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A comparative evaluation of communication apprehension among pharmacy and non-pharmacy undergraduates

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2 Department of Pharmacy, Island college of technology, Malaysia

Abstract

The goals of the present study were to assess and compare the level of communication apprehension (CA) among pharmacy undergraduate and non-pharmacy undergraduate students. To accomplish this aim a modified version of Zimbardo’s scale was used. A total of 501 students showed participation in this study. A higher participation was observed from the respondents from the age group 21-25 years. About 235 (46.9%) of the respondents were Chinese followed by Malay, Indian and other ethnic minorities. Majority 53.5% of the students were from school of pharmacy. Findings demonstrate a high level of CA among pharmacy students. However, in general Chinese female were found at a high risk of CA. Race, gender and study discipline were found to the factor associated with CA.

Key words: Communication apprehension, pharmacy undergraduate, non-pharmacy undergraduate

Introduction

Communication is a dynamic way to share information and feelings to others (Cathcart, 1988). Communication can be either intentional or unintentional by adopting a either verbal or non-verbal way (Berko et al., 1992). According to Berko et al., 1992 as an adult, one spend 42% of the communication time as a listener and 40% as a speaker. However, about 15 % of the time is spent in reading and 1% in writing (Berko, et al., 1992).

Nowadays good communication skills are the assets of a professional. Especially in pharmacy practice effective communication skill are vital for a pharmacist (Baldwin et al. 1979). Whilst offering the pharmacy practice services pharmacist interact with different individuals like patients, their family member, medical staff and other pharmacists. For affective patient care it is essential for a pharmacist to have good communication skill. However, sometimes an affective communication is hindered due to the shyness or lack of confidence to communicate. In other words CA on the part of pharmacist act as a barrier to affective communication (Baldwin et al. 1979). According to Baldwin et al. 1979 this CA can be a possible factor compelling a pharmacist to avoid; patient communication, counseling or discussion forums with professional peers.

McCroskey, 2001 has defined CA as “The level of fear or anxiety associated with either real or anticipated communication with another person or a group of person” (McCroskey, 2001). There are two types of CA; writing apprehension and oral CA (Elias, 1999). According to Stanga and Ladd (1990) oral CA is due to an intense personal fear or anxiety about communicating. In other words, experts view oral CA as a deficiency to communicate verbally with other people which afterward distort effectual communication. However, Zimbardo, 1977 has associated CA with the shyness. Shyness is seen as, the lack of tendency to talk and engage in communication with others, Which ‘may result from high CA, lack of verbal skills, or other causal factors (Mc,Croskey & Ri-
Oral CA is considered to be an issue of more importance. Oral CA can be reduced by means of cognitive intercession to ensure better quality future professionals. The cognitive intercession strategies consist of the systematic desensitization; cognitive restructuring and assertiveness training (Stanga & Ladd, 1990).

Communication apprehension exists in everyone; the level of shyness or hesitation to participate in the discussion is a marker to define the CA in to different level (Mc, Croskey & Richmond, 1980). This study aims to evaluate and compare the level of CA among the pharmacy undergraduates and non pharmacy undergraduates’ students.

**Methodology**

In August 2007 a cross sectional study was conducted among the pharmacy and non-pharmacy students at university Sains Malaysia (USM). USM is a public university with an estimated student’s number five thousand over. Mainly four groups are at USM Malays, Chinese, Indians and foreigners. However, at undergraduate level there is a high percentage of Malays, Chinese and Indians.

**Participants**

This study encompasses a non-experimental method. A cluster random sampling method was used to approach the potential participants. Two clusters were defined on the basis of types of participants; pharmacy undergraduates and non-pharmacy graduate. The non-pharmacy graduates were mainly from the school of arts, social sciences, maths, computer sciences, management and linguistics. Those willing to participate were the part of study. Ethical approvals from the research ethics committee of University Sains Malaysia were taken for this study. Moreover, a verbal consent was also taken from the respondents in order to assure the confidentiality of the information.

**Study tool**

Face to face interviews were conducted using a prevalidated Zimbardo’s scale. Zimbardo’s, 1977 comes up with a scale to evaluate the CA among the students. This was scale previously validated by McCroskey 1970; 1977 & FlcCroskey, 1982. In order to make the Zimbardo’s scale compliant with the Malaysian students’ content validation was conducted.

The content validation process was comprised of two phases; phase one was the preliminary content validation conducted by the professionals at the school of pharmacy, USM. After phase one twenty two items out of twenty four were selected to be the best to attain the objectives of the study. A three item likert scale (Agree, Undisclosed and Disagree) was used in order to calculate the level of communication apprehension among the students. After the phase one content validation the questionnaire was translated in to Malay language in order to make the questionnaire easier to understand by the respondents. The translation of the questionnaire to Malay language was done by the experts at the school of linguistics, USM. The translation was rechecked by the professionals at school of pharmacy in order to check the appropriateness of the word according the study objectives. After the phase one content validation the questionnaire was subjected to the phase two validation. The phase two content validations involves a pilot survey conducted among the USM students. For the pilot study two clusters were defined; one pharmacy undergraduates and two non-pharmacy undergraduates. A total of fifty students were approached (twenty five from every cluster). Keeping in view the responses the reliability scale was applied and internal consistency of the study tool was estimated on the basis of Cronbach’s Alpha (α = 0.63). Furthermore to assure the validity of the contents factor analysis was carried out. The content validity was estimated by using Bartlett’s test of sphericity and Kaiser-Mayer-Olkin measure of sampling adequacy. The results appear that Bartlett’s test of sphericity was significant 0.0000 and Kaiser-Mayer-Olkin measure of sampling adequacy was 0.790. According to Sheridan and Lyndall (2001), a measure of more than 0.6 reflects the adequacy of the contents of the questionnaire. Thus these results showed a considerable evidence of reliability and validity of the sampling tool.
Contents of the questionnaire

The questionnaire comprised of two parts. One demographic part and second the part evaluating the shyness level. The demographic part comprises of four questions i.e age, sex, race and school. However, the second part comprise of twenty two items. Of these twenty, only sixteen items were used to evaluate the level of CA among the students. Furthermore on the basis of the responses form this section scoring was done. The list of the items considered for scoring are illustrated in Table 2. However, self evaluation and personal perception about shyness was estimated by using two items i.e Are you facing some problem in communication with your colleagues and teachers and what do you think communication apprehension is a problem. The personal perception of the respondents about the importance of communication was evaluated by using a four item mentioned in Table 1.

Response for the survey and Scoring of the responses

A total of seven hundred participants were approached using the cluster random sampling method (n=350 from every cluster). Of seven hundred respondents, n=501 respondents participated in this survey. The responses obtained from the items mentioned in Table 2 were used to evaluate the level of communication apprehension.

Table 1. Personal perception about the importance of communication

<table>
<thead>
<tr>
<th>Statement</th>
<th>Not important</th>
<th>Moderately important</th>
<th>Very important</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. How you rate the importance of good communication in conversation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. How you rate the important one to one interpersonal communication</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. How you rate importance of good group communication</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. How you rate importance of good public speaking</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 2 Evaluation of the shyness level among students

<table>
<thead>
<tr>
<th>Statements</th>
<th>Scoring of responses</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Agreed</td>
</tr>
<tr>
<td>1. I dislike to participate in the group discussion</td>
<td>2</td>
</tr>
<tr>
<td>2. I feel nervous and tense while participating in a group discussion</td>
<td>2</td>
</tr>
<tr>
<td>3. Group discussion with new people makes me more tense and nervous</td>
<td>2</td>
</tr>
<tr>
<td>4. Usually I am nervous when I have to participate in a meeting</td>
<td>0</td>
</tr>
<tr>
<td>5. I am very calmed and relaxed when I am called upon to express my opinion at a meeting</td>
<td>0</td>
</tr>
<tr>
<td>6. I feel afraid to express myself at meetings</td>
<td>2</td>
</tr>
<tr>
<td>7. Communication at meeting with my colleagues make me uncomfortable</td>
<td>2</td>
</tr>
<tr>
<td>8. I stay relaxed and confident while answering the questions in a meeting</td>
<td>0</td>
</tr>
<tr>
<td>9. Participation in a conversation with a new colleague make me nervous</td>
<td>2</td>
</tr>
<tr>
<td>10. I feel confident in a conversation and express my views without any fear</td>
<td>0</td>
</tr>
<tr>
<td>11. I have no fear in giving speech</td>
<td>0</td>
</tr>
<tr>
<td>12. I feel tense while giving speech</td>
<td>2</td>
</tr>
<tr>
<td>13. My body shake while giving speech</td>
<td>2</td>
</tr>
<tr>
<td>14. I have confused and jumbled thoughts when I am giving a speech</td>
<td>2</td>
</tr>
<tr>
<td>15. I face the prospect of giving a speech with confidence</td>
<td>0</td>
</tr>
<tr>
<td>16. while giving speech I get so nervous , I forget eh facts I really know</td>
<td>2</td>
</tr>
</tbody>
</table>
These responses were scored in order to categorise the communication apprehension in to further levels. The maximum possible score for the questionnaire was 32. However, the maximum score attained by the respondents was 21. Quartiles were applied to classify the communication apprehension in to sub levels i.e no communication apprehension, slight communication apprehension, moderate communication apprehension and high communication apprehension. Those score zero were in the criteria of no communication apprehension. However, those scored 1-5 ranked with slight communication apprehension, 6-10 ranked with moderate communication apprehension, 11-15 ranked with high communication apprehension and those with 16 and over with the highest communication apprehension.

Data analysis

For the purpose of data analysis, the Statistical package for social sciences (SPSS13.0®) was used. A parametric statistics has been used. In order to compare the difference in CA in gender and among the non pharmacy and pharmacy students’ student t-test was applied. However, in order to compare the CA level among the ethnic groups One way ANOVA was used. Moreover, to identify the communication among the different racial groups Post-Hoc analysis was conducted.

Results

A total of N=501 respondents participated in the survey with a response rate of 71.6%. Majority 302 (60.3%) of the respondents were females. A higher participation was observed from the respondents from the age group 21-25 years. About 235 (46.9%) of the respondents were Chinese followed by Malay, Indian and other ethnic minorities. Details about the demographics of the respondents are mentioned in table 3.

<table>
<thead>
<tr>
<th>Demographics</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>199 (39.7%)</td>
</tr>
<tr>
<td>Female</td>
<td>302 (60.3%)</td>
</tr>
<tr>
<td>Race</td>
<td></td>
</tr>
<tr>
<td>Malay</td>
<td>218 (43.5%)</td>
</tr>
<tr>
<td>Chinese</td>
<td>235 (46.9%)</td>
</tr>
<tr>
<td>Indian</td>
<td>22 (4.4%)</td>
</tr>
<tr>
<td>Other</td>
<td>26 (5.2%)</td>
</tr>
<tr>
<td>Pharmacy Students</td>
<td>268 (53.5%)</td>
</tr>
<tr>
<td>Non-Pharmacy Students</td>
<td>233 (46.5%)</td>
</tr>
<tr>
<td>Age [Range=18-40]</td>
<td>Mean=22 ±3.4</td>
</tr>
<tr>
<td>18-20</td>
<td>207 (41.3%)</td>
</tr>
<tr>
<td>21-25</td>
<td>252 (50.3%)</td>
</tr>
<tr>
<td>26-30</td>
<td>26 (5.2%)</td>
</tr>
<tr>
<td>31-35</td>
<td>10 (2.0%)</td>
</tr>
<tr>
<td>36-40</td>
<td>6 (1.2%)</td>
</tr>
</tbody>
</table>

Table 4. Students perceptions towards the importance of communication

<table>
<thead>
<tr>
<th>Statement</th>
<th>Students</th>
<th>Not important</th>
<th>Moderately important</th>
<th>Very important</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. How you rate the importance of good communication in conversation</td>
<td>Pharmacy (268) Non-Pharmacy (233)</td>
<td>9</td>
<td>30</td>
<td>229</td>
</tr>
<tr>
<td></td>
<td></td>
<td>16</td>
<td>56</td>
<td>157</td>
</tr>
<tr>
<td>2. How you rate the importance of interpersonal communication</td>
<td>Pharmacy (268) Non-Pharmacy (233)</td>
<td>9</td>
<td>50</td>
<td>209</td>
</tr>
<tr>
<td></td>
<td></td>
<td>10</td>
<td>66</td>
<td>157</td>
</tr>
<tr>
<td>3. How you rate importance of good group communication</td>
<td>Pharmacy (268) Non-Pharmacy (233)</td>
<td>9</td>
<td>90</td>
<td>169</td>
</tr>
<tr>
<td></td>
<td></td>
<td>6</td>
<td>92</td>
<td>135</td>
</tr>
<tr>
<td>4. How you rate importance of good public speaking</td>
<td>Pharmacy (268) Non-Pharmacy (233)</td>
<td>29</td>
<td>111</td>
<td>128</td>
</tr>
<tr>
<td></td>
<td></td>
<td>33</td>
<td>190</td>
<td>110</td>
</tr>
</tbody>
</table>
Perception about the importance of communication

Overall, most of the students consider good communication as a very vital factor for the oral, group and interpersonal communication. However, the turn out for the importance of communication in general public communication was low. Details about the student’s perceptions toward the importance of communication are described in Table 4.

