic inflammation (20-25 ppb) was determined in 10/44 patients (22,73%), moderate eosinophilic inflammation (25-50 ppb) was determined in 4/44 (9,09%) and 30/44 (68,18%) had good results of FENO.

Conclusion: After five months of treatment 34/44 (77,27%) patients included in study were moved from uncontrolled and partly controlled to controlled asthma. In the end of treatment 30/44 patients (68,18%) had FENO < 20 ppb.

In this study we reached good controlled asthma and eosinofilic inflammation of airway with ciclesonide – new inhaled corticosteroid and that was confirmed with results of FENO.

Key words: asthma , fractional concentaracion of exaled nitric oxid (FENO)

1. Introduction

Bronchial asthma is defined as an inflammatory airway disease characterized by intermittent obstruction of airway and hyper responsiveness to the pharmacological and physical stimuli. Current concept of pathogenesis of asthma involves chronic inflammatory process that causes the development of limitation air flow in the airways and increased response to allergens. Inflammation of the airways is characterized by an increased number of activated eosinophils, mast cells and T-lymphocytes within the airway mucosa and lumen. Activity of these cells leads to damage of epithelium, swelling, mucous secretion and contraction of smooth musculature of airways. These inflammatory cells and mediators cause symptoms of asthma. Studies have shown persistence of the inverse correlation between the concentration of eosinophils and integrity of the epithelium of airways in persons with atopic asthma, which suggests that inflammation plays an important role in the remodeling of the airways. Chronic inflammation is partly reflected in an increase in the number of eosinophils between mucosa and lumens of airways. To determine the inflammation of airways was introduced non-invasive methods such as determining exhaled nitrogen oxide (NO). NO fraction in expired air (FENO) is a marker of asthma; FENO-magnitude increases in proportion to the inflammation or induced-sputum eosinophils and hypersensitivity of airways. FENO-increase is associated with deterioration of asthma control and level-FENO and decreases depending on the regime find out anti-inflammatory treatment. ^(1,2,3,4)

The goal of asthma therapy is to remove the symptoms of asthma but also reduce inflammation. Inhaled corticosteroids (ICS) as an effective anti-inflammatory drugs are widely represented in the treatment of asthma. Studies have demonstrated that ICS leads to reduction of symptoms and frequency of asthma exacerbation improving lung function. Level of exhaled NO as a hyperreactivity of the airways are sensitive to steroid treatment.⁽¹⁾

Inhaled corticosteroids have a marked effect on exhaled NO in keeping with their anti-inflammatory properties. The response to corticosteroids is both rapid (within 1 week, potentially as early as 48 hours) and dose-dependent. The higher the exhaled NO value, the higher the ICS dose needed to normalize it.

Previous research on the impact ciclesonide to FeNO have shown that treatment with ICS resulting in a significant reduction of exhaled NO-a (47 ppb difference in comparison with placebo). Thanks to these characteristics, ciclesonide a potent inhaled corticosteroid with extended anti-inflammatory effect in the lungs and reduced the number of systemic and local side effects. Ciclesonide can be used in patients with different degrees of severity of asthma. (7)

This study aimed to show the possibilites of ciclesonide as inhalaled corticosteroids in controlling asthma and eosinophilic inflammation of the bronchi, where we used level of exhaled NO (FENO) as a marker of eosinophilic inflammation.^(1,4,5,6)

2. Materials and methods

Retropsektivno-prospective study included 44 patients were aged 12 to 17 years who were treated by ciclesonide or a combination of ciclesonide and oral antileukotrien and controlled through the pulmonary counseling KCUS Pediatric Clinic in the second half of the 2008th year. In group of 44 patients included in the study, 22 were male and 22 female. Criteria for inclusion in the study were patients with a diagnosis of asthma, while the tests excluded patients with respiratory infections,

complicated asthma and physical mass above the 95 percentile because in these cases the results of FENO would be unreproducibility. All subjects at the beginning and end of the five months treatment by ciclesonide determine the degree of asthma control in accordance with the revised GINA guidelines from 2011. and the level and NO in expired air (FENO) as a marker of eosinophilic inflammation. All participants involved in the study were treated by ciclesonide 160 μ g once daily, with that in 36 of 44 respondents included ciclesonide as monotherapy while the other 8 patients with ciclesonide included oral and selective receptor antagonist of leukotrien the strength of 5 or 10 mg once a day.

FENO determination is done on the device "NIOX" produced by Swedish company "Aerocrine." Patients who have used "NIOX" system had to inhaled clean, filtered air, after which they exhaled air in the mouth space which is connected to the computer system using a flexible tube. Patients have repeated this procedure three times, after which are the computer automatically calculated and displayed the mean of all three results. The basic method of determining exhaled NO in the above apparatus is chemiluminiscentia gas analysis with integrated software that uses a highly sensitive and highly specific chemiluminiscentia gas analyzers is the most precise analytical method that is available to determine the NO molecules in very low concentrations. Chemiluminiscentia is a chemical reaction which occurs as a product of light. When a NO molecules react with ozone to oxidize exciting state NO2. Small fraction of molecules in exciting state decays by emitting a photon near infrared spectrum. NO concentration in the sample is proportional to the amount of emitted light. This method is highly sensitive and selective. (7,8,9)

3. Results

In retrospective - prospective study we assigned 44 patients with asthma 12 to 17 years old who had been receiving treatment with ciclesonide. All data were analysed in statistical program SPSS and presented tables and figures.

In Table 1 it is possible to see the number of patients investigated, numbers of male and female, the mean and standard deviation age, height, body weight, FeNO-a, and numbers of the pati-

Parameters	Ciclesonid 160 µg 1 x 1
Number of patients	44
• Sex, male/female	22/22
• Age (years); male/female (X ± SD)	13,05±1,46 / 12,86±1,21
• Height (cm); male/female (X ± SD)	154,55±8,99 / 148,00±10,72
• Mass (kg); male/female (X ± SD)	45,64±6,40 / 52,82±15,62
• FENO before the treatment $(X \pm SD)$	45,94±25,74
FENO < 20 ppb	4
FENO 20-25 ppb	5
FENO 25-50 ppb	25
FENO > 50 ppb	10
Monotherapy/Combi therapy	36 / 8
• FENO after 5 months of treatment $(X \pm SD)$	15,54±6,24
FENO < 20 ppb	30
FENO 20-25 ppb	10
FENO 25-50 ppb	4
FENO > 50 ppb	0

Table 1. The values of parameters in the study group patients suffering from asthma (N = 44)

X - mean

SD - Standard deviation

FENO – forced exaled nitric oxide concentraction (ppb)

ents classified to FENO-values before and after five months treatment by ciclesonide. Before the treatment with ciclesonide the level of FENO < 20 ppb was determined in 4/44 patients (9,09%) - which is good result for this ages according to Taylor et al 2006; mild eosinophilic inflammation (FENO = 20-25 ppb) was determined in 5/44 patients (11,36%); moderate eosinophilic inflammation (FENO = 25-50 ppb) was determined in 25/44 patients (56,82%); severe eosinophilic inflammation (FENO > 50 ppb) was determined in 10/44 patients (77,27%). As can be seen in Table 1, the representation of male and female in the study group is identical, in this study included the 22 (50%) patients of both sexes.