Evaluation of communication apprehension

Communication apprehension among both groups was evaluated on the basis of the sixteen items mentioned in Table 2. The minimum score of the respondents was two and maximum was 21. Those score zero were in the criteria of no communication apprehension. However, those scored 1-5 ranked with slight communication apprehension, 6-10 ranked with moderate communication apprehension, 11-15 ranked with high communication

Table 5. Students responses about communication apprehension

<table>
<thead>
<tr>
<th>Statements</th>
<th>Students</th>
<th>Scoring of responses</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Agree</td>
<td>Undisclosed</td>
</tr>
<tr>
<td>1. I dislike to participate in the group discussion</td>
<td>Pharmacy (268)</td>
<td>35</td>
</tr>
<tr>
<td></td>
<td>Non-Pharmacy (233)</td>
<td>38</td>
</tr>
<tr>
<td>2. I feel nervous and tense while participating in a group discussion</td>
<td>Pharmacy (268)</td>
<td>72</td>
</tr>
<tr>
<td></td>
<td>Non-Pharmacy (233)</td>
<td>48</td>
</tr>
<tr>
<td>3. Group discussion with new people makes me more tense and nervous</td>
<td>Pharmacy (268)</td>
<td>126</td>
</tr>
<tr>
<td></td>
<td>Non-Pharmacy (233)</td>
<td>71</td>
</tr>
<tr>
<td>4. Usually I am nervous when I have to participate in a meeting</td>
<td>Pharmacy (268)</td>
<td>135</td>
</tr>
<tr>
<td></td>
<td>Non-Pharmacy (233)</td>
<td>80</td>
</tr>
<tr>
<td>5. I am very calmed and relaxed when I am called upon to express my opinion at a meeting</td>
<td>Pharmacy (268)</td>
<td>66</td>
</tr>
<tr>
<td></td>
<td>Non-Pharmacy (233)</td>
<td>84</td>
</tr>
<tr>
<td>6. I feel afraid to express myself at meetings</td>
<td>Pharmacy (268)</td>
<td>125</td>
</tr>
<tr>
<td></td>
<td>Non-Pharmacy (233)</td>
<td>62</td>
</tr>
<tr>
<td>7. Communication at meeting with my colleagues make me uncomfortable</td>
<td>Pharmacy (268)</td>
<td>90</td>
</tr>
<tr>
<td></td>
<td>Non-Pharmacy (233)</td>
<td>54</td>
</tr>
<tr>
<td>8. I stay relaxed and confident while answering the questions in a meeting</td>
<td>Pharmacy (268)</td>
<td>57</td>
</tr>
<tr>
<td></td>
<td>Non-Pharmacy (233)</td>
<td>86</td>
</tr>
<tr>
<td>9. Participation in a conversation with a new colleague make me nervous</td>
<td>Pharmacy (268)</td>
<td>142</td>
</tr>
<tr>
<td></td>
<td>Non-Pharmacy (233)</td>
<td>73</td>
</tr>
<tr>
<td>10. I feel confident in a conversation and express my views without any fear</td>
<td>Pharmacy (268)</td>
<td>68</td>
</tr>
<tr>
<td></td>
<td>Non-Pharmacy (233)</td>
<td>93</td>
</tr>
<tr>
<td>11. I have no fear in giving speech</td>
<td>Pharmacy (268)</td>
<td>49</td>
</tr>
<tr>
<td></td>
<td>Non-Pharmacy (233)</td>
<td>82</td>
</tr>
<tr>
<td>12. I feel tense while giving speech</td>
<td>Pharmacy (268)</td>
<td>96</td>
</tr>
<tr>
<td></td>
<td>Non-Pharmacy (233)</td>
<td>58</td>
</tr>
<tr>
<td>13. My body shake while giving speech</td>
<td>Pharmacy (268)</td>
<td>167</td>
</tr>
<tr>
<td></td>
<td>Non-Pharmacy (233)</td>
<td>104</td>
</tr>
<tr>
<td>14. I have confused and jumbled thoughts when I am giving a speech</td>
<td>Pharmacy (268)</td>
<td>133</td>
</tr>
<tr>
<td></td>
<td>Non-Pharmacy (233)</td>
<td>81</td>
</tr>
<tr>
<td>15. I face the prospect of giving a speech with confidence</td>
<td>Pharmacy (268)</td>
<td>70</td>
</tr>
<tr>
<td></td>
<td>Non-Pharmacy (233)</td>
<td>94</td>
</tr>
<tr>
<td>16. while giving speech I get so nervous , I forget eh facts I really know</td>
<td>Pharmacy (268)</td>
<td>144</td>
</tr>
<tr>
<td></td>
<td>Non-Pharmacy (233)</td>
<td>83</td>
</tr>
</tbody>
</table>
apprehension and those with 16 and over with the highest communication apprehension. Detailed evaluation of the respondents is mentioned in Table 5 & Table 6. Overall, a high communication apprehension was found among the pharmacy students in comparison to non-pharmacy students and the difference were found statistically significant (p = <0.001, t=-51.538) (Table 6). In term of gender female (p=<0.001, t=-53.430) were found to face CA more in comparison to males (Table 6). However, on racial grounds Chinese student were found to have higher communication apprehension in comparison to others (Table 7).

### Discussion

**Philosophy of Communication apprehension**

CA is found in almost every individual at a certain level. Not only the students they face problems but any one involve in any type of social or professional communication is at risk (McCroskey, 1977). Those facing CA are not only at the risk of low academic profile but also at the risk of poor self esteem and lack of social skills. Friedman, 1980 has associated CA with anxiety; few relate it to personality problem while McCroskey,

<table>
<thead>
<tr>
<th>Demographics</th>
<th>Slight CA 1-5</th>
<th>Moderate CA 6-10</th>
<th>High CA 11-15</th>
<th>Highest CA 16 and over</th>
<th>Total</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Race</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Malay</td>
<td>24</td>
<td>49</td>
<td>97</td>
<td>48</td>
<td>218</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Chinese</td>
<td>13</td>
<td>43</td>
<td>97</td>
<td>82</td>
<td>235</td>
<td></td>
</tr>
<tr>
<td>Indian</td>
<td>4</td>
<td>7</td>
<td>8</td>
<td>3</td>
<td>22</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>5</td>
<td>8</td>
<td>11</td>
<td>2</td>
<td>26</td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>46</td>
<td>107</td>
<td>213</td>
<td>135</td>
<td>501</td>
<td></td>
</tr>
</tbody>
</table>

| Gender       |               |                 |               |                        |       |         |
| Male         | 23            | 59              | 87            | 30                     | 199   | <0.001* |
| Female       | 23            | 48              | 126           | 105                    | 302   |         |
| **Total**    | 46            | 107             | 213           | 135                    | 501   |         |

| School       |               |                 |               |                        |       |         |
| Pharmacy     | 19            | 40              | 113           | 96                     | 268   | <0.001* |
| Graduates    | 27            | 67              | 100           | 39                     | 233   |         |
| Non-Pharmacy | 46            | 107             | 213           | 135                    | 501   |         |

Mean score= 12.5 ± 4.6, (range; Minimum 2, Maximum 21),  student t-test,  one way ANOVA, p-value significant at 0.05

### Table 7 Comparison of Communication apprehension among racial groups

<table>
<thead>
<tr>
<th>Race (A)</th>
<th>Compared Race group (B)</th>
<th>Mean Difference (A-B)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malay</td>
<td>Chinese</td>
<td>-1.15075</td>
<td>0.036*</td>
</tr>
<tr>
<td></td>
<td>Indian</td>
<td>2.196831</td>
<td>0.134</td>
</tr>
<tr>
<td></td>
<td>Other</td>
<td>2.343684</td>
<td>0.062</td>
</tr>
<tr>
<td>Chinese</td>
<td>Malay</td>
<td>1.150752</td>
<td>0.036*</td>
</tr>
<tr>
<td></td>
<td>Indian</td>
<td>3.347582</td>
<td>0.005*</td>
</tr>
<tr>
<td></td>
<td>Other</td>
<td>3.494435</td>
<td>0.001*</td>
</tr>
<tr>
<td>Indians</td>
<td>Malay</td>
<td>2.19683</td>
<td>0.134</td>
</tr>
<tr>
<td></td>
<td>Chinese</td>
<td>-3.34758</td>
<td>0.005*</td>
</tr>
<tr>
<td></td>
<td>Other</td>
<td>0.146853</td>
<td>0.999</td>
</tr>
<tr>
<td>Others</td>
<td>Malay</td>
<td>-2.34368</td>
<td>0.062</td>
</tr>
<tr>
<td></td>
<td>Chinese</td>
<td>-3.494444</td>
<td>0.001*</td>
</tr>
<tr>
<td></td>
<td>Indian</td>
<td>-0.14685</td>
<td>0.999</td>
</tr>
</tbody>
</table>

*Post Hoc tukey, p-value significant at 0.05*
1977 has associated CA with the situation. However, McCroskey, 1980; Bond, 1984 believe that CA can be a result of the following seven items.

- Lack of intellectual skills or low intellectual skills
- Poor speech skills
- Social shyness
- Social isolation
- Nervousness while conducting a communication
- Low social self-esteem
- Ethnic/cultural issues

In spite of all these facts, one cannot ignore the Negative Cognitive Appraisal Model (NCAM) (Glaser, 1981). In NCAM, Glaser, 1981 stated that CA is a result of poor early language performance of the individual. In response to the poor language performance that individual fear to speak and this lead to CA. Bond, 1984 has further refined this aspect of CA and associated it with the negative remarks on the poor language performance by the classmates, teacher or family member. Such response put an individual at risk of high CA (Bond, 1984).

InNCAM, Glaser, 1981 stated that CA is a result of poor early language performance of the individual. In response to the poor language performance that individual fear to speak and this lead to CA. Bond, 1984 has further refined this aspect of CA and associated it with the negative remarks on the poor language performance by the classmates, teacher or family member. Such response put an individual at risk of high CA.

Findings of this study report a higher CA among pharmacy students. Majority 60.3% of the respondents were female and in term of ethnic majority 46.9% were Chinese. About a half of the respondents 53.5%, were from school of pharmacy (Table 2). In response to evaluation of the student’s perception regarding communication majority has positive perception toward the importance of communication (Table 4). Rating of responses in terms of educational background i.e (Pharmacy and Non-Pharmacy), the importance of; good communication in conversation, interpersonal communication, group communication & good public speaking was observed higher among pharmacy students in comparison to non-pharmacy students. However, CA among professional peers, meetings, speech and group discussion pharmacy students were on the top (Table 5). Especially if the evaluation is done on the basis of problems faced while delivering a speech, majority facing these problems were pharmacy students. Scoring on the basis of the responses mentioned in table 5 revealed the significant CA among pharmacy and non-pharmacy students (<0.001, t=-51.538) (Table 6). Further exploration on the basis of gender showed that the CA was significant among female (0.001, t=-53.430) (Table 6) (Rosan, 1994). Findings demonstrated that regardless of gender and school, Chinese students were found to have a higher level of CA than Malays and Indians (Table 7). Majority (64.2%) of the pharmacy students were facing the problem of communication apprehension.

<table>
<thead>
<tr>
<th>Statement</th>
<th>Response</th>
<th>Pharmacy (268)</th>
<th>Non-Pharmacy (233)</th>
<th>t</th>
<th>df</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Are you facing some problem in communication with your colleagues and teachers</td>
<td>Yes</td>
<td>172</td>
<td>119</td>
<td>1.420</td>
<td>500</td>
<td>0.156</td>
</tr>
<tr>
<td>What do you think communication apprehension is a problem</td>
<td>Yes</td>
<td>147</td>
<td>90</td>
<td>5.991</td>
<td>289</td>
<td>&lt;0.001*</td>
</tr>
</tbody>
</table>

*Student t-test, p-value significant at 0.05*
possibility that the communication apprehension among the pharmacy students is a blend of the social and cultural factors. As the findings of the study revealed that majority reporting a higher level of CA were Chinese. May be the some underlying cultural issues are the possible factors behind this. However, from my teaching experience and the experience of my other professional peer at different Malaysian universities, Chinese students were found at a higher risk of CA than others. Overall a lack of participation is observed among the Chinese students in the question answer session in the lecture hall, however Chinese students are observed to be more comfortable in asking the questions and discussing problems individually with the lecturer in his office or discussion room instead of asking the questions in the class. While discussing the issue of CA among the pharmacy and non-pharmacy graduates a possible reason can the lack of participation of pharmacy students in the extracurricular activities in the campus. The students from the other disciplines were found more involved in the games, cultural shows, and recreation in comparison with the pharmacy students. Lack of participation of pharmacy students can be a possible factor contributing to the high level of CA.

Conclusion

Findings demonstrate a high level of CA among pharmacy students. However, in general Chinese female were found at a high risk of CA. Race, gender and study discipline were found to the factor associated with CA.

Recommendation

There is an immediate need to focus on the communication aspect of pharmacy. Negligence in this regards may result lack of confidence in the future pharmacist to conduct an affective counselling session for the patients (ZmagoTurk & Eva-Turk, 2009). Moreover, the communication apprehension also hinders the learning process of the pharmacist which will result inability to share and retrieve patient and pharmacy oriented knowledge from the professionals and colleagues. Furthermore future studies should focus on the exploration of the factors responsible for the communication apprehension among the pharmacy students. In addition to this evaluation of the academic staff attitude with the students is also essential which may be one of the main factors.
Reference


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Vaginal douching practices in women and influential factors

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2 Cumhuriyet University, Faculty of Health Sciences, Department of Midwifery, Turkey
3 Cumhuriyet University, Faculty of Health Sciences, Department of Health Management, Turkey

Abstract

Objective: Vaginal douching can be very harmful to women’s health and can lead to health problems because of the introduction of many pathogenic microorganisms into the ascending pathways. This research was conducted to investigate the vaginal douching practices of women and influential factors of this practices.

Materials and methods: The research population of this cross-sectional research, consisted of 665 women, attending a primary healthcare centre, between March - May in 2006. A questionnaire, developed by researchers, was used as a data collection tool.

Results: The prevalence of vaginal douching of the women was found to be 54.3%. The major reason for douching was found to be for general body hygiene. In total, 83.1% of the women applied vaginal douching after each elimination (defecation and urination). Of the participants 12.2% reported that they have learned this practice from health care personnel.

Conclusion: the prevalence of vaginal douching was found to be high. Practicing vaginal douching after each elimination may expose high risk to various genital infections.

Key words: Perineal hygiene; Traditional intravaginal practices; Vaginal douching

Background: Vaginal douching is a commonly applied, traditional practice among women as a means of ‘cleansing’ the vagina. It is defined as washing the inside of the vagina (inserting of fingers into vagina) with water or another liquid. Women in many developed and developing countries use vaginal douching for personal cleanliness and general hygiene, for decreasing complaints related to genital infections, preventing sexually transmitted diseases, preventing pregnancy, and for esthetic and religious reasons (Çalışkan, 2005; Demirbağ, 2000; Foch, McDaniel & Chacko, 2001; Karatay & Özvarış, 2006; Ness et al., 2002; Rupp, Short, Head-Caroll & Rosenthal, 2006).

International studies on this subject have reported a prevalence of vaginal douching between 27% and 80% (Cottrell, 2006; Foch, McDaniel & Chacko, 2001; Kim Oh, Merchant & Brown, 2002; Simpson, Merchant, Grimley & Kim Oh, 2004; Vermund et al., 2001). Nationally, although it is a well known and common practice among Turkish women, only five studies have been found and none of them was carried out in a health centre. These studies reported prevalence of vaginal douching as 50.2% (Çalışkan, 2005), 58.0% (Karaer, Avşar, Özkan, Bayır & Sayan, 2005), 61.5% (Ege, Timur, Zincir & Egri, 2007), 64.0% (Hodoglugil, Aslan & Bertan, 2000; Karaer, Boylu & Avsar, 2005). In these studies it was reported that Turkish women practice vaginal douching as part of personal hygiene, as part of religious practices, or after menstruation. Previous works have shown that vaginal douching can be very harmful to women’s health and can lead to health problems from the introduction of many pathogenic microorganisms into the ascending pathways. Vaginal...
douching disturbs the normal vaginal flora that exists in the vagina to protect it against infection and leads the foundation for infection. Vaginal douching causes many health problems including complaints of vulvovaginal irritation, such as itching, burning and dyspareunia, infection, vulvovaginal candidiasis, trichomonas vaginalis, abnormal and malodorous vaginal drainage, cervical erosion, pelvic inflammatory disease (PID) and related health problems, ectopic pregnancy, decreased fertility and infertility, risk of sexually transmitted diseases, bacterial vaginosis, chlamydia, Herpes Simplex Type II, Chlamydia, Human Papilloma virus (HPV), preterm birth, low birth weight, and cervical cancer (Chiaffarino, Parazzini, De Besi & Lavezzari, 2004; Cottrell, 2006; Fiscella, Franks, Kendrick, Meldrum & Kieke, 2002; Fiscella, Franks, Kendrick & Bruce, 1998; Foch, McDaniel & Chacko, 2001; Joesoef et al., 2001; Karatay & Özvans, 2006; Misra & Trabert, 2007; Ness et al., 2002; Newton, Piper, Shain, Perdue & Pairs, 2001; Scholes et al., 1998; Sun et al., 2005; Vermund et al., 2001).

There are various investigations about the origin of knowledge about vaginal douching. Simpson, Merchant, Grimley and Kim Oh (2004) proposed that 43% of women learned about this practice from close relatives. However Cottrell (2006) found that 70.5% of women learned from close relatives and 6.2% from physicians and nurses. In a study by Foch, McDaniel and Chacko (2001) 70% of the women learned about this practice from their mothers.

Research Questions: What are the frequency (timing of the vaginal douching), prevalence and the reasons behind vaginal douching practices among women in Sivas province.

Methods

Design: This study was a cross-sectional type. The research population was comprised of all married, divorced and widowed women who attended a Primary Health Center (PHC) in Sivas province between March-May 2006. Information obtained from employees of the health center and from the health center records revealed that March and May is the busiest season for the health center. Therefore, data was collected during this period. Sampling method was not used, all 665 women who agreed to participate in this study were included. Single women were not included due to strong cultural values placed on having an intact hymen. That is, single women, who are not virgins, are not approved of in society and would not openly admit that they were not virgins. Therefore, they were not included in the research sample.

The PHC, where the research carried out, serves some 20,000 people around the centre. In Turkey PHCs are the important parts of providing primary health care services. Health protection, health promotion and outpatient treatment are given to all people covered by centre. Patients, who do not have health insurance or have low income, prefer these centers since they provide cheaper health care services as compared with hospitals. Especially women and children have priority in using these services provided by PHCs. Nurses and midwives employed in PHCs, work closely with women in the community, and play an increasingly prominent role in the provision of health care. They have a significant role in health education, advice and counselling, and in preventing harmful traditional practices such as vaginal douching.

The region covered by the PHC, where the research is performed, is a rural area and have primarily lower socio-economic level residents. In such regions, it is well known that vaginal douching practice is widespread.

Measures: A questionnaire was developed by the researchers used as a data collection tool. In the questionnaire, there were 20 descriptive questions about the women’s age, occupation, educational level, number of children, as well as questions about the women’s vaginal douching practices and factors that may have an influence on vaginal douching. The questionnaire was piloted, in another PHC in Sivas province, in order to ensure the validity and reliability of the questionnaire. In the main study, the questionnaire was applied using a face-to-face interview technique with the women. The questionnaire was administered to the research population by the researchers. The interviews took place in an appropriate place in the health center so that the women could be alone with the interviewer in a quiet environment. Before collecting data from the women they were informed
by the interviewer about the purpose and length of the interview, and that the results would not be used for any other purpose. It was also explained that the participation to the research was voluntarily. All research data were obtained by asking the women themselves. Health center records and other sources of data were not used.

Before beginning data collection written permission was obtained from the relevant authorities. The women gave their verbal consent to participate in the research.

Statistical Analysis Data was evaluated in the SPSS 13.0 software program using percentage and Chi square. Statistical tests were conducted at the 5% significance level.

Results

The descriptive characteristics of the women are shown in Table 1. One fifth of the women were under 25 years of age. The percentage of women in the 26-30 (40.4%) and over 40 year old (40.8%) age groups were nearly the same. The majority of the women (97.2%) were housewives, 33.5% had less than a primary school education, more than half (58%) had a primary or middle school education, 13.5% had no social security health insurance, 66.3% were in nuclear families, 32.5% were in extended families, one third had four or more children, and 27.8% described their income level as low. In the examination of their husbands’ demographic data, it was seen that 62.9% had primary to middle school level education, and 5.1% were unemployed.

In this study, 6.9% of the women did not use any method of family planning method, and 54.6% used some method. However 22.9% of the second group used ineffective methods, such as withdrawal. Furthermore, the prevalence of vaginal douching of the women was found to be 54.3%. Of the women who use vaginal douching (inserting of fingers into vagina), 89.5% used just water and 10.5 % use soapy water. The women used vaginal douching while cleaning the perineum, after sexual intercourse, while bathing, and at the end of their menstrual cycles (Table 2).

<table>
<thead>
<tr>
<th>Table 1. Descriptive Characteristics of Women Included in the Research</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Descriptive Characteristics</strong></td>
</tr>
<tr>
<td>Age</td>
</tr>
<tr>
<td>≤25</td>
</tr>
<tr>
<td>26-39</td>
</tr>
<tr>
<td>≥40</td>
</tr>
<tr>
<td>Educational level</td>
</tr>
<tr>
<td>&lt;Primary school</td>
</tr>
<tr>
<td>Primary-middle school</td>
</tr>
<tr>
<td>≥High school</td>
</tr>
<tr>
<td>Occupation</td>
</tr>
<tr>
<td>Housewife</td>
</tr>
<tr>
<td>Civil servant</td>
</tr>
<tr>
<td>Laborer</td>
</tr>
<tr>
<td>Self-employed</td>
</tr>
<tr>
<td>Farmer</td>
</tr>
<tr>
<td>Husband’s educational level</td>
</tr>
<tr>
<td>&lt;Primary school</td>
</tr>
<tr>
<td>Primary-middle school</td>
</tr>
<tr>
<td>≥High school</td>
</tr>
<tr>
<td>Husband’s occupation</td>
</tr>
<tr>
<td>Unemployed</td>
</tr>
<tr>
<td>Civil servant</td>
</tr>
<tr>
<td>Laborer</td>
</tr>
<tr>
<td>Self-employed</td>
</tr>
<tr>
<td>Farmer</td>
</tr>
<tr>
<td>Retired</td>
</tr>
<tr>
<td>Not answered</td>
</tr>
<tr>
<td>Social security health insurance</td>
</tr>
<tr>
<td>Yes</td>
</tr>
<tr>
<td>No</td>
</tr>
<tr>
<td>Family type</td>
</tr>
<tr>
<td>Nuclear</td>
</tr>
<tr>
<td>Extended</td>
</tr>
<tr>
<td>Broken</td>
</tr>
<tr>
<td>Number of children</td>
</tr>
<tr>
<td>None</td>
</tr>
<tr>
<td>One child</td>
</tr>
<tr>
<td>Two children</td>
</tr>
<tr>
<td>Three children</td>
</tr>
<tr>
<td>≥Four children</td>
</tr>
<tr>
<td>Income level</td>
</tr>
<tr>
<td>Low</td>
</tr>
<tr>
<td>Middle</td>
</tr>
<tr>
<td>High</td>
</tr>
<tr>
<td>Total</td>
</tr>
</tbody>
</table>
Table 2. Time When Women Did Vaginal Douche (n=361)

<table>
<thead>
<tr>
<th>Vaginal douche time</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>While washing perineum</td>
<td>300</td>
<td>83.1</td>
</tr>
<tr>
<td>After having sex</td>
<td>278</td>
<td>77.0</td>
</tr>
<tr>
<td>While bathing</td>
<td>260</td>
<td>72.0</td>
</tr>
<tr>
<td>During menses and at the end</td>
<td>209</td>
<td>57.9</td>
</tr>
<tr>
<td>All the time</td>
<td>18</td>
<td>12.2</td>
</tr>
<tr>
<td>When doing ritual cleansing</td>
<td>4</td>
<td>1.1</td>
</tr>
<tr>
<td>When having extra drainage</td>
<td>1</td>
<td>0.3</td>
</tr>
</tbody>
</table>

In the examination of the reasons why women use vaginal douching, it was determined that the overwhelming majority (82.5%) used vaginal douching for cleanliness, but 6.4% used vaginal douching for religious reasons (Table 3).

Table 3. Reasons Why Women Used Vaginal Douche

<table>
<thead>
<tr>
<th>Reasons for vaginal douche</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ensure cleanliness</td>
<td>298</td>
<td>82.5</td>
</tr>
<tr>
<td>Ensure cleanliness and protect from disease</td>
<td>36</td>
<td>10.0</td>
</tr>
<tr>
<td>Religious belief</td>
<td>23</td>
<td>6.4</td>
</tr>
<tr>
<td>Doesn’t know</td>
<td>3</td>
<td>0.8</td>
</tr>
<tr>
<td>To prevent pregnancy</td>
<td>1</td>
<td>0.3</td>
</tr>
<tr>
<td>Total</td>
<td>361</td>
<td>100.0</td>
</tr>
</tbody>
</table>

When the women were asked where they learned about vaginal douching, it was determined that 40.9% learned on their own, 31.3% from relatives, and 12.2% from health care personnel (nurses, midwives and physicians) (Table 4).

Table 4. People From Whom the Women Learned about Vaginal Douching

<table>
<thead>
<tr>
<th>People from whom learned vaginal douching</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Learned on her own</td>
<td>148</td>
<td>40.9</td>
</tr>
<tr>
<td>Relatives</td>
<td>113</td>
<td>31.3</td>
</tr>
<tr>
<td>Health personnel (midwife, nurse and physician)</td>
<td>44</td>
<td>12.2</td>
</tr>
<tr>
<td>Neighbors</td>
<td>32</td>
<td>8.9</td>
</tr>
<tr>
<td>Religious publication</td>
<td>18</td>
<td>5.0</td>
</tr>
<tr>
<td>Husband</td>
<td>4</td>
<td>1.1</td>
</tr>
<tr>
<td>TV, magazine, book</td>
<td>2</td>
<td>0.6</td>
</tr>
<tr>
<td>Total</td>
<td>361</td>
<td>100.0</td>
</tr>
</tbody>
</table>

There was a significantly higher percentage of vaginal douching application in the following groups (Table 5): younger women under 25 years old, those with lower educational level (primary school or lower), those whose husbands were farmers or self-employed, those without health insurance, those with a low income level, those living in an extended family, those with four or more children, and those who used Intra Uterin Devices (IUD) or injection as their method of family planning.