Chart 1. Number of patients according to the degree of asthma control before and after 5 month treatment

Chart 1 show the number of those with good controlled, partly controlled and uncontrolled asthma before and after 5 month treatment. Before the treatment 5 of 44 patients (11,36%) had uncontrolled asthma, 36/44 (81,82) had partly controlled asthma and 3/44 (6,82%) had controlled asthma. After 5 months of treatment by ciclesonide 34/44 (77,27%) had controlled asthma, 10/44 (22,73%) had partly controlled asthma.

In Table 2 shows the number of patients with different degree of eosinophilic inflammation of the Taylor DR et al. (2006). Before the treatment three patients had mild eosinophilic inflammation (6.81%), most of them had moderate eosinophilic inflammation (25-50ppb) 27/44 (61.36%) and severe eosinophilic inflammation had 11/44 (25.00%). After 5 month treatment by ciclesonide 7 / 44 patients had moderate eosinophilic inflammation (15.91%), 7 / 44 patients had mild eosinophilic inflammation (15.91%) while the other 30/44 (68.18%) had good level of NO to expire <20ppb.

As shown in Chart 2, mean FENO a significantly reduced from 44.86 ppb, as was before therapy by ciclesonide (1), to 15.54 ppb as measured after 5 months treatment (2).

Eosinophilic inflammation FENO values (ppb)*	Number of patients before the treatment	Percentage (%)	Number of patients after 5 month treatment	Percentage (%)
Without <20	4	9,09	34	77,27
Mild 20-25	5	11,36 %	10	22,73
Moderate 25-50	25	56,82	4	9,09
Severe >50	10	22,73	0	0
Ν	44	100	44	100

Table 2. Patients in relation to the degree of eosinophilic inflammation of bronchial mucous

*Classification by Taylor et al., 2006.



Chart 2. Mean value of FENO changes during treatment of 5 months

4. Discussion

Results of retrospective - prospective studies that have comprised 44 patients diagnosed with asthma aged 12 to 17 years showed a significant influence monotherapy by cicesonide and therapy by combination of ciclesonide and selective and orally active leukotriene receptor antagonist on impairment FENO. Forty four patient were required, 22 of them were men (50%) with mean weigh of 45,64 \pm 6,40 kg (M \pm SD) and 22 of them were women (50%) with mean weigh of $52,82 \pm 15,62$ kg (M \pm SD). Monotherapy was included in 36 of 44 patients (88.82%), other 8 of 44 patients (11.18%) were treated by ciclesonide in combination with oral antileukotrien. As could perceive in shown results of 44 patients 11 (25%) ago beginning treatments by ciclesonide had uncontrolled asthma, 30/44 (68.18%) had partially controlled asthma while 3 / 44 (6.82 %) had well controlled asthma. At the beginning of treatment by ciclesonide, level of FENO (<20ppb) was determined in 3 / 44 patient and it is a good result for this age (Taylor et al. 2006.), mild eosinophilic inflammation (FENO=20-25ppb) had 3 / 44 patients (6.82%), while moderate eosinophilic inflammation (FENO=25-50ppb) had 27/44 patients (61.36%). Severe eosinophilic inflammation (FENO>50ppb) was found in 11/44 patients (25%). After 5 month treatment by ciclesonide, 30/44 (68.18%) had controlled asthma, while 14/44 (31.82%) had partially controlled asthma, mild eosinophilic inflammation (20-25ppb) had only 7/44 patients (15.91%), moderate 7 / 44 (15.91%), while other patients 30/44 (68.18%) had a good level of NO in expired air (FENO <20ppb).

After 5 month of treatment of asthma in this group of patients 27 of 44 have been translated from uncontrolled or partially controlled in the controlled asthma (61.36%). At the end of the treatment 30/44 (68.18%) patients had value of nitric oxide in expired air <20ppb.

The concomitant effect of inhaled steroid on markers of airway inflammation and exhaled NO hes been examined in many studies. The autors concluded that exaled NO might be useful in guiding dose adjustments of inhaled corticosteroids in patients with persistent asthma.(7,8,9)

Many study showed that exaled NO levels were higher in patients in whom asthma control was insufficient and significant impruvment in exaled NO after inhaled and oral anti-inflamatorory therapy (10,11).

5. Conclusion

After five months of corticosteroid treatment 34/44 (77,27%) patients included in study were moved from uncontrolled and partly controlled to controlled asthma. In the end of treatment 30/44 patients (68,18%) had FENO < 20 ppb.

In this study we reached good controlled asthma and eosinofilic inflammation of airway with inhaled corticosteroid and that was confirmed with results of FENO.

Clinical applications of exhaled NO measurement unclude monitoring compliance and response to treatment, disease activity, and the notification of loss of control.

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Sexual Compulsivity, Promiscuity and Phallic Stage of Psychosexual Development Fixation

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Abstract

This research explored the correlation between sexual compulsivity and the phallic stage fixation and promiscuous sexual behavior in the sample N=1711 participants, in young people from Serbia and B&H (19-25 years old). Standard regression analysis showed that the phallic stage fixation was the best predictor of sexual compulsivity (beta=0.347). The entire model explained only around 14% of the total variance, but only two predictors were significant: the phallic stage fixation and anal stage fixation - the former showing a higher beta coefficient (beta=0,347; p<0,001 and beta=0,092; p<0,001, respectively). Man-Whitney U test showed significant difference in the sexual compulsivity level between the fixated (Md=32, n=66) and non-fixated subjects (Md=14, n=1634), U=26785; p=0,000; z=-6,987; r=0,169. Sexually compulsive individuals showed greater proneness to the phallic stage fixation than non compulsives. Additionally, sexually compulsive and phallicstage-fixated individuals were more promiscuous and preferred the sex organs of their sexual partners as desired body parts.

Key words: Sexual compulsivity, phallic stage fixation, promiscuous sexual behavior, psychosexual development

Introduction

Sexual compulsivity presents the phenomenon which was explored in the last three decades predominantly in Western societies and under different terms. In literature, authors simultaneously use terms which determine problematic hypersexual behavior: sexual addiction¹⁻⁴, sexual compulsivity⁵⁻⁷, sexual impulsivity⁸, sexual promiscuity⁹, problematic hypersexuality¹⁰, paraphilia-related disorders¹¹⁻¹³, hypersexual behavior¹⁴, but the most frequently used terms are sexual addiction and sexual compulsivity. In DSM-IV-TR¹⁵ there is no explicitly mentioned hyperactive sexual desire disorder, while in ICD-X some archean terms such as "nymphomania" (if the disorder is related to female population) or "satyriasis" (if the disorder is related to male population), are still in use¹⁶. It is about clinical syndrome which is characterized by loss of control of sexual fantasies, drives and behaviors, intending multiple negative consequences on psychological well-being of an individual, as well as higher levels of distress^{12,17}.