Of the women, 71.4% had symptoms of genital infection. This prevalence of genital infection was 55.2% in women who used vaginal douching. Comparative overview of Table 5 exhibited that 61.3% of the women, who used vaginal douching, had itching, 58.1% had pain, burning and leakage when urinating, 55.3% had pain in the abdomen or groin, the same percentage had odor, and 54.3% had abnormal drainage.

Discussion

Douching or douche products may disrupt the normal vaginal microbial flora, increasing susceptibility to pathogenic microorganisms capable of rapid proliferation. The repetitive and frequent use of douche products over time may change the pH of vaginal secretions and reduce the prevalence and concentration of hydrogen peroxide-producing lactobacilli, creating a less protective vaginal environment (Bruce, Fiscella & Kendrick, 2000).

The prevalence of vaginal douching was found to be 54.3%. Karaer, Avsar, Özkan, Bayır and Sayan (2005) also proposed the similar results. Demba et al. (2005) determined that 57.6% used just water and 22.2% used soapy water for vaginal douching. Misra, Trabert and Atherly-Trim (2006) proposed that 90.8% of African American women used vaginal douching with vinegar and water. Rupp, Short, Head-Caroll and Rosenthal (2006) exhibited that 92% of the population, most of which was composed of African American women, used the commercial douche products. On the other hand, in a similar work, these commercial products were used by 58% of the research group, 55% of whom were African American (Cottrell, 2006). Sun et al. (2005) suggested that women, who used salty water or detergent, had a higher HPV positivity than women who used tap water.

In the examination of time when women use vaginal douching (Table 2), it was seen that the
Table 5. Characteristics of Women According to Douching Practice (n=665)

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Women who douche</th>
<th>Women who don’t douche</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤25</td>
<td>73</td>
<td>58.4</td>
<td>52</td>
</tr>
<tr>
<td>26-39</td>
<td>147</td>
<td>54.6</td>
<td>122</td>
</tr>
<tr>
<td>≥40</td>
<td>141</td>
<td>52.0</td>
<td>130</td>
</tr>
<tr>
<td>Educational level</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;Primary school</td>
<td>133</td>
<td>59.6</td>
<td>90</td>
</tr>
<tr>
<td>Primary-middle school</td>
<td>206</td>
<td>53.4</td>
<td>180</td>
</tr>
<tr>
<td>≥High school</td>
<td>22</td>
<td>39.3</td>
<td>34</td>
</tr>
<tr>
<td>Husband’s education</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;Primary school</td>
<td>38</td>
<td>55.1</td>
<td>31</td>
</tr>
<tr>
<td>Primary-middle school</td>
<td>242</td>
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<td>176</td>
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<tr>
<td>≥High school</td>
<td>81</td>
<td>45.5</td>
<td>97</td>
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<tr>
<td>Husband’s occupation*</td>
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<td></td>
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<tr>
<td>Unemployed</td>
<td>18</td>
<td>52.9</td>
<td>16</td>
</tr>
<tr>
<td>Civil servant</td>
<td>38</td>
<td>43.7</td>
<td>49</td>
</tr>
<tr>
<td>Laborer</td>
<td>65</td>
<td>46.8</td>
<td>74</td>
</tr>
<tr>
<td>Self-employed</td>
<td>163</td>
<td>61.3</td>
<td>103</td>
</tr>
<tr>
<td>Farmer</td>
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<td>68.0</td>
<td>8</td>
</tr>
<tr>
<td>Retired</td>
<td>53</td>
<td>52.5</td>
<td>48</td>
</tr>
<tr>
<td>Social security health insurance</td>
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<td></td>
</tr>
<tr>
<td>Yes</td>
<td>300</td>
<td>52.2</td>
<td>275</td>
</tr>
<tr>
<td>No</td>
<td>61</td>
<td>67.8</td>
<td>29</td>
</tr>
<tr>
<td>Family type</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nuclear</td>
<td>237</td>
<td>53.7</td>
<td>204</td>
</tr>
<tr>
<td>Extended</td>
<td>120</td>
<td>55.5</td>
<td>96</td>
</tr>
<tr>
<td>Broken</td>
<td>4</td>
<td>50.0</td>
<td>4</td>
</tr>
<tr>
<td>Number of children</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>20</td>
<td>42.6</td>
<td>27</td>
</tr>
<tr>
<td>One child</td>
<td>45</td>
<td>56.2</td>
<td>35</td>
</tr>
<tr>
<td>Two children</td>
<td>91</td>
<td>53.8</td>
<td>78</td>
</tr>
<tr>
<td>Three children</td>
<td>71</td>
<td>43.6</td>
<td>92</td>
</tr>
<tr>
<td>≥Four children</td>
<td>134</td>
<td>65.0</td>
<td>72</td>
</tr>
<tr>
<td>Income level**</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>105</td>
<td>56.8</td>
<td>80</td>
</tr>
<tr>
<td>Middle</td>
<td>244</td>
<td>53.9</td>
<td>209</td>
</tr>
<tr>
<td>High</td>
<td>12</td>
<td>44.4</td>
<td>15</td>
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<tr>
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<td></td>
<td></td>
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<tr>
<td>IUD</td>
<td>69</td>
<td>61.1</td>
<td>44</td>
</tr>
<tr>
<td>Condom</td>
<td>64</td>
<td>58.2</td>
<td>46</td>
</tr>
<tr>
<td>Withdrawal</td>
<td>38</td>
<td>45.8</td>
<td>45</td>
</tr>
<tr>
<td>Tubal ligation</td>
<td>17</td>
<td>58.6</td>
<td>12</td>
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<tr>
<td>Pill</td>
<td>12</td>
<td>52.2</td>
<td>11</td>
</tr>
<tr>
<td>Injection</td>
<td>3</td>
<td>60.0</td>
<td>2</td>
</tr>
<tr>
<td>Symptoms of genital infection</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain, burning with urination</td>
<td>140</td>
<td>58.1</td>
<td>101</td>
</tr>
<tr>
<td>Abdominal, groin pain</td>
<td>182</td>
<td>55.3</td>
<td>147</td>
</tr>
<tr>
<td>Abnormal drainage</td>
<td>146</td>
<td>54.3</td>
<td>123</td>
</tr>
<tr>
<td>Odor</td>
<td>109</td>
<td>55.3</td>
<td>88</td>
</tr>
<tr>
<td>Itching</td>
<td>100</td>
<td>61.3</td>
<td>63</td>
</tr>
<tr>
<td>Pain during sexual intercourse</td>
<td>2</td>
<td>100.0</td>
<td>-</td>
</tr>
</tbody>
</table>

* 13 women did not provide any answer
** Defined according to women’s own statements
top four were while cleaning the perineum, after sexual intercourse, while bathing, and at the end of their menstrual cycles. The overwhelming majority (82.5%) use vaginal douching for cleanliness (Table 3). It was also determined that 6.4% of the women use vaginal douching for religious reasons. In many studies, similar reasons were reported by women for douching: to feel clean, for personal hygiene, to remove blood and odor at the end of menstruation, after sexual intercourse, and to eliminate symptoms of odor and drainage (Blythe, Fortenberry & Orr, 2003; Cottrell, 2006; Foch, McDaniel & Chacko, 2001; Simpson, Merchant, Grimley & Kim Oh, 2004). A lower percentage of women stated that they learned about vaginal douching on their own compared to the Karaer and his co-workers’ findings (Karaer, Avsar, Özkan, Bayır & Sayan, 2005). Even though approximately 41% of the women in this study stated that they learned about vaginal douching on their own, it can be said that this practice is learned during the socialization process from those around them, including their relatives and friends. In spite of the fact that many health problems, primarily infections, are related to vaginal douching, it is an interesting finding that in this research 12.2% of the women were encouraged to douche by health care personnel. The majority of these were nurses and midwives (7.5%), followed by physicians (2.5%), and “health workers” (2.2%). This finding makes it clear that all health care personnel, particularly nurses and midwives, need to be taught about this subject in continuing educational programs.

In some studies, the percentage of women at an early age who used vaginal douching was found to be lower than those in older age groups (Blythe, Fortenberry & Orr, 2003; Karaer, Avsar, Özkan, Bayır & Sayan, 2005). However in this study, although not reaching statistical significance, a higher percentage of the younger women were found to use vaginal douching. This result can be explained for reasons such as the younger women being more active sexually and menstruating, because a significant number of women stated that they practiced vaginal douching for cleanliness during and after menstruation and after sexual intercourse (Tables 2 and 3). For this reason, young women, who are menstruating and sexually active, would practice vaginal douching more than older women.

The prevalence of women using vaginal douching was found to be higher in women with low educational level in this study. This result is similar to that reported from other studies (Cottrell, 2006; Karaer, Avsar, Özkan, Bayır & Sayan, 2005).
similar result was found in the evaluation of their husbands’ educational level. Both results were found to be statistically significant. It is known that as educational level increases, the likelihood of individuals practicing negative behaviors in the health area, as in other areas, decreases.

When the prevalence of douching was compared to the occupations of the women’s husbands, it was observed that there was a higher prevalence of vaginal douching in the wives of men who were farmers and self-employed. This was followed by the wives of men who were unemployed and retired. The lowest prevalence was in the wives of men who were civil servants and laborers. This result may be related to the higher educational level of civil servants and laborers compared to farmers and self-employed people. A statistically significant relationship was found according to husband’s occupation.

In the comparison of those who use vaginal douching with the presence of social security health insurance and income level, it was determined that women, who did not have social security health insurance and women with a low income level, had higher prevalence of vaginal douching. The difference between those who did and did not have social security health insurance was found to be statistically significant. This result is likely to be related to the fact that women, who do not have social security health insurance, generally have low income levels and are unable to benefit from health care services (Cottrell, 2006; Karaer, Avsar, Özkan, Bayır & Sayan, 2005; Simpson, Merchant, Grimley & Kim Oh, 2004).

Comparative investigation of vaginal douching prevalence exhibited that women living in extended families had a higher prevalence of vaginal douching, but this difference was not found to be statistically significant. The increased prevalence of this traditional health practice in extended types of families may have caused this result. For this reason, priority needs to be given to educate women living in extended families.

Prevalence of vaginal douching with number of children was striking that the women with four or more children had a higher prevalence of vaginal douching. This was followed by women with one and two children. The difference between these groups was found to be statistically significant. It is suggested that as the number of children increase the number of women who use this practice to prevent pregnancy also increases. This theory is supported by the finding that 77% of the women who used vaginal douching did so after sexual intercourse. However in the examination of reasons for vaginal douching it was seen that only 0.3% of the women use vaginal douching to prevent pregnancy (Table 3). Although more women stated that they use vaginal douching for cleanliness, they may include the removal of sperm from the vagina to prevent pregnancy as a basis for this cleanliness when they douche after sexual intercourse.

No statistically significant difference was found for practicing vaginal douching according to whether or not the women used a method of family planning (p = 0.35). Although the difference was not statistically significant, the percentage of women who used vaginal douching was higher in women who use IUD and injections as a method of family planning. The reason why women with IUDs may practice vaginal douching may be more related to the IUD causing an increase in vaginal drainage and for this reason the women would use vaginal douching for the purpose of genital hygiene. In the study by Karaer, Avsar, Özkan, Bayır and Sayan (2005) it was determined that more women use vaginal douching who have IUDs, but in the study by Hodoglugil, Aslan and Bertan (2000) no difference was found in prevalence of vaginal douching between women who did and did not use IUD.

Karaer, Avsar, Özkan, Bayır and Sayan (2005) found a significantly higher prevalence of symptoms of vaginal infection in women who use vaginal douching and of complaints of vulvovaginal irritation, such as itching, burning and dyspareunia. Although the women, in this study, who used vaginal douching, had a higher prevalence of symptoms of genital infection, only the difference for itching between those, who did and did not use vaginal douching, was found to be statistically significant (p = 0.05). However, many other studies have found a correlation between vaginal douching and genital infections (Blythe, Fortenberry & Orr, 2003; Chiaffarino, Parazzini, De Besi & Lavezzari, 2004; Corsello et al., 2003; Cottrell, 2006; Joesoef et al., 2001; Karaer, Boylu & Avsar, 2005; Newton, Piper, Shain, Perdue & Peairs, 2001; Sun et al., 2005; Vermund et al., 2001).
Conclusion

There are several clinical implications of this study. First, the practice of vaginal douching was more prevalent in women under 25 years of age, who had low educational and income levels, who did not have health insurance, whose husband was a farmer or self-employed, and who had four or more children. Second, the most common reason for vaginal douching application was for general hygiene. A significant percentage of women who practice vaginal douching did so after they had a bowel movement. Therefore, this practice brings with it many potential health dangers. For this reason, nurses and midwives can help women, who attend to PHC, by informing them about problems that can occur from vaginal douching and can encourage them to give up this practice. Third, the primary basis for the practice of vaginal douching was religious beliefs. Therefore it is suggested that the health care personnel should cooperate with religious leaders when they plan public educational programs for women as they work to change incorrect beliefs about this practice. Finally, some of the women had been encouraged to practice vaginal douching by health care personnel. Thus doctors, nurses and midwives need to be taught about this subject in continuing education programs. In addition assessment of women on vaginal douching in details, by nurses and midwives, during their visit to the HCSs, should be as part of routine health history taking activity.

References


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Relationship between sociodemographic characteristics and migraine in working women

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Abstract

Migraine is the most common type of headache in working women of reproductive age. It is classified according to the internationally recognized criteria. Menstrual migraine is not included into the main body of the classification, but in its appendix, indicating the need for further research in this field.

The aim of the study was to determine the prevalence of migraine and its subtypes in working women and to evaluate the significance of sociodemographic characteristics.

The study was done on a sample of 715 working women aged 20-65 years who filled in a questionnaire. The general questionnaire was used to collect relevant data. The collected data were analyzed using appropriate mathematical and statistical methods.

The results obtained show the prevalence of migraine in working women to be 20.69%. Among the women suffering from migraine, 4.73% had pure menstrual migraine and 56.76% had menstrually-related migraine, while non-menstrual migraine was present in 38.51%. We found a significant difference among some of the three studied subtypes of migraine in relation to age, level of education, family history of headache, and presence of another chronic disease. On the other hand, the three studied subtypes of migraine did not show significant differences in relation to marital status, children, type of employment, overtime work, or smoking. Migraine in women deserves special attention. Migraine subtypes differ in certain sociodemographic characteristics.

Key words: migraine, women, working population, sociodemographic characteristics

Introduction

Migraine is a type of primary headache, manifested as intermittent, usually unilateral headache accompanied by vegetative disturbances, and frequently also by transient neurological symptoms (1). Migraine is diagnosed using the International Classification of Headache Disorders (ICHD-II) criteria, published in Cephalalgia, Vol. 24, Suppl.1, 2004 (2, 3). The classification encompasses three parts. Part one presents primary headaches, coded 1-4; part two presents secondary headaches, coded 5-12; and part three, i.e., chapter 13, presents cranial neuralgias and central causes of facial pain. Headache types and subtypes that do not fulfill the diagnostic criteria stated in the chapters 1-13 are listed in chapter 14 (14.1 Headache not else classified), including headaches that need more information in order to be classified (14.2 Headache unspecified). At the end of the classification there is an appendix, which has been introduced in the second edition with the main purpose of providing research criteria for the new entities that still need further validation in order to be formally accepted (4).

In women, migraine without aura is frequently closely associated with menstruation. Based on the current knowledge menstrual migraine is classified into two subtypes: pure menstrual migraine and menstrually-related migraine (5). Pure menstrual
migraine occurs only during menses. MacGregor has proposed the following definition of menstrual migraine: an attack of migraine without aura that occurs regularly on the first day of menstruation or on two days before or after that day, and at no other times (6). There is another opinion, that this is migraine headache occurring regularly every month and only in the period between two days before menstruation and the end of menstruation (7). Menstrually-related migraine may occur as pure menstrual migraine during the perimenstrual period, as well as at other times during a menstrual cycle (8). Since it is not clear whether these two types of migraine are different entities, menstrual migraine is included in the appendix, suggesting the need for further elucidation.

All epidemiological research of migraine clearly indicates that the prevalence of migraine is associated with sex and age (9). The most frequently reported data is that migraine is three times more common in women than in men, although some studies present different ratios. In China, Zhao et al found this ratio to be 5:1 to the disadvantage of female sex (10). The prevalence of migraine does not change significantly throughout childhood, however, in adolescence it increases in women (11). Given the ratio of migraine in women and men, the question arises as to whether and how ovarian hormones affect migraine. Abnormal response of the central nervous system exposed to normal hormonal fluctuations during a menstrual cycle is probably the mechanism underlying menstrual migraine (12, 13). It has been established that oscillations in the oestrogen levels are the key factor in the increased prevalence of migraine in women. The absolute oestrogen levels are not so important as are the sudden changes in the levels occurring, among others, in physiological states such as a menstrual cycle and after childbirth.

The prevalence of menstrual migraine has been reported to range from 4% to 73%, depending on the criteria used for defining the onset of migraine attack (14, 15).

Our paper, therefore, focuses on migraine in working women in our environment, and aims at contributing to the research of this important medical problem.

Material and methods

The study was done on a sample of 715 working women aged 20-65 years, using a general questionnaire. The questionnaire contained general questions and questions about sex, age, type of employment, marital status, children, level of education, overtime work, smoking, family history of headache, and presence of another chronic disease. The last two questions of the questionnaire were about the occurrence of headache during the previous year and month. Subjects who answered positively to one or both of these questions, i.e., who had had a headache in the previous year and/or month, were included for further study. The questionnaire was made on the basis of our clinical experience and scientific research findings, respecting the accepted knowledge about headache, with an emphasis on primary headache.

The data was analyzed using multivariate analysis of variance (MANOVA), discriminative analysis, and other parametric procedures and methods. Univariate analyses included Roy’s test, Pearson’s contingency coefficient ($\chi$), and the multiple correlation coefficient (R). Calculation of discrimination coefficients discriminates characteristics that determine specificity of subsamples. The purpose of the mathematical and statistical analysis was to determine characteristics of each subsample and the homogeneity and distance between subsamples in relation to the discriminative characteristics.

The collected data were checked for possible formal or logical errors. The data obtained through the statistical analysis are presented in tables and figures, accompanied by comments.

Results

The results of the study show that out of 715 subjects 148 (20.69%) had migraine (Figure 1). Of the 148 women suffering from migraine, 7 (4.73%) had pure menstrual migraine (PMM), 84 (56.76%) had menstrually-related migraine (MRM), and 57 (38.51%) had non-menstrual migraine (NMRM).
Table 1 and table 2 show cumulative responses to general questions. Multivariate analysis of variance (MANOVA) showed a significant difference between the three studied migraine subtypes for some of the general questions (p = 0.008).

Table 3 shows that in subjects suffering from pure menstrual migraine the most prevalent was age 41-50, present in 57%.

Regarding menstrually-related migraine, the prevalence of ages 41-50 years was 38%, which is significantly higher than the prevalence of ages 20-30, in 14.3% of subjects suffering from migraine (p=0.001), and the prevalence of ages 51-60, in 13.1% of subjects suffering from migraine (p=0.000).

Regarding non-menstrual migraine, the prevalence of ages 41-50 was 35.1%, which is significantly higher than the prevalence of ages 20-30, in 10.5% of subjects suffering from migraine (p=0.002).

Since p = 0.078 it can be said that there is an association, with an increased risk for making conclusions, between the migraine subtypes and age structure.

Table 1. Cumulative responses to general questions (age, marital status, children, education)

<table>
<thead>
<tr>
<th>Age</th>
<th>Marital status</th>
<th>Children</th>
<th>Education</th>
</tr>
</thead>
<tbody>
<tr>
<td>20-30</td>
<td>Single</td>
<td>yes</td>
<td>114 Elementary school</td>
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<tr>
<td>31-40</td>
<td>Married</td>
<td>no</td>
<td>34 Secondary school</td>
</tr>
<tr>
<td>41-50</td>
<td>Divorce</td>
<td></td>
<td>17 2-year college</td>
</tr>
<tr>
<td>51-60</td>
<td>Widower</td>
<td></td>
<td>35 University education</td>
</tr>
</tbody>
</table>

Table 2. Cumulative responses to general questions (type of company, overtime work, smoking, family history, and chronic disease)

<table>
<thead>
<tr>
<th>Type of company</th>
<th>Overtime work</th>
<th>Smoking</th>
<th>Family history</th>
<th>Chr. disease</th>
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</thead>
<tbody>
<tr>
<td>Public</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Private</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Mixed</td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

Table 3. Prevalence of migraine subtypes across age, expressed as numbers (n) and percentage (%)

<table>
<thead>
<tr>
<th></th>
<th>51-60</th>
<th>41-50</th>
<th>31-40</th>
<th>20-30</th>
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<tbody>
<tr>
<td>PMM</td>
<td>0</td>
<td>4</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>MRM</td>
<td>11</td>
<td>32</td>
<td>29</td>
<td>12</td>
</tr>
<tr>
<td>NMRRM</td>
<td>18</td>
<td>20</td>
<td>13</td>
<td>6</td>
</tr>
<tr>
<td>Total</td>
<td>29</td>
<td>56</td>
<td>45</td>
<td>18</td>
</tr>
</tbody>
</table>

Table 4. Prevalence of migraine subtypes across levels of education

<table>
<thead>
<tr>
<th>Education</th>
<th>Elementary school</th>
<th>Secondary school</th>
<th>2-year college</th>
<th>University education</th>
</tr>
</thead>
<tbody>
<tr>
<td>PMM</td>
<td>1</td>
<td>5</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>MRM</td>
<td>2</td>
<td>49</td>
<td>10</td>
<td>23</td>
</tr>
<tr>
<td>NMRRM</td>
<td>5</td>
<td>34</td>
<td>6</td>
<td>12</td>
</tr>
<tr>
<td>Total</td>
<td>8</td>
<td>88</td>
<td>17</td>
<td>35</td>
</tr>
</tbody>
</table>

Figure 1. Prevalence of migraine and migraine subtypes in working women
Since \( p = 0.078 \) of \( \chi^2 \) - test, and \( \chi = 0.267 \) with confidence interval (0.141-0.393) it can be said that there is weak association between migraine subtypes and age structure.

By observing presented data (Table 4), it can be noticed that in the whole sample of working women suffering from migraine in relation to educational level, the most prevalent was secondary school 59.46%, which is significantly higher than the prevalence of university education 23.65% \( p=0.000 \), 2-year college 11.49% \( p=0.000 \), and elementary school education 5.41% \( p=0.000 \). Regarding individual migraine types, the results obtained for pure menstrual migraine were the most different.

Since \( p = 0.396 \) it can be said that the method of \( \chi^2 \) test did not determine association between migraine subtypes and educational level.

Since \( p = 0.396 \) of \( \chi^2 \) - test, and \( \chi = 0.201 \) with confidence interval (0.077 - 0.325) it can be said that there is weak association between migraine subtypes and educational level.

Since (Table 5) \( p > 0.1 \), this means that no significant difference was observed between the three migraine subtypes for responses related to type of employment (\( p=0.258 \)), marital status (\( p=0.328 \)), family status (\( p=0.158 \)), overtime work (\( p=0.286 \)), or smoking (\( p=0.843 \)).

Since \( p < 0.1 \), this means there was a significant difference between some of the three migraine subtypes in responses related to age structure (\( p=0.007 \)), level of education (\( p=0.056 \)), family history of headache (\( p=0.069 \)), and presence of another chronic disease (\( p=0.030 \)).

Discriminative analysis was applied, where \( p=0.009 \), which means there is a significant difference and a clear delineation between some of the migraine subtypes.

Discrimination coefficient shows that the greatest contribution to discriminating migraine subtypes (i.e. that the difference was greatest) with regard to the responses obtained to the questions about family history of headache (0.053), followed by age structure (0.051), level of education (0.045), family status (0.045), marital status (0.033), another chronic disease (0.022), type of employment (0.016), overtime work (0.014), and smoking (0.011).

**Discussion**

Primary headaches are the most prevalent among professionally and reproductively active population. Over the past two decades significant advances have been made in the data collection and understanding of the pathophysiology, pharmacology, genetics and epidemiology of migraine, although there are still numerous issues that need further clarification. New developments in each of these fields will contribute to a more comprehensive understanding of this significant medical problem. However, in our region epidemiological data that could shed light on the magnitude of the problem are still scarce, and our study therefore aimed at contributing to clarification of the problem. The results we obtained are in accord with other similar studies.

The most frequently reported data is that over 10% of the world’s populations suffer from migraine, with migraine being three times more prevalent in women than in men (16, 17). American Migraine Study II (AMS II) published in 2001 and based on the research done in 1999, ten years after the first study (AMS I), shows the prevalence of migraine in women to be 18.2%. An epidemi-

<table>
<thead>
<tr>
<th>Table 5. Significance of differences between migraine subtypes in relation to responses to general questions</th>
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<tbody>
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<tr>
<td>Age</td>
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<td>Type of employment</td>
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<td>Marital status</td>
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<td>Children</td>
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<td>Education</td>
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<td>Overtime work</td>
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<td>Smoking</td>
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<td>Family history</td>
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<td>Chronic disease</td>
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</table>
ological study of migraine carried out in Sivas, Turkey, in the first half of 1999, by interviewing 1320 persons suffering from headache older than 7 years, showed migraine prevalence in women of 17.1% (18).

In our study of working women aged 20-65 years, 148 (20.69%) out of 715 subjects had migraine. We can therefore conclude that the prevalence of migraine in our region is similar to that found in other studies, and a somewhat higher prevalence was expected considering the age of the studied population in our study.

The significantly higher prevalence of migraine in women and its decline with advancing age indicates that migraine attacks in women are associated with the hormonal status. Numerous physiological mechanisms during a menstrual cycle have been proposed as a possible basis of menstrual migraine. Decrease in oestrogen levels, magnesium deficiency and changes in the neurotransmission system during menses are possible causes of attacks of menstrual migraine (19).