Until now, three models were used to explain uncontrolled or hyperactive sexual behavior: addiction model, obsessive-compulsive disorder model and impulse-control disorder model. Each of the mentioned models was formed to explain etiological mechanisms and efficient treatment, but some significant determinants of models overlapping were also found, which suggests that models are not mutually exclusive¹⁸. The common feature of all models explaining this clinical syndrome is that it intends disinhibited and uncontrolled sexual behavior, which is acted on because of specific emotional states, and such behavior intends negative consequences, disordered everyday functioning and significant clinical distress¹⁰.

A lot of researchers concord that several symptoms of this clinical syndrome intend disregulation of behavior, disordered everyday functioning, maladaptive coping strategies and discordance with the individual's own believes and values¹⁴. There is no universally accepted and clear definition of uncontrolled sexual behavior¹⁹. It is about heterogenic psychological construct which intends preoccupation of sexual desires and behaviors until the degree of disordered social relations, job difficulties and everyday life functioning²⁰, but it intends multiple forms and etiology.

Sexual compulsivity is not a measure of sexual behavior frequency, rather it is a sexual behavi-

or pattern which is initially pleasurable, but with time, it becomes unsatisfying, self-destructive and the individual is not able to stop it any more; he/ she loses control over his/her sexual behavior²¹.

Compulsive sexuality was probably first mentioned in Freud's work at the end of XIX century. He described masturbation as the original, primary addiction, while other addictions such as alcoholism, drug addiction, smoking, gambling and the like, are just a compensation of masturbatory activities²². Traditionally, psychoanalytically oriented theorists consider that all disorders in adulthood could be explained by several fixations and regressions to previous stages of psychosexual development (oral, anal, phallic). The phallic stage, characteristic for preschool period of psychological development was significantly considered as very important issue, since it is a period where sexual identification and oedipal conflict occur. Because of maladaptive strategies in resolution of oedipal situation in preschool period, some discrepancies in later sexual behavior might appear. Freud coined the term "polymorphic perversion", which is characteristic of preschool children, meaning the children in phallic stage of psychosexual development²³. The importance of oedipal conflict in the phallic stage of psychosexual development is reflected through the occurrence of fear and castration in boys²⁴, or penis envy in girls²⁵. Castration anxiety intends a fear that the father will punish oedipal boy because of his masturbatory fantasies by cutting his penis, and penis envy in girls intends blaming a mother for "defect" of not having a penis, when unconscious love toward a father occurs^{22,26-28}. If this oedipal situation is not resolved adequately, fixation to this stage in adulthood could lead to promiscuous sexual behavior^{26,27}. In males, this fixation is manifested by overemphasizing masculinity, wantonness, bragging, ambitiousness, imprudence and the like; in females, this fixation is manifested by seductive sexual behavior, proneness to flirt, increased desires for male partners²⁶, usually older. Many sexual paraphilias (i.e. exhibitionism, voyeurism) are related to castration anxiety which is characteristic of phallic stage of psychosexual development²⁹.

This study aimed to answer the question of whether individuals who show phallic stage fixation are more likely to develop sexual compulsive behavior in adulthood than their non-fixated counterparts. The question which was raised in this study was: Which stage of psychosexual development best predicts and explains the occurrence of sexual behavior? Are sexual promiscuous individuals more likely to develop sexual compulsivity than those who are not sexually promiscuous? The influences of sexual promiscuity and phallic stage of psychosexual development fixation on the sexual compulsivity level were explored.

Two hypotheses of this study were:

- 1. Individuals who show higher levels in phallic stage of psychosexual development fixation are more likely to develop sexual compulsivity, so we hypothesized that the phallic stage of psychosexual development best predicts the sexual compulsivity occurrence in adulthood, comparing to all other psychosexual development stages.
- 2. According to the theoretical consideration that phallic stage of psychosexual development fixated individuals show sexual promiscuous behavior in adulthood, we hypothesized that sexual compulsives would show characteristics not only of phallic stage fixation, but also characteristics of sexually promiscuous behavior.

Method

The study was performed during the spring semester of 2010, on the student sample in Serbia and B&H. The study obtained data of 1711 subjects from Universities in Belgrade and Novi Sad (Serbia), and Universities of Sarajevo and Tuzla (B&H). Fixation to psychosexual development stages was explored by the questionnaire of libido fixations of Ignjatovic et al., named FR-3, sexual compulsivity was explored by Kalichman's Sexual Compulsivity Scale, SCS. Likeliness to sexual promiscuous behavior was determined by Sociosexual Orientaion Inventory, Revised form (SOI-R) subscale of sexual partners. Several sexual preferences were explored by the questionnaire of sexual preferences for males and females, constructed for this study purposes only.

Sexually compulsive individuals, phallic stage fixated and individuals prone to sexual promiscuous behavior were determined according to the principle of two standard deviations above the mean sample score on SCS, FR-3 and SOI-R sexual partners' subscale. Consistency coefficients (Kronbach's alpha) showed that scales had had acceptable internal consistency: 0.943 for SCS; 0.886 for FR-3 questionnaire and 0.814 for a phallic stage fixation subscale; 0.93 for a subscale of sexual partners in SOI-R.

Sexual Compulsivity Scale, SCS³⁰ was developed to assess the tendency toward sexual preoccupation and hypersexuality. Subjects who scored above two standard deviations of mean sample score (which meant cut off score of 32) were classified in sexual compulsives group. Scale consists of ten items scored on four-degree Likert scale. The lowest score is 10 and the highest is 40. Higher scores indicate higher sexual compulsivity levels. Research of psychometric properties of this scale showed acceptable internal consistency, alpha=0.79, as well as acceptable construct and criterion validity¹⁹.

FR-3 libido fixation questionnaire of Ignjatovic et al., was developed to measure different libido fixations at the stages of psychosexual development. It is consisted of 64 items, whose subsets present indicators of fixations to: oral-passive stage, oral-sadistic stage, anal stage, urethral retentiveness with the shame because of enuresis and phallic stage fixation³¹. In all studies in which FR-3 questionnaire was used for determining correlations between libido fixation and dimensions of diverse personality traits systems, significant correlations between measurement spaces were obtained, which indicated empirically based hypotheses of the role of some personality traits in primary cathexes³².

Revised form of Socio-sexual Orientation Inventory, SOI-R³³ is a nine item questionnaire, developed to assess three facets of socio-sexual orientation: previous sexual behavior (number of sexual contacts and sex partners), explicit attitudes toward optional sex and sexual desire for people for whom intimate relationships do not exist. Each facet is explored by three questions with the answers on nine-degree Likert scale. Analyses confirmed that SOI-R was an adequate instrument for individuals of every education and age level (18 do 60 years old),³³ as well as it has good and acceptable internal consistency and test-retest reliability³⁴.

Statistical analysis

The collected data were entered in a specially created database on a personal computer. Statistical analysis was performed using software SPSS, version 12.0. To test hypotheses of the research, standard regression analysis, two-way ANOVA, Kruskal-Wallis, and Man-Whitney U Test were performed, as well as other parametric and nonparametric statistical techniques.

Results

To explore which fixation or fixation to which stage of psychosexual development explains the highest sexual compulsivity variance rate, multiple regression analysis was performed. Independent variables in this case were: total score on the oral-passive stage fixation subscale; total score on the oral-sadistic stage fixation subscale; total score on the anal stage fixation subscale; total score on the urethral-retentive stage fixation subscale and total score on the phallic stage fixation subscale. Since multiple regression analysis requires normal distribution, the transformation of total SCS score was performed by logarithm function log10, diminishing as much as possible the skewness and kurtosis of the results distribution. For multiple regression analysis, as dependent variable was used the new variable of total SCS score, transformed by logarithm function log10.

Table 1 shows that the highest correlation was obtained between the phallic stage of psychosexual development fixation as the independent variable and the total SCS score as the dependent variable (r=0.364). Since there were no independent variables with very high correlations to the dependent variable, all of them were included in further analysis.

Multicolinearity diagnostics did not show significant deviations. The value of Tolerance is not low - it is higher than 0.10, which means that there is no high correlation to other variables, that is – there is no multicolinearity. Values of VIF (variance inflation factor) are not higher than 10, which means that the hypothesis about multicolinearity non-existence was not impaired. Scree plot revealed several atypical points, but with the performance of Mahalanobis's and Cook's distan-

		SCS score	Oral-passive stage	Oral-sadistic stage	Anal stage	Urethral-ret. stage	Phallic stage
	SCS score	1,000	,110	,077	,205	,178	,364
	Oral-passive stage	,110	1,000	,598	,118	,231	,274
Pearson	Oral-sadistic stage	,077	,598	1,000	,229	,304	,307
correlation	Anal stage	,205	,118	,229	1,000	,442	,382
	Urethral-reten. stage	,178	,231	,304	,442	1,000	,479
	Phallic stage	,364	,274	,307	,382	,479	1,000

Table 1. Correlation matrices of independent variables and independent variables and dependent variable

ces, it was concluded that including all those cases in further analysis would not impair final analysis results. Table 2 shows data about model significance, and table 3 shows regression coefficients of variables included in the model.

Table 2. Model significance

Model	R	R squared	R squared corr.	Stand. error
1	,377ª	,142	,139	,16326

a. Predictors: constant, phallic stage, oral-passive stage, anal stage, urethral-retentive stage, oral-sadistic stage. b. Dependent variable: SCS score (log10)

The model was significant on the level p < 0.0005, so the determination coefficient and corrected determination coefficient was r=0.14 r=0.139, respectively, which means that the model (which intends the phallic stage, urethral-retentive stage, anal stage, oral-sadistic stage and oral-passive stage as predictors) explains around 14% of the total sexual compulsivity variance, which is not a very high rate, but it is significant. After including the predictor variables, the model explained around 13.9% of the total variance, but only two predictors of sexual compulsivity were found to be significant: the phallic stage and the anal stage fixation. The phallic stage fixation predictor had a higher beta coefficient (beta=0.347; p<0.001) than the anal stage fixation predictor (beta=0.092, p<0.001).

Phallic stage fixated individuals to be considered as fixated, must have had the score two standard deviations above the mean sample score on the FR-3 subscale. Results showed positive but low correlation (r=0.236) between sexual compulsivity and the phallic stage of psychosexual development fixation.

The mean sexual compulsivity scores are shown in table 4. The table shows that prevalence rate of the phallic stage fixation in present sample was lower than the sexual compulsivity prevalence rate. A total

Table 3. Regression coefficients

Model	Non-st: coeffi	andard. cients	St. coeff.	E	Citra C	95,0% cor	ısist.inter.	C	orrelation	S	Colinea statisti	rity ics
IDDOLA	В	Stand. error	Beta	-	-IIBIC	Lower	Upper	Pearson	Partial	Semi- partial	Tolerance	VIF
Constant	,991	,019		52,500	,000	,954	1,028					
Oral-passive stage	,001	,000	,054	1,906	,057	,000	,002	,110	,046	,043	,630	1,588
Oral-sadistic stage	-,001	,000	-,077	-2,635	,008	-,002	,000	,077	-,064	-,059	,601	1,665
Anal stage	,001	,000	,092	3,571	,000	,001	,002	,205	,087	,080	,758	1,318
Urethral- retentive stage	,000	,001	-,018	-,672	,502	-,001	,001	,178	-,016	-,015	,674	1,484
Phallic stage	,003	,000	,347	12,895	,000	,003	,004	,364	,299	,291	,703	1,423

of 66 subjects (3.88%) were identified as phallic stage fixated individuals. Man-Whitney U test revealed significant difference in sexual compulsivity levels between fixated (Md=32; n=66) and non-fixated individuals (Md=14, n=1634), U=26785; p=0,000; z= -6.987. The mean sexual compulsivity score of the phallic stage fixated (M=26.47; SD=10.997) was significantly higher than the mean score of those who were not identified as phallic stage fixated (M=16,35; SD=7,46).

Table 4. Mean scores on SCS in relation to phallic stage fixation

	SCS	5 scores		
Phallic stage fixation	М	N	SD	Median
Non-fixated	16,35	1634	7,459	14,00
Fixated	26,47	66	10,997	32,00
Total	16,75	1700	7,869	14,00

To determine the influences of two independent variables (the phallic stage fixation and promiscuous behavior) on the dependent variable of total sexual compulsivity score, two-way ANOVA was performed. This statistical technique intended the use of transformed distribution of results by the logarithm function (log10), as it was the case with multiple regression analysis. Promiscuous individuals were those who scored two standard deviations above the mean sample score on the subscale of sex partners on the SOI-R. This research revealed a total number of 113 promiscuous and 1587 non-promiscuous subjects.

Table 5 shows mean scores on the Sexual Compulsivity Scale (after transforming results distribution) in relation to sexual promiscuity and the phallic stage fixation. Promiscuous subjects scored higher on SCS (M=1.47; SD=0.155) than their non-promiscuous counterparts (M=1.165; SD=0.16), and those identified as fixated and promiscuous had higher SCS mean scores (M=1.546; SD=0.123) than those who were promiscuous but not fixated to the phallic stage of psychosexual development (M=1.446; SD=0.157).