Migraine without aura in women is frequently associated with menstruation. The latest classification of headache disorders includes menstrual migraine without aura in its appendix, indicating that further research in this field is needed before this entity can be moved into the main body of the classification (4). Inconsistent classification criteria are one of the reasons why the prevalence of menstrual migraine ranges from 4% to 73% in literature data, depending on the criteria used for defining the onset of a migraine attack (14, 15). As mentioned before, menstrual migraine can be classified into two types: pure menstrual migraine and menstrual-related migraine (5). In our study we divided migraineurs into those suffering from pure migraine, those suffering from menstrually-related migraine, and those suffering from non-menstrual migraine. This division was governed by the assumption that pure menstrual migraine occurs only during menstruation. For the diagnosis of pure menstrual migraine, we used MacGregor’s definition that distinguishes menstrual migraine as an attack of migraine without aura, occurring regularly on the first day of menstruation or on two days before or after menstruation, and at no other times (6). By these criteria, 4.73% of all women migraineurs in our study had pure menstrual migraine.

The prevalence of menstrually-related migraine has been reported to range between 35% and 68% (20, 21). In our study, the prevalence of this type of migraine was 56.76%, whereas non-menstrual migraine was present in 38.51% of subjects suffering from migraine. Moreover, we found a significant difference between the three studied subtypes of migraine in relation to age, level of education, family history of headache, and presence of another chronic disease.

The prevalence of migraine varies with age, it starts increasing with menarche and reaches its peak at the age of 42, after which it declines (9, 12). The prevalence is the highest during the fourth decade of life in both sexes, and according to Lipton et al it is 7.4% in men and 24.4% in women (22). In the AMS I the highest prevalence was found between the ages of 35 and 45 years (12). The age groups in our study were formed using a different methodology and subjects were only women, so our comparison can only be indirect. Our results show that 68.25% of women suffering from migraine were 31-50 years old; 30.41% in the age group 31-40 years, and 37.84% in the age group 41-50. Moreover, we found significant differences in the prevalence of the three migraine subtypes in relation to age. Namely, no subject in the age categories 20-30 and over 50 years suffered from pure menstrual migraine. The groups of subjects suffering from menstrually-related migraine and non-menstrual migraine had a typical distribution of prevalence that first increases with age and then declines. In addition, in the group with non-menstrual migraine the prevalence in the oldest age category was significantly higher compared to the other two types of migraine, which was expected considering menopause.

Previous studies have not found association between the level of education and the prevalence of migraine (18). Our study corroborates that the level of achieved education has no significant impact on the occurrence of migraine; however, it can contribute to differentiation of migraine subtypes. Namely, regarding education, there was no difference in the distribution of prevalence.
between the whole study sample and the sample of migraineurs, with the prevalence being the highest among subjects with secondary education, followed by those with college and university education, whereas the lowest prevalence was found among those with elementary school education. Regarding the distribution across the levels of education in relation to migraine subtypes, only pure menstrual migraine showed deviation from this pattern of distribution. Namely, in pure menstrual migraine, the highest number of subjects had completed secondary school education, there were no subjects with a university diploma, and there were equal numbers of subjects with college and elementary school education, with the difference between pure menstrual migraine and other migraine subtypes being significant only in relation to the prevalence of subjects with elementary school education.

A strong genetic predisposition to migraine has been well established. If only parents and children with migraine are taken into account, 46% have a positive family history of migraine (23), and the percentage further increases with inclusion of other relatives. The information about the presence of headache in relatives is of great importance for prediction of migraine, and it can be of use in determining the subtype of migraine. In contrast to menstually-related migraine and non-menstrual migraine, in which almost two thirds of sufferers have relatives who also suffer from headache, in pure menstrual migraine only 14.3% of sufferers have relatives with headache, which is similar to the percentage present in healthy population. This finding requires a larger study sample suffering from pure menstrual migraine.

A thorough history of previous and current diseases is essential for a complete insight into possible contraindications and for the choice of a treatment option. Moreover, a complete medical history is necessary for determining possible presence of more than one type of headache and indications for supplementary diagnostic procedures in order to exclude or confirm a secondary headache (24, 25). In our study 33% of migraine sufferers had a chronic disease. Furthermore, we found that other chronic diseases were less frequent in menstually-related migraine (26.2%) than in non-menstrual migraine (45.6%). Chronic diseases were the least frequent in subjects suffering from pure menstrual migraine (14.3%), with a statistically significant difference compared to the other studied subtypes.

The analysis of study results did not show a significant difference between the three migraine subtypes in relation to marital status, family status, type of employment, overtime work, and smoking.

A study of 1320 residents of Sivas, Turkey, suggested that marital status had no significance for the prevalence of migraine (18). We found that both in the overall study sample and individual migraine subtypes the greatest number of sufferers was among those who were married, followed by single women, divorcees, and widows. However, there was no significant difference among the groups, or between each group and the whole sample.

In addition to marital status, we investigated the influence of family status, i.e., the subjects were asked whether they had any children, and if so, how many. The analysis of results did not show association between the presence and subtypes of migraine on one hand and family status on the other.

Considering that our country is in a state of social and political turmoil, our study paid attention to the type of enterprise the subjects were employed at: public, private or mixed. The greatest number of subjects, both in the overall sample and migraineurs, were employed in public companies; however, there was no significant association between the type of employment and the presence of migraine or its subtype.

An everyday occurrence nowadays is that a considerable number of employees work overtime, either voluntarily or compulsory and we took this fact into account in our study. Among our subjects suffering from migraine, 37.84% reported overtime work, while significantly higher percentage, 62.16%, did not work overtime. However, we found no association between overtime work and migraine subtype.

It is well known that healthy lifestyles can contribute to reducing frequency and severity of headache. It is recommended that a person suffering from migraine should avoid smoking and staying in smoky rooms, caffeine and alcohol, and stressful situations, and should practice regular physical exercise and respect normal rhythm of sleep.
and rest (23). While some of the factors can be influenced and corrected, others cannot.

Smoking is a bad habit, to say the least, and it is also a significant risk factor for numerous diseases, and in some cases it is also an addiction disorder. Given the limited number of studies on the relationship between smoking and headache, we analyzed the structure of our subjects in relation to smoking. In the overall sample of women migraineurs, there were an equal number of smokers and non-smokers. Regarding the migraine subtype, the highest number of smokers was found among women with non-menstrual migraine (52.6%) and the lowest among those with pure menstrual migraine (42.9%). However, there was no significant association between the studied migraine subtypes and smoking.

Conclusion

Migraine in women deserves special attention. The prevalence of migraine in professionally active women in our region is 20.69%. Among the women suffering from migraine, 4.73% have pure menstrual migraine, 56.76% have menstrually-related migraine, and 38.51% have non-menstrual migraine.

Our study corroborates the relationship between sociodemographic characteristics and migraine. The established specificities and differences between the migraine subtypes in relation to sociodemographic characteristics among working women suggest the need for further more extensive research in this file.

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Abbreviations:
ICH - International Classification of Headache Disorders
MANOVA - multivariate analysis of variance
PMM - pure menstrual migraine
MRM - menstrually-related migraine
NMRM - non-menstrual migraine
AMS - American Migraine Study

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The impact of various factors on self-care of elderly

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Abstract

Introduction: This study is focused to describe the self-care of home-dwelling elderly people living in Slovenia and factors affecting to self-care. The purpose is to describe the experiences of the elderly people’s ability to manage at home.

The aim of this study was to produce new knowledge about the self-care of home dwelling elderly people living in Slovenia and the factors connected with it. The knowledge could be used to develop elderly care and support elderly people who live at home and the knowledge could be also used to educate nurses to care for the elderly people.

Methods: The quantitative structured data was collected by interview of home-dwelling elderly people all over Slovenia. The sample consisted of 302 home-dwelling elderly people who were clients in domiciliary care. The selection criteria were: aged 75 years or over and the ability to communicate, no hearing problems, no severe mental problem/cognitive disability and gave full consent for their participation. Community nurses selected elderly people in their homes. Descriptive statistics was used for presentation of sample background information and cross tabulations for presentation of results. Factors were extracted by factor analysis.

Results: Extracted self-care factors (handling of everyday tasks, relationship with health care staff, medication handling, and medical treatment) were often in significant relations to elderly people’s perceptions concerning either their past or their future (physical condition, family relations, meaningful and stimulating ageing, working habits etc).

Discussion and conclusions: Self-care is combined with functional capacity, stimulative ageing and acceptance of the future. Quality old age depends a great deal on the habits and approaches to life in the previous active years. A general preventive and other measures, and strivings for healthy habits and lifestyle, are the way to healthy ageing. It is upon each of us how the process will be directed.

The results may present the basis for care planning by caregivers, especially community nurses. On the basis of this results the model of nursing and social care for home-dwelling elderly people living in Slovenia could be planned.

Key words: self-care, factors, home-dwelling, elderly people

Introduction

At the start of the twenty-first century, one of the most profound social changes to occur in developing societies is that the population is older (Backman, Hentinen 1999; Čačinovič Vogrničič, 2000; Zeleznik, 2005; Dragoš, 2004; Hendry in McVittie, 2004, Kempen et al., 2006). This change is a result of social and scientific developments over the course of the previous century, resulting in the addition of 25 years to life expectancy (Ravovš, 2003; Dean, 2003). This demographic trend has meant that, in Europe, elderly people represent twenty per cent of the total population and demographic projections anticipate significant increases in this section of the population; these projections predict that the proportion of the elderly people in Europe as a whole will increase to twenty five per cent by the year 2025 (European
Commission, 2000). According to (Cheng, 2006; Baltes in Baltes, 1990), ageing is more than a series of biological changes. It is defined by gender, class, social standing, and culture rather than year alone. Ageing is for the individuals regarded as something unpleasant, useful, and unnecessary and above all, unwanted. Owing to economical crisis the whole relationship to people in older years has been changed. The old aged people feel themselves to be useless. There are still some stereotypes that old aged people are unnecessary and inferior (Mesec, 2000; Zupančič, 2004).

One important factor allowing an elderly people to live at home is self-care. Self-care means to take care of his/her own self it is a part of an individual lifestyle, which is shaped by values and beliefs learned in specific cultures (Slovar slovenskega knjižnjega jezika, 2005). Self care practices are seen to reflect elderly people’s individual styles and adaptations specific to their personal histories, current circumstances and views of the future. According to Backman in Hentinen, (2001), self-care seems to be connected with the personal experiences of each old woman or man. Self-care is the personal care that individuals require each day to regulate their own functioning and development (Orem et al., 2001; Allender in Spradley, 2001). Self-care is supposed to be the key to health and illness care (Aggleton in Chalmers, 1985; Orem, 2001; Toljamo in Hentinen 2001; William, 2004, Parissopoulos in Kotzabassaki, 2004). The theory of self-care proposes that individuals learn and deliberately perform for themselves or have performed for them (dependent care) on a continuous basis those actions that are necessary to protect human integrity, physical and mental functioning, and development within norms essential for promoting life, health and well-being (McAuley et al. 2000; Denyes et al. 2001; Tomey in Alligood 2002; Allison, 2007). Physical activity seems to be an important factor when older people assess their health (Leinonen in Jylhä 2001). According to Teel in Leenerts, (2005), self-care responses appear to be learned within the social context early in life, be reinforced through the life cycle, and evolve through cooperation with both professional and lay persons.

Self-care has traditionally been defined as activities associated with health promotion (Backman, Hentinen 1999; Backman, 2003). It represents the range of behaviours undertaken by individuals to promote or restore their health. The activities of daily living, such as exercise, nutrition and relaxation, are often used to measure self-care. Orem, (1991) has started: “self-care means care that is performed by oneself for oneself when one has reached a state of maturity that enables consistent, controlled, effective, and purposeful action”. The aim of such rational self-care is to maintain health. In this way, self-care is seen as a rational, conscious way to operate. In this presentation, self-care activities are not seen merely as rational ways to maintain health. Self-care is not only a conscious way to act, but partly also a subconscious routine that has been shaped in the course of life. Self-care is not a separate part of old men’s or women’s lives. It is associated closely with both their past life and the future. Such knowledge of the self-care of elderly people helps us to understand many aspects of self-care and its associations with vulnerability in later life.

**Methods**

Quantitative research method was used. Quantitative study is needed to get a general picture and to describe what the self-care of home-dwelling elderly people is like in Slovenia, because we don’t have any knowledge of that. Quantitative research methods assume that the world is stable and predictable, and phenomena can be measured empirically (Christensen, Kackrow, 2003). The positivist tradition of quantitative research derives from the biomedical sciences (Topping, 2006). Quantitative researchers focus on a very specific area and plan every detail (Polit, Beck, Hungler 2006). The purposive sample involves the conscious selection by a researcher of a certain criterion.

**Data collection**

The data was collected in Slovenia by interviewing elderly people in their homes by structured instrument. The community nurses selected and interviewed the elderly people in their homes who fulfilled the criteria (over 75 years old, does not
have a profound hearing problem, does not have a severe mental problem/cognitive disability, can speak Slovene, can give fully informed consent of their participation). All the home–dwelling elderly people in this study were capable of describing their experiences of self-care and they were very interested to discuss and share their opinions.

**Instrument**

The whole instrument consists of 91 items and covers background data, and the following subscales measuring the following factors: types of self-care, self care orientation, functional ability, life satisfaction and self-esteem. The original instrument had been used previously in the Finnish language, it was based on Backman’s theory of the self-care of elderly people and it was used and tested in Finland. The reliability and validity was found to be good (Räsänen, Backman, Kyngäs, 2007). In order to use the instrument in this study, it had to be translated from Finnish into English and then to Slovene language following instructions by Harkness, (2003). Before using the instrument, it was pre-tested by five elderly people. The researcher asked the participants to read the instrument very carefully and give their comments. In their opinion, units, sentences and statements were logical, understandable and unambiguous.