Two-way ANOVA (table 6) was performed to explore the influences of sexual promiscuity and the phallic stage fixation of psychosexual development on the sexual compulsivity level. Subjects were divided into two groups according to promiscuity: promiscuous and non-promiscuous; and into two groups according to the phallic stage fixation: fixated and non-fixated. Leven's test showed statistical significance, meaning that the dependent variable variance was not equal in all groups. Interaction between the subscale sex partners score and the phallic stage fixation score was not significant (p=0.598). This intends that there is no significant difference in influence of promiscuous sexual behavior on sexual compulsivity of phallic stage fixated and non-fixated individuals, F(1, 1699)=0.278, p=0.598. However, separate influences of promiscuity and the phallic stage fixation were significant, F (1, 1699)=152.457; p=0.000; F (1, 1699)=25.397; p=0.000; respectively. Those influences are low (partial eta squares 0.082 and 0.015). This means that promiscuous individuals differ from non promiscuous in sexual compulsivity levels, and that phallic stage fixated differ from phallic stage non-fixated in sexual compulsivity levels.

	Dependent variable: SC	CS score (log10)		
Promiscuity	Phallic stage fixation	Μ	SD	Ν
	Non-fixated	1,1614	,15681	1544
Non-promiscuous	Fixated	1,2844	,20238	43
	Total	1,1648	,15939	1587
	Non-fixated	1,4459	,15682	90
Promiscuous	Fixated	1,5456	,12273	23
	Total	1,4661	,15533	113
	Non-fixated	1,1771	,16967	1634
Total	Fixated	1,3754	,21745	66
	Total	1,1848	,17592	1700

Table 5. Descriptive statistics of two-way ANOVA

	Depender	nt variable	e: SCS score (lo	g10)		
Source	Type III sum of squares	Df	M squared	F	Sign.	Partial eta squared
Model corrected	10,396ª	3	3,465	139,330	,000	,198
Intercept	376,643	1	376,643	15143,676	,000	,899
SOI-R sex partners	3,792	1	3,792	152,457	,000	,082
Phallic stage fixation	,632	1	,632	25,397	,000	,015
SOI-R sex partners * Phallic stage fixation	,007	1	,007	,278	,598	,000
Error	42,182	1696	,025			
Total	2438,976	1700				
Total corrected	52,578	1699				

Table 6. Two-way ANOVA: SSK score prediction on the basis of fixation and promiscuity

a. R squared = ,198 (R squared corr. = ,196)

Table 7 shows mean values of total sex partners' numbers in sexual compulsives and sexual non-compulsives. The mean value of sex partners is significantly different in sexual compulsives (M=22.22; SD=49.385) than in sexual non-compulsives (M=2.48; SD=4.746). Man-Whitney U test revealed significant difference between sexual compulsives (Md=9, n=153) and sexual non-com-

Table 7. Number of sexual partners and sexual compulsivity

	Sexual compulsivity	N	Μ	SD	Stand.error
Number of sev pertners	Sexually non-compulsives	1557	2,48	4,746	,120
Number of sex partners	Sexually compulsives	153	22,22	49,385	3,993

Table 8. Sex partner's body part preference in sexual compulsives and sexual non-compulsives

	· · · ·	· · · ·	Sexual con	npulsivity	
			Sexual non- compulsives	Sexual compulsives	Total
	Ling	Frequencies	679	41	720
	Lips	% within sexual compulsivity	43,6%	26,8%	42,1%
	Amus	Frequencies	28	7	35
	Allus	% within sexual compulsivity	1,8%	4,6%	2,0%
	Say argan (ganitala)	Frequencies	275	82	357
	Sex organ (genitals)	% within sexual compulsivity	17,7%	53,6%	20,9%
Desired body part	Breast	Frequencies	45	7	52
		% within sexual compulsivity	2,9%	4,6%	3,0%
	Buttocks	Frequencies	21	4	25
in sex		% within sexual compulsivity	1,3%	2,6%	1,5%
partner	Other body parts	Frequencies	91	5	96
		% within sexual compulsivity	5,8%	3,3%	5,6%
	Nothing	Frequencies	378	1	379
		% within sexual compulsivity	24,3%	,7%	22,2%
	Everything	Frequencies	35	6	41
	Everyuning	% within sexual compulsivity	2,2%	3,9%	2,4%
	Prost and buttooks	Frequencies	4	0	4
	Dieast and buttocks	% within sexual compulsivity	,3%	,0%	,2%
Total		Frequencies	1556	153	1709
10101		% within sexual compulsivity	100,0%	100,0%	100,0%

pulsives (Md=1, n=1557) in mean sex partners' number, U=31091, p=0.000; z= -15.669; r=0.38.

Within the questionnaire about sexual preferences for males and females, participants could select one of the given alternative answers. Among them, one of the given alternatives was a sex organ and others were: lips, anus, breast, buttocks or some other body part (table 8). Results showed that sexual compulsives mostly preferred the sex organ as the most desired body part in their sex partners (53.6%), while sexual non-compulsives mostly preferred lips as a desired body part in their sex partners (43.6%). Sexual non compulsives mostly answered that they are not interested in a specific body part of their sex partners, which was the case in only 0.7% of sexual compulsive cases.

To determine if there were similarities or differences in special body part preferences in sexual compulsives and those phallic stage fixated, chisquare test was performed. Very similar results were obtained, so the phallic stage fixated mostly preferred the sex organ (42.4% of fixated vs. 20% non-fixated) of their sex partners, while the phallic stage non fixated preferred lips as the desired body part of their sex partners (42.8% of non-fixated vs. 28.8% of fixated), χ^2 (8, n=1698) =28.895; p=0.000, phi=0.13. Similar results were obtained in difference analysis between promiscuous and non-promiscuous, where promiscuous individuals more often than non promiscuous preferred the sex organ as the desired body part of their sex partners (56.6% of promiscuous vs. 18.4% of nonpromiscuous), while non-promiscuous preferred the oral zone more than promiscuous (43.5% of non-promiscuous vs. 22.1% of promiscuous), χ^2 (8, n=1709) = 144.005; p=0.000, phi=0.290. Preference of the sex organ as the desired body part in sex partners was shown as common characteristic of sexual compulsives, sexually promiscuous and phallic stage fixated individuals.

Discussion

Multiple regression analysis was performed to analyze contribution of libido fixations in the prediction of sexual compulsivity level as dependent variable. Results showed that independent variables (libido fixations) explain only 14% of total variance, and that the best predictors of sexual compulsivity level were the phallic stage and anal stage fixations. It was hypothesized that sexual compulsivity is correlated to the phallic stage fixation, so further influence of this variable on the total score on sexual compulsivity was explored. Only these two predictors were significant in explaining sexual compulsivity level, but higher percentage rate of total variance was explained by a phallic stage fixation predictor. This result partially confirmed the hypothesis that sexual compulsive behavior could be correlated to the phallic stage of psychosexual development fixation. It could mean that individuals who show sexual compulsivity symptoms would be more likely to have oedipal conflicts, reflected in castration anxiety in males and penis envy in females. Fulgosi²⁶ aims that the characteristics of phallic stage fixated adult men are boastfulness, overemphasizing masculinity, likeliness to frequently change sex partners, as well as the dominance of the genital zone (phallus) in which specific conflicts are present. Sexual compulsive males could have such characteristics, because frequent change of sex partners (promiscuity) intends insecurity in his own sexuality, so they permanently seek new sex partners to fortify their sexual power (but sexual power is actually sexual weakness manifested as external sexual power). However, persistent overemphasizing their masculinity and showing that they could have as many sexual intercourses as they want to, they do not resolve conflicts occurred in preschool (oedipal) stage of (psychosexual) development. It is possible that sexually compulsive men, being fixated to the phallic stage of psychosexual development, develop some kind of pathological relation to their mothers, which could result in insecure attachment styles in adulthood. Zapf, Geiner and Caroll³⁵ revealed that sexual compulsive males were more likely to develop insecure attachment styles than those who are not sexual compulsives. Sexually compulsive men tend to have high anxious and avoiding behaviors in intimate relationships in adulthood³⁵, and sexually compulsive individuals whose demeanor is characterized by sexual promiscuity (not all sexual compulsives are promiscuous), behave in anxious and avoiding ways when they try to form intimate relationships. As they are not able to adequately attach to a close person, their emotional relationships are of short term duration and unstable, and the only close relationship would be the one with their mother. That could be one of the reasons why some young men who are phallic stage fixated seek a mother figure in adult females. However, this only relates to heterosexual males. In phallic stage fixated homosexual males identification inversion occurs, so man identifies with a mother, instead with a father. This could be the case especially when father's love was not adequate, or he (father) was physically or psychologically absent²⁸. This explanation contributes to the fact that homosexual males in this, as in other research, scored significantly higher on sexual compulsivity than their heterosexual counterparts³⁶. Phallic stage fixated heterosexual women are prone to seducing (usually older) men, frequent change of sex partners; they are prone to sexual promiscuous behavior²⁶. Homosexual females are not as prone to develop sexual compulsivity as are their male counterparts, but more research needs to be done about this phenomenon. Sexual compulsive young women have more sexual intercourses than their male counterparts, but the letter tend to have more sexual intercourses than the former³⁷. Sexually compulsive young women have more sexual partners during their adolescent period of life than sexually compulsive young men, but the letter tend to have more sexual partners than the former³⁷.

Phallic stage fixated individuals scored two standard deviations above the mean sample score. The total number of the phallic stage fixated was 66 subjects, which is around 3.8% prevalence rate of the phallic stage fixation in the whole sample. Phallic stage fixated subjects scored significantly higher on sexual compulsivity than their non fixated counterparts. The relation between sexual promiscuity, the phallic stage fixation and sexual compulsivity was explored. The highest sexual compulsivity levels were obtained in the phallic stage fixated who were also sexually promiscuous (they had more than 20 partners in the last year, or they were likely to frequently change sex partners during their life-span). However, no significant influence of promiscuous behavior on the sexual compulsivity of fixated or non-fixated subjects was found. Promiscuous sexual behavior intends greater number of sex partners during the life-span. Sexually compulsives were significantly more likely to have more sex partners (approximately more than 22) than sexually non-compulsives (who tend to have less than three partners during their life-span). Kafka and Hennen¹³ emphasized the importance of protracted promiscuity as a special subcategory of paraphilia related disorders, even frequent change of sex partners is mentioned as one of various "symptoms" of sexually compulsive behavior^{17,38}.

In sexual compulsives who are phallic stage fixated, the dominant erogenous zone would be the zone of genitalia. In this research, the sexually compulsive individuals had mostly preferences toward the sex organ of their sex partner, which was obtained in other research³⁹ of Reece and Dodge who claimed that the sexually compulsive subjects usually reported behaviors primarily focused on their genitals, including solo masturbation, mutual masturbation and oral interaction. The second dominant erogenous zone in this research was the oral zone, so the result of focusing on oral sexual interaction was partially confirmed in this research, too. Probably, in sexually compulsives and/or phallic stage fixated individuals, there is a constant fear of having sexual intercourse, but they try to prove to others that this kind of fear does not exist at all, but this fear is actually castration fear or fear of losing the genitals. In females, there is penis envy, that is the fear of not having the penis, so they constantly seek other sexual experiences, trying to get the penis they were deprived from by their mother²⁶⁻²⁸. Vainly search for a lost father or lost mother could lead to promiscuous behavior and promiscuous behavior could lead to development of sexual compulsivity.

Conclusion

This study revealed some relations of sexual compulsivity to sexual promiscuity and the phallic stage fixation. Results showed significant modest correlation between sexual compulsivity level and the phallic stage fixation. Sexually compulsive individuals are more likely to have a phallic stage fixation than their non-compulsive counterparts. The former are also more likely to develop sexually promiscuous behavior than the letter. Phallic stage fixated and sexually compulsive individuals are more likely to develop promiscuous sexual behavior and they more frequently prefer the sex organ (genitals) as the desired body part of their sexual partner than it is the case with phallic stage nonfixated and sexually non-compulsive individuals. There are two main conclusions of this study:

- 1. Individuals who score higher on the phallic stage fixation, are more likely to develop sexual compulsivity and the phallic stage of psychosexual development best predicts the occurrence of sexual compulsivity in adulthood.
- 2. Sexual compulsive individuals were more likely to exhibit characteristics of the phallic stage fixation and sexual promiscuous behavior, than their non-compulsive counterparts.

However, more research needs to be done on the sex differences in their likeliness to sexual promiscuous or sexual compulsive behavior, as to fixations of phallic stage of psychosexual development in relation to developing sexual compulsivity in adulthood. On the other side, it would be interesting to do the research on the sample of young people who work or did not go to the university to see if there are differences between them and their university college peers.

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Display of antibiotic sensitivity of Staphylococcus epidermidis isolates in the smears of surfaces in a hospital environment

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Abstract

The skin of patients and health workers, medical equipment, clothes of medical staff and other surfaces in hospitals can be the source of resistant strains of S.epidermidis. It is considered that the main risk of infections caused by MRCNS is linked to the complex environment in hospitals. The aim of this work is to show the antibiotic resistance of Staphylococccus epidermidis strains isolated from 36 smeras of surfaces which include smears of hands and uniforms of medical staff as well as smears of beds in the hospital environment of RMC "Dr.Safet Mujić" and to examine the prevalence of MRSE in regards to MSSE. The testing of antibiotic resistance was done using the disk diffusion Bauer-Kirby method on Mueller-Hinton agar, and the sensitivity to penicillin and other beta-lactam antibiotics was determined by the oxacillin screenig test. It is concluded that the MRSE isolates (67%) were prevalent in regards to MSSE isolates (37%).