Cronbach’s alpha coefficient for the reliability of the instrument in this study was highly accepted for self-care orientation. The alpha values were as follow: self-care 0.75, self-care orientation 0.60, self-esteem 0.75, life-satisfaction 0.84 and functional capacity 0.95.

**Data analyses**

The data were analysed by exploratory factor analyses - principal component analyses with varimax rotation and an unlimited number of factors (Burns in Grove 2005; Gillis in Jackson 2001). Before the final exploratory factor analyses, all items with low correlation coefficients (under 0.400) were omitted (Polit, Beck, Hungler 2006; Gillis in Jackson 2001). Items with factor loadings under 0.400 were also omitted, and missing values were excluded likewise. Factors were extracted using the following guidelines: eigenvalues were greater than one in all factors and the factors showed a reasonable structure in terms of the theory underlying the instruments (Gillis in Jackson 2001; Holloway in Wheller 2002; Gerrish in Lacey 2006). Sum variables have been made for each factor of self-care of home-dwelling elderly people and separated them into three 3 categories (good, moderate, poor), using percentiles. The procedures of sum variables calculations was done by adding together all the items of each factor divided by the total number of those items (Teeri et al. 2008). The relations between the factor variables were analyzed using cross-tabulations and χ² tests.

The statistical calculation was made by SPSS (Statistical Package for the Social Sciences) 12.0.1. SPSS supported all statistical methods used in this study. P-value<0.05 was considered significant.

**Ethical considerations**

The Board of the Ethical Committee in Slovenia approved this research study into home–dwelling elderly people. The permission to use the instruments was given by the Ethical Committee in Slovenia. In this study it was emphasized that participation was completely voluntary. Written consent was obtained from each elderly person. Anonymity and confidentiality were assured and permission. Participants were advised that their participation was entirely voluntary and that they had the right to withdraw from the study at any time. Participants were assured that their confidentiality would be protected and findings reported anonymously. Quantitative information was obtained using anonymous instruments.

**Results**

The factor analysis started with 42 items and 6 items were omitted based on the criterion. A twelve-factor solution was specified, 4 factors described self-care and 8 factors describe elderly people’s perceptions concerning either the past or the future. For all extracted factors sum variables
were calculated and, according to percentiles, separated into 3 equal categories (poor, moderate and good). The relations between the factor variables were analysed using χ² tests. There were statistically significant connections between the self-care behaviour and experiences of health and ageing and attitudes towards other people (table 1, cells include p-values). These connections were present in nearly all calculations. Some relations were also found to ageing and the future and to elderly people’s background.

The results of χ²-tests for the first extracted self-care behaviour factor (handling of everyday tasks) showed statistically significant connections to physical condition, family relations, meaningful and stimulating ageing and to working habits (table 2). More than 80% of the elderly people who managed everyday tasks well had good (52%) or moderate (30%) physical condition. 60% of the elderly people and more who managed everyday tasks well had good family relations. More than 80% of the elderly people who managed everyday tasks well

<table>
<thead>
<tr>
<th>Elderly people background</th>
<th>physical condition</th>
<th>family relations</th>
<th>meaningful and stimulating ageing</th>
<th>future perceptions</th>
<th>working habits</th>
<th>past events</th>
<th>confidence</th>
<th>future perspectives</th>
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</thead>
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<td>&lt;.001</td>
<td>&lt;.001</td>
<td>&lt;.001</td>
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<td>.497</td>
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<td>.003</td>
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<td>.708</td>
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<td>.901</td>
<td>.002</td>
<td>.033</td>
<td>.241</td>
<td>.124</td>
<td>.229</td>
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<td>.019</td>
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<td>.262</td>
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<td>.076</td>
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<th>χ²</th>
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<td></td>
<td>Poor n</td>
<td>%</td>
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<td>Physical condition</td>
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<td>36</td>
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<td>27</td>
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<td>Working habits</td>
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<tr>
<td>Total</td>
<td>75</td>
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</tbody>
</table>
had meaningful and stimulating ageing (good 40 % and moderate 43 %). Also nearly 80 % of the elderly people who managed everyday tasks well had good (50 %) or moderate (30 %) working habits.

The results of χ²-tests for the second extracted self-care behaviour factor (relationship with health care staff) showed statistically significant connections to physical condition, family relations, meaningful and stimulating ageing, working habits and future perspectives (table 3). Nearly 80 % of the elderly people who enjoyed good relations with health care staff had good (48 %) or moderate (29 %) physical condition. More than 60 % of the elderly people with good relationships with health care staff had good family relations. Over 80 % of the elderly people with good relationships with health care staff had meaningful and stimulating ageing (good 43 % and moderate 41 %). More than 80 % of the elderly people with good relationships with health care staff had good (54 %) or moderate (30 %) working habits. All results confirmed the results of the first self-care behaviour factor (handling of everyday tasks).

The only contradiction represented factor future perspectives, describing ageing and the future with only one item: “I am going to continue living at home, no matter how sick I may become”. Nearly 90 % of the elderly people with good relationships with health care staff had poor (62 %) or moderate (26 %) future perspectives. The elderly people who had good relationships with health care staff (and also in most cases practice healthy self-care behaviour) had difficulty to accept that they will probably have to leave their homes at some stage.

The results of χ²-tests for the third extracted self-care behaviour factor (medication handling) showed statistically significant connections to physical condition, meaningful and stimulating ageing and future perceptions (table 4). Nearly 80 % of the elderly people with poor medication handling had good (37 %) or moderate (36 %) physical condition. These results show that the elderly people in good physical condition show some signs of irresponsible self-care, but correlation was not strong. More than 80 % of the elderly people with good medication handling had good (26 %)

### Table 3. Relations with health care staff and factors connected to them (N=302)

<table>
<thead>
<tr>
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<th>n</th>
<th>%</th>
<th>n</th>
<th>%</th>
<th>n</th>
<th>%</th>
<th>χ²</th>
<th>P-value</th>
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<td></td>
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<tr>
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<td>30</td>
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<td>26</td>
<td>33</td>
<td>48</td>
<td></td>
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<td></td>
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<tr>
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<td>100</td>
<td>69</td>
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<td></td>
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<td>&lt;0.001</td>
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<td>Moderate</td>
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<tr>
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<td>69</td>
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<tr>
<td>Meaningful and stimulating ageing</td>
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or moderate (55 %) family relations. Nearly 80 %
of the elderly people with good medication han-
dling had good (38 %) or moderate (30 %) future
perceptions, but also correlation was not strong.

The results of χ²-tests for the fourth extrac-
ted self-care behaviour factor (medical treatment)
showed statistically significant connections to fami-
ly relations, meaningful and stimulating ageing and
to future perceptions (table 5). The elderly people
with good medical treatment had good (38 %) or
moderate (38 %) family relations. More than 80 %
of the elderly people with good medical treatment
had meaningless and unstimulating ageing (poor 35
% and moderate 46 %). More then 70 % of the el-
derly people with good medical treatment had good
(42 %) or moderate (34 %) future perceptions.

Discussion

Noted by Fung in Carstensen (2002), any syn-
thesis of the self-care of the elderly people and
related factors based on the existing research
knowledge is hampered by the fact that self-care
and related factors have been defined from diffe-
rent theoretical viewpoints and operationalized in
a number of different ways. Roughly speaking,
it can be said that advancing age and declining
functional capacity are likely to affect self-care at
some point of the life span (Norburn et al., 1995).
The knowledge of elderly people home–dwelling
self-care is not clear. Most studies are quantitative
which measure and compare two or more factors
which have been defined and measured in diffe-

Table 4. Medication handling and factors connected to it (N=302)

<table>
<thead>
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<th>Medication handling</th>
<th>χ²</th>
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<td>Total</td>
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Table 5. Medical treatment and factors connected to it (N=302)

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rent ways. Because of the lack of knowledge of the levels of self care of home-dwelling elderly people this study is based on Backman’s theory 1999 of the self care of home-dwelling elderly people. According to Backman’s study 2003 and some other studies (Zasuszniewski, 1996; Rabiner et al., 1997), the self-care of elderly people is found to be linked to functional capacity, satisfaction with life and self-esteem (Toljamo, Hentinen, 2001; Isola et al., 2003; Fagerström et al., 2007). These factors were also studied here.

Based on factor analyses, four factors were found which described the self-care. All other factors described elderly people’s perceptions concerning either the past or the future. The elderly people who were able to manage their daily activities/routines had good functional capacity, good family relations, live qualitatively, accept the future positively and clearly and are satisfied with their life because they can take care of themselves. Elderly people, whose life was full of heavy labour, are more responsible for self-care with high levels of life satisfaction. They are responsible for their health, therapies and maintaining functional capacity and they are satisfied with their own life. Careful treatment with medicaments is connected with stimulative ageing and clear acceptance of the future.

The elderly people who had good relations with health care staff were in good physical condition, had good family relations and had meaningful and stimulating ageing. They were also proud of their past and present working performance. The future perspectives factor describes the elderly people’s desire to stay at home at any cost; this is the only negative experience of their self-care.

Estimation of elderly people should be founded on the level of their functionality and not according to chronological age. Functional level is the accurate indicator of the difficulties experienced by elderly people and the required interventions. Functional capabilities range from complete independence to complete dependence, accompanied by different/various physical, cognitive, psychological and emotional deprivation (Hagberg et al., 2004).

According to Gerson, Berg, (2004) the increase in size of older groups of the population has set new demands for the development of existing established means of providing support to the elderly people which, at the same time, calls for an organised approach to the development of new forms of care - educational forms in the field of gerontological nursing.

In order to understand self-care of the elderly people living in Slovenia it is necessary to understand that elderly people would like to live as long as possible at home and care for themselves in daily living. According to (Hobbs Leenerts et al., 2002; Teel in Leenerts, 2005; Allison, 2007), self-care consists of the action systems performed by individuals in time and in conformity with health care requirements that are associated with their growth and development, their state of health and health-related conditions, the environment, and other influencing factors.

**Conclusion**

The self-care of home-dwelling elderly people who are able to manage their daily activities, are in good functional capacity and who have good family relations, live qualitatively and have meaningful stimulating ageing. They are proud of their past and present working performance. Their self-care is at a high level. Elderly people whose life was full of heavy labour are more responsible for self-care with high levels of life satisfaction. They are responsible for their health, therapies and maintaining functional capacity and they are satisfied with their own life.

In the process of planning public care for the elderly population it is of vital importance that the middle generation of today becomes prepared for their old age. Otherwise, social problems of the elderly population will be impossible to manage. Healthy way of life, better human and generational relationships, respectfulness, tolerance, solidarity, and before all, treating old age as equally valuable period of life are important for one’s self-care in old age.
References


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Generic medicines: Perceptions of Pharmacists in Basrah, Iraq

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Abstract

Background: The use of cheaper generic medicines is a strategy promoted in many countries to reduce rising health care costs. The objective of this study was to investigate generic medicine dispensing trends and substitution practice from the perspective of pharmacists in Basrah, Iraq.

Methodology: A qualitative approach was used to gather information from the pharmacists in the city of Basrah, Iraq. A purposive sample of ten pharmacist practicing in Basrah was interviewed face to face using a semi-structured interview guide.

Results: A total of ten pharmacists were interviewed. Thematic content analysis of the interviews identified five major themes: Generic Medicines substitution practices, Knowledge about generic medication, Quality and safety of generic medicines, Patient education by pharmacists regarding generic medicines, and Strategies to improve generic medicine utility.

Conclusion: The present study suggested that, in general pharmacists interviewed in Basrah city were positive towards the use of generic medicines. Patient should be educated to increase the use of generic medicines in the future.

Key words: Generic medicine, bioequivalence, perceptions, substitution

Introduction

Generic medicines provide the opportunity for major savings in healthcare expenditure to both government and consumers, given that they are generally lower price than their counterpart branded.

In Iraq, the Ministry of Health (MOH) is responsible for importing medicines from companies that are previously registered with KIMADIA (the state company for importation and distribution of drugs and medical appliances). The MOH distributes imported pharmaceuticals to the public and private sectors (private pharmacies) after obtaining permission from the Drug National Quality Control Laboratories (DNQCL). Iraqi law requires all drugs to be marketed via the KIMADIA system. For over 20 years, KIMADIA has been the sole body authorised to carry out management, planning, selection, quantification, procurement, storage and distribution of medicines and medical equipment. In 1989, it was estimated that 70% of drugs were imported. The other 30% came from Samara Drugs Industries (SDI), a government agency. Until 1994; the supply of medicines was dominated by the public sector. Approximately 90% of the drugs purchased using public funding was allocated to the public sector. Currently, there is no social health insurance system exist in Iraq. There are very small, isolated health insurance programs for employees of specific companies. At present, however, there is no system for reimbursement for money spent by public on private prescriptions in the country. Thus, ensuring the availability of high-quality drugs at affordable prices in Iraq is a public health priority. Prescribing drugs by generic name and encouraging pharmacists to dispense prescriptions with generic medicines is one frequently suggested means for lowering the costs of healthcare. Various articles have discussed the implications of generic substitution and other strategies to reduce pharmaceutical expenditure. The concept of dispensing and using generic medicines has been controversial, however. Concern has been expressed by pharmacists elsewhere about the efficacy of generic medication. This debate has centered on issues...
related to bioequivalence and potential confusion that might arise when changes of medicine brands occur in some patient populations.\textsuperscript{14,9} The theoretical framework for this study calls on bounded rationality theory which predicts that the quality of the decisions we make are limited by the available information and our ability to synthesize that information.\textsuperscript{15} A review of the available literature revealed that a few studies have been carried out in the USA and France, but no studies have been performed in Iraq to explore pharmacists’ perceptions regarding the use of generic medications by the consumer. As a result of differences in pharmacy practices and the health care system between Iraq and western countries, the results of such a study would be a significant contribution to the field. Therefore, the aim of this study was to explore perceptions held by Iraqi pharmacists towards the use of generic medicines.