Key words: MRSE, MSSE, smears of surfaces

Introduction

For *Staphylococcus epidermidis* can be said to live on the border between commensalism and pathogenicity. As such, these organisms have developed an interesting strategy for winning the hospital environment as their new ecological niches. Various external factors that are associated with medical progress, continue to assist the development of this microorganism. Immunocompromised patients for this organism are highly susceptible hosts, as well as medical devices that are suitable habitats for colonization. Bacteria in the hospital environment are under selective pressure from the heavy use of antibiotics and disinfectants, so that resistant strains are very frequent. Multiply resistant strains of coagulase-negative staphylococci frequently colonize hospitalized patients, hospital staff (Archer *et al.*, 1991) and a variety of surfaces in hospitals, which represent potential reservoirs of these bacteria (Aires *et al.* 2000; Hedin, 1993). Many studies showed that the main risk of MRCNS is associated with the complex environment in hospitals (Diekema *et al.*, 2001).

Since S.epidermidis is primary a normal inhabitant of healthy human skin and mucosal microflora, as a commensal bacterium it has a low pathogenicity potential. Indeed, S.epidermidis rarely causes disease in immunocompetent patients. But in recent decades, this organism has become a common cause of many hospital infections (Lim and Webb, 2005). These infections are usually associated with the use of medical devices such as intravascular catheters, pacemaker electrodes, catheters and a variety of other polymeric and metallic implants. Infections caused by Staphylococcus epidermidis usually occur in immunocompromised patients who have long been hospitalized and are critically ill (Ziebuhr, 2001). Increased resistance to antibiotics in nosocomial isolates poses a major problem for the control of hospital infections in general (Goossens, 2005; Laurie and Angeletti, 2003). Because of the ubiquitous distribution of S.epidermidis as a commensal bacteria, it is often difficult to determine whether the isolation of *S.epidermidis* is due to infection or a non-specific contamination. To better understand the hospital infections caused by S.epidermidis it is crucial to know whether the pathogenic strain originates from the hospital environment or outside it, since these strains are significantly different genetically and physiologically.

According to literature *Staphylococcus epidermidis* strains circulating hospitals may be up to 70% resistant to meticillin (Zork *et al.*, 1996). Most of meticillin-resistant strains are also resistant to other antimicrobial drugs (Paulsen *et al.*, 1997). The aim of this paper is to present the antibiotic sensitivity of isolates of *Staphylococcus epidermidis*, which were isolated from 36 smears taken from surfaces in hospital environment and examine the prevalence of MRSE compared to MSSE. These smears include: 24 smears of hands, 6 smears of work clothes of hospital personnel and six smears of hospital beds in the hospital environment RMC "Dr. Safet Mujić."

Material and methods

We analyzed a total of 36 smears of surfaces in the hospital environment which include 24 smears taken from hands of hospital personnel, 6 smears of work clothes and 6 smears of beds. To create the antibiograms for *S.epidermidis* we used following antibiotics from the manufacturer Liofilchem: penicillin, ampicillin, amoxicillin / clavulanic acid, oksacillin, cefoxitin, erithromycin, azitromycin, bactrim (co-trimoxasole, trimethroprim and sulph a metoxazol), clindamycin, gentamicin (garamycin) and vankomycin.

S.epidermidis isolates were identified based on colony morphology and other characteristics of the growth me d ium (blood agar and mannitol salt), gram stain, catalase and coagulase test (coagulation of the plate and tube). In some cases the Api-Staph identific a tion system was used according to the manufacturer's instructions (Biomerieux).

To creat e the antibiograms the preparation of bacterial suspension was made with a sterile physiological solution and a final bacterial concentration was adjusted by comparing with 0.5 McFarland standard. *S.epidermidis* isolates, taken from smears of surfaces in the hospital environment, were tested for selected antibiotics using disc diffusion Kirby-Bauer method on Mueller-Hinton agar. Sensitivity to penicillin and other beta-lactams was determined by the oxacillin-screening test.

Kirby-Bauer method is a standardized system that takes into account all the variables. The recommended medium is Mueller-Hinton II agar, which has a pH value between 7.2 and 7.4 Inoculation of the medium surface with a suspension of bacteria was performed with a sterile swab. Discs with antibiotics were placed on the agar surface with sterile tweezers. After 16 to 18 hours of incubation at 37 $^{\circ}$ C the measuring of diameter of the zone of inhibition of bacterial growth was carried out around the discs with antibiotics. The measured values were presented in millimeters.

Results

We analyzed 36 isolates of *Staphylococcus epidermidis* that were isolated from smears of hands, work clothes of hospital staff and hospital beds. According to the oxacillin screening test 12 isolates (33%) were meticillin sensitive (MSSE), while 24 isolates (67%) were meticillin resistant MRSE (Fig. 1).



Figure 1. Percentage of MSSE and MRSE

Analysis of antibiotic susceptibility of isolates of *S.epidermidis* from smears taken from work clothes showed that all isolates were meticillin resistant (100%). Analysis of antibiotic susceptibility of *Staphylococcus epidermidis* isolates from hand smears showed that 15 isolates were resistant to meticillin (62.5%), while 9 isolates were meticillin sensitive (37.5%). Analysis of antibiotic susceptibility of isolates of *Staphylococcus epidermidis* from bed smears showed an equal proportion of meticillin resistant (50%) and meticillin-sensitive isolates (50%) (Table 1).

× 1			1		
Smears	R	%	S	%	Total
Work clothes	6	100	0	0	6
Hands	15	62,5	9	37,5	24
Beds	3	50	3	50	6
Total	24	-	12	-	36

Table 1. Meticillin sensitivity of isolates of Staphylococcus epidermidis by samples

For isolates of *Staphylococcus epidermidis* we determined the following percentages of resistance: for penicillin and ampicillin 100%, amoxicillin / clavulanic acid and oxacillin 66.66%, cefoxitin and eritromycin 50%, azithromycin 41.66%, clindamicin 8.33%, trimethroprim-sulphametoxazol and garamycin 58.33% and for vankomycin 0% (Table 2). *Table 2. Display of antibiotic sensitivity of isolates of S.epidermidis isolated from smeras of surfaces in a hospital environment*

Antibiotic	R	R%	Ι	I%	S	S%
Р	36	100%	0	0%	0	0%
Amp	36	100%	0	0%	0	0%
Amc	24	66,66%	0	0%	12	33,33%
Ox	24	66,66%	0	0%	12	33,33%
Fox	18	50%	0	0%	18	50%
Er	18	50%	6	16,66%	12	33,33%
Az	15	41,66%	9	25%	12	33,33%
Cc	3	8,33%	3	8,33%	30	83,33%
TSH	21	58,33%	0	0%	15	41,66%
Ga	21	58,33%	0	0%	15	41,66%
Va	0	0%	0	0%	36	100%



Picture 1. The submitted samples: Smear of hands of hospital personnel, smear of hospital beds, smear of work clothes. Isolated: MRSE (668, 669, 673) and MSSE (679)

Discussion

Within coagulase-negative staphylococci from human samples 18 species were isolated, and only 7 of them was repeatedly associated with nosocomial infections. Among them *Staphylococcus epidermidis* is the most common cause of hospital infections. The skin of patients and health workers, medical equipment, clothes for hospital staff and a variety of surfaces in hospitals can be a source of resistant strains of *Staphylococcus epidermidis* (Aires *et al.* 2000; Hedin, 1996). To better understand the hospital infections caused by *S.epidermidis* it is crucial to know whether the pathogenic strain originates from the hospital environment or outside it, since these strains are significantly different genetically and physiologically.

The incidence of meticillin resistance varies depending on the origin of the population of coagulase-negative staphylococci. Resistance to meticillin typically ranges from 75% -80% in nosocomial infections caused by CNS isolates and infections that occur in the intensive care unit (Li *et al.*, 2009; Claesson *et al.*, 2007). In contrast to primary care centers where the observed resistance of 27% was reported (Claesson *et al.*, 2009). For coagulase-negative staphylococci the prevalence of meticillin resistance is usually in correlation with resistance to other classes of antibiotics (Miragaia *et al.*, 2002).

According to that most of meticillin-resistant strains were also resistant to other antimicrobial drugs (Paulsen et al., 1997). The emergence of strains that are resistant to glycopeptides is particularly worrisome. Moreover meticillin-resistant strains of S.epidermidis are considered reservoirs of genes responsible for the occurrence of antimicrobial resistance, that can be transfered to other staphylococci by horizontal gene transfer (Archer and Climate, 1994; Wielders et al., 2001). The transfer of these genes to other pathogenic species, particularly S.aureus, causes great concern. However, unlike resistance to meticillin in Staphylococcus aureus, little attention has been devoted to meticillin resistant Staphylococcus epidermidis isolates, especially in hospital settings. For MRSE intensive hygiene measures are not used as with MRSA. As a result, we are faced with a high prevalence of resistant isolates of Staphylococcus epidermidis in the world.

Accordingly, 75%-80% of isolates of *Staphyloco-ccus epidermidis*, which cause infections associated with medical devices, are resistant to meticillin and multiple resistant to many antibiotics. By contrast commensal strains isolated outside the hospital environment show good sensitivity to antibiotics (Ko-zitskaya *et al.*, 2004).

Genomic sequencing of meticillin-resistant Staphylococcus epidermidis RP62a revealed the presence of SCCmec type II cassette (Gill et al., 2005). There was an identity of 98% at the nucleotide level of type II SCCmec cassette of Staphylococcus epidermidis and the same element in Staphylococcus aureus. This is a good indicator of horizontal gene transfer between these two species (Gill et al., 2005). This hypothesis is supported by a series of studies that confirm the presence of primordial SCCmec-like elements in the coagulase-negative staphylococci, which can be transferred to other strains and species (Hanssen et al., 2004; Wielders et al., 2001; Katayama et al. 2003; XX Ma et al., 2004; Katayama et al., 2005). SCCmec are mobile genetic elements in which intense recombination and gene transfer takes place. It is obvious that these elements serve not only as a means of transmission of meticillin resistance but also for the transmission of other staphylococcal genes. According to recent estimates Staphylococcus epidermidis and other coagulase-negative staphylococci are the "gene pool" for the next generation of new SCC types from which meticillin resistance in Staphylococcus aureus occurred in the first place. Given this, it is necessary to seriously consider the multiresistant strains of Staphylococcus epidermidis and coagulase-negative staphylococci as a reservoir that is responsible for the spread of genes responsible for resistance to antibiotics within a microbial community. Therefore, they should be controlled by appropriate hygiene measures, such as is done for meticillin-resistant Staphylococcus aureus.

Previously it was thought that the origin of infections caused by coagulase-negative staphylococci was endogenouse (McGowan, 1985). During the past two decades database of molecular epidemiology of hospital infections caused by *Staphylococcus epidermidis* have increased. There is considerably less data on other types of infections caused by coagulase-negative staphylococci. Several studies, devoted to hospital strains of *Staphylococcus epider*- midis, show high genetic diversity of strains (Spare et al., 2003; Boisson et al., 2002; Lang et al., 1999). But in most of these studies clusters of coagulase-negative staphylococci were usually detected, mostly meticillin-resistant Staphylococcus epidermidis, which persists in the hospital environment (de Silva et al., 2001; Burnie et al., 1997; Krediet et al., 2004; Miragaia et al., 2002; Nouwen et al., 1998; Raimundo et al., 2002; Sloos et al., 1998; Spiliopoulou et al., 2003; Villari et al., 2000; Aires De Sousa et al., 2000; van Belkum et al., 1996; Vermont et al., 1998; Worthington et al., 2000). Most of these genotypes were detected within a single department in a relatively short period of time (Burnie et al., 1997; Raimundo et al., 2002; Sloos et al., 1998), and resistance to antibiotics is largely proportional to the use of antibiotics in a particular department (Burnie et al., 1997). Several studies have also detected unrecognized genotypes in isolates taken from different departments (Spiliopoulou et al., 2003, Worthington et al., 2000) or hospitals (Milisavljevic et al., 2005; Aires De Sousa et al., 2000). Before 2003, only one study was dedicated to the strains of Staphylococcus epidermidis isolated from different countries (Miragaia et al., 2002). One of these studies reported the persistence of clones of Staphylococcus epidermidis in a hospital environment as much as 11 years (Huebner et al., 1994).

Conclusions

Using the oxacillin- screening test, it was noted that in smears taken from surfaces in the hospital environment among *Staphylococccus epidermidis* isolates 66.66% was resistant to meticillin (MRSE), while 33.33% was meticillin sensitive (MSSE). The analysis of antibiotic sensitivity of *Staphylococcus epidermidis* isolates in smears of surfaces in the hospital environment using disc diffusion Kirby-Bauer method according to 11 selected antibiotics are as follows: the majority of strains was resistant to penicillin and ampicillin (100%), resistance to amoxicillin / clavulanic acid and oxacillin was 66.66%, to TSH and garamycinu 58.33%, to cefoxtinu 50%, to azithromycin 41.66%, clindamycin 8.33%.

The analysis of antibiotic sensitivity of isolates from smears taken from work clothes showed that all isolates of *Staphylococcus epidermidis* were meticillin-resistant (100%). Analysis of antibiotic susceptibility of *Staphylococcus epidermidis* in smears of hands showed that 15 isolates were resistant to meticillin (62.5%), while 9 isolates were meticillin sensitive (37.5%). Analysis of antibiotic susceptibility of isolates of *Staphylococcus epidermidis* in bed smears showed an equal proportion of meticillin resistant (50%) and meticillin-sensitive (50%) isolates.

Staphylococcus epidermidis, commonly isolated as an opportunistic pathogen, is gaining increasing importance in the hospital environment, and it is very important to continue monitoring its antibiotic sensitivity.

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