Method

Since little research has been carried out in Iraq to identify pharmacists’ perceptions of generic medicines, qualitative methods were used to gain understanding of this issue.\textsuperscript{16,17} A qualitative approach was adopted because it allows a flexible exploration of informants’ attitudes and experiences and produces a richness of data that allows the researcher to gain a deeper understanding of social phenomena., \textsuperscript{18,19} One of the challenges faced in the process of recruitment was to obtain a varied sample of informants to participate in the interviews. To address this, purposive sampling procedure was used. The advantages of purposive sampling are that it is cheaper and time-saving to implement in comparison to other sampling procedure. Semi-structured interviews were conducted with pharmacists until we reached saturation of themes.\textsuperscript{20,21} The interview guide was developed following an extensive review of the literature on similar studies conducted elsewhere. Pharmacists were approached personally by the researcher at their private pharmacy hospital. Ten pharmacists consented to be interviewed. The interviews focused on the following issues: generic medicine dispensing preferences, knowledge about and confidence in the generic medication, and patients’ acceptance of generic prescriptions. Follow-up questions were used when necessary to get a more in-depth explanation and to draw out more complete ideas from the participants. They were given freedom to express additional views on the subject at the end of the interview time.\textsuperscript{22}

All interviews were conducted at a place suitable for the participants: eight at their private pharmacy and two in hospital pharmacy in Basrah province. Interviews took an average of 20-30 minutes. They were conducted by the investigator in his native language (Arabic). Interviews were documented and transcribed verbatim by qualified transcribers. Transcripts were confirmed by the researcher, corrections (if needed) were made before copies of the transcripts were sent to the respective physicians for their endorsement. The researcher manually analysed all of the transcripts line-by-line for relevant content and themes.\textsuperscript{23,24} Ten interviews were required to achieve saturation of the themes, and no new themes emerged in the last three interviews.

Results

Characteristics of participants

Ten pharmacists were interviewed. Eight of them worked in urban areas, and the other two were in rural settings. Demographic characteristics are summarised in Table 1.

\textbf{Table 1. Pharmacists’ demographic characteristics (n=10)}

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<td>Female</td>
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<td>Mosul University</td>
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<td>Work place</td>
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<td>College of pharmacy (lecturer)</td>
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<td>Government hospital</td>
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<td>Private pharmacy</td>
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<td>More than 10 years</td>
<td>7</td>
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<tr>
<td>Less than 10 years</td>
<td>3</td>
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</table>
All the interviews were conducted at the pharmacists’ workplaces (two in hospital pharmacies and the others at the pharmacists’ private pharmacies).

Themes

Five major themes emerged when the interview content was reviewed: generic medication substitution practices, knowledge of and confidence with generic prescriptions, quality and safety of generic drugs, pharmacist’s roles in educating patients regarding generic substitutions and strategies to improve their use of generic medications. The themes are presented below.

Theme 1
Generic Medicines substitution practices

Nearly, all the pharmacists interviewed have recommended generic medications to consumers.

“Normally, we dispense generic medicines, unless the patient requests to have of innovative medicine” (p01)

“I recommend the generic and innovative medicines and leave the choice to the patient” (p03)

Interestingly, the relatively inexpensive cost of generic medications leads pharmacists and patients to choose generic over innovative drugs.

“Medicine price is one of the important factors that makes the patient favour the generic medicine. For example, the price of Zantac® (Ranitidine 150 mg) is ID15000 (US$=12.5) for sixty tablets, while the price of Histac is ID 2000 (US$ 1.6)” (p10)

“I recommend generic medicine because it is cheap for the patient and more profitable to the pharmacy” (p07)

A patient’s income status affects the pharmacists’ recommendations.

“Patients with low income request a cheaper medicine; therefore offering generic medicine will help patients to buy such medicines” (p06).

Another factor which encourages pharmacists to dispense generic medications is the availability of generic medicines in drug stores. Innovative drugs are more difficult to obtain.

“The availability of generic medicines in drug stores constantly encourages the pharmacist to recommend them to the patients, in contrast to the innovator medicines, which are difficult to obtain continuously “ (p02)

Though most pharmacists recommend generic medications, certain circumstances make them reluctant to use the generic over the innovative drug. When the physician does not want generic medicines, pharmacists respect the physicians’ recommendations. Furthermore, the nature of the disease affects pharmacists’ willingness to use the generic form of a drug.

“The doctor does not agree to switch medicines is one of the factors that prevent me from offering generic medicines to the patients “(p01)

“If the patient was satisfied and stabilized with the innovator medicine, I don’t offer generic medicines, especially in the cases of chronic disease” (p05)

In Iraq, patients’ trust in their physicians’ choice of innovative medicine was seen as a barrier to offering generic medicines.

“Some patients are convinced with what the physician prescribes to them, so I don’t offer generic medicine to these patients” (p 03).

Confusion is one barrier that prevents pharmacists from recommending generic medications. This is especially pertinent with respect to elderly patients and patients treated with multiple medications.

“I don’t offer generic medicine to the elderly people who use innovative medicine and they are comfortable with it, or to those who take more than one type of medicine to avoid getting them confused “ (p04).

“I do not offer generic medicines to any refill prescription because I am afraid of confusing the patient” (p09).
Some pharmacists have realised that many patients, especially from those from rural areas, do not believe that generic medications are effective.

“Actually, in my pharmacy I don’t recommend generic medicine to patients (especially those patients from rural areas) who do not believe in the effect of generic medicines” (p03).

**Theme 2**
**Knowledge about generic medication**

Pharmacists were questioned about the bioequivalence criteria required by the WHO and/or FDA, KIMADIA and DNQCL in Iraq, for approval of a generic medication. We found that the pharmacists have little or no knowledge about the bioequivalence requirements.

“I don’t have any idea” (p02).
“I do not care about these things, I depend on the DNQC “(p01).

**Theme 3**
**Quality and safety of generic medicines**

Pharmacists were asked about their belief in therapeutic equivalence when comparing a brand-name (innovative) medication with generic medicine. Generally, the pharmacists expressed their belief that quality of a particular generic medication depends on the reputation of the company that produced it. In addition, all of the pharmacists included in this study reported a lot of confidence in the laboratory control program in Iraq (DNQCL).

“I have great confidence in the generic medicines which come from European origin as well as the medicines that are being tested by the DNQCL” (p09.)

**Theme 4**
**Patient education by pharmacists regarding generic medicines**

One of the most important responsibilities of the pharmacist is to educate patients about proper use of their medications. All of the pharmacists interviewed in this study agreed that educating patients about generic medicines may reduce misunderstandings about brand substitution when using generic drugs.

“Answering the patients’ questions, if any is the most important duties of the pharmacist, also giving the patients all the information on the medicine leads to reduce the risk of the misuse of medications and confusion due to different brands of medications” (p07).

**Theme 5**
**Strategies to improve generic medicine utility**

All of the pharmacists commented on the need for a law to regulate the substitution of generic medicines.

“Legislating a law to regulate generic medicines substitution made by the pharmacist leads to increase the use of generic medicine by the patients and helps them to save money. This is because the price different between innovative and generic medicine” (p08).

Furthermore, some pharmacists noted the usefulness of a drug guide that would contain a list of the generic equivalent of commonly-used innovative drugs. This guide could be used to guide brand substitutions in Iraq.

“A drug guide containing all the innovative medicine and the medicines which are equivalent leads to regulate the generic medicine substitution. This will convince the physician to follow the proposed guide” (p10).

Some pharmacists suggested that the use of the scientific name or “INN” in prescription writing by Iraqi physicians would increase the use of ge-
Generic medicine. In addition, this would decrease patient confusion caused by name variations between brand-name and generic forms of a medication.

“Many names of branded medicines confuse the patients, physicians and pharmacist and thus, the use of scientific names is the best” (p06).

Currently, the Iraqi market is inundated with counterfeit medicines, which patients often confuse with generic medications. Decreasing the availability of counterfeit medication, by increasing oversight of pharmaceutical production, would help to prevent this confusion.

“The large numbers of the counterfeit medicines adversely affect the use of generic medicine and these counterfeit medicines are considered by most patients as generic medicines, and this is not true” (p03).

Discussion

Generic substitutions positively impact medication usage by making necessary prescriptions more affordable. Pharmacists play an important role in educating patients about generic medicines. This exploratory study of Iraqi pharmacists’ perceptions about the use of generic medication highlights factors that interfere with utilising generic medicines in Iraq. Some of these issues include bio- and therapeutic equivalence, substitution practices, confusion due to the usage of different generic brands, and product labelling.

There is not currently any law in Iraq which regulates generic substitution. This decision is currently dictated by two main factors: the relationship between the pharmacist and physician and the relationship between the pharmacist and patient. In general, all of the pharmacists interviewed were willing to recommend generic medicines because generics are lower in price than their brand equivalents and supplier consistency enables pharmacists to feel secure that they are recommending a quality replacement. This supports previous studies published by Segal, Sanborn, and Hassali all of which highlighted the influence of price and supplier consistency in pharmacists’ decisions whether to recommend a generic substitution.25-27 (Segal et al, 1989; Sanborn and White, 1993; Hassali et al, 2005).

Patients’ reluctance to deviate from what their physicians have prescribed for them, and the reluctance of some physicians to recommend generic substitutions are two of the main barriers to the widespread usage of generic medicine.28,29 (Mott and Cline, 2000; Ludin, 2000). In addition, previous studies have reported that many physicians are unwilling to recommend generic medications to avoid confusing their patients, especially elderly patients, those with chronic diseases, or those on multiple medications.27 (Hassali et al., 2005). These were the main pharmacist-reported patient concerns regarding medication substitution.

All of the pharmacists interviewed agreed that generic medications obtained from European or reputable Arab companies are bio and therapeutic equivalents of the innovative medicines. However, there are a lot of counterfeit medicines in the Iraqi market, which makes it very difficult to distinguish legitimate medications from counterfeit drugs. Ultimately, this may negatively affect the usage of generic medicines in Iraq.

When counselled by a pharmacist, patients are generally amenable to using generic medicine. Most Iraqi patients hold the baseless belief that generic medications are less effective than innovative medicines because generic versions are less expensive. Patients should be educated by their pharmacist about the equivalence of generic medicines to innovative medicines to prevent such misunderstandings. For example, an American study reports that only 35% of patients over 65 years of age believe that the quality of generic medicines does not equal that of innovative medicines.30 (Rosendahl, 1994).

Some of the pharmacists involved in this study suggested that using the scientific name (INN) for medications may increase the usage of generic medicine. This aligns with previous studies by Lagarce and Segal, which reported that pharmacists are more likely to dispense generic medicines for patients with a low income or when the physician writes the prescription using INN.25,31 (Segal et al., 1989; Lagarace et al., 2005) to this end, the WHO International Non-proprietary Names
(INN) Committee works to develop generic names that will be accepted worldwide.\(^{32}\) (WHO, 2003)

Similar results have been reported in the United Kingdom.\(^{33}\) (Pharmacopia, 2003).

Discussions between physicians and pharmacists regarding the availability of generic medications in pharmacies can increase prescriptions for generic medicines. A study by Knowlton and Knapp found out that pharmacists’ interference led to a 6% increase in prescriptions for generic medicines.\(^{34}\) (Knolton and Knapp, 1994). Institution of a law to regulate generic substitutions in Iraq would likely increase the use of generic medications. In addition, a medicine guide containing innovative drugs and their therapeutically equivalent generics would facilitate generic substitution by both physicians and pharmacists.

**Study limitation**

One of the limitation of qualitative methods is that the results cannot be extrapolated to the wider population.\(^ {35}\) (Creswell et al., 2004). This study was conducted in Basrah city in Iraq and the findings may not apply to Pharmacists living in other province in Iraq. We were unable to include pharmacists from other province due to limited funding.

**Conclusion**

In general, the pharmacists interviewed in this study were positively inclined towards generic substitution because it gives the pharmacist an expanded role in the education and healthcare of the patient. The pharmacists felt that this process could change the negative predisposition that patients have toward pharmacists as businessmen or dispensers of drugs. This study shows the perceptions of ten pharmacists about the use of generic medicines. An understanding of these perceptions will be important to policy makers when they strategies to improve the utilisation of generic medicines in Iraq. In addition, an extra effort should be taken by regulatory and professional bodies to educate pharmacists on bioequivalence requirements, which currently cause confusion among Iraqi pharmacists.

**Reference**


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Salt content in meals of boarding schools and students’ restaurants in Novi Sad

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2 School of Medicine University of Novi Sad, Republic of Serbia

Abstract

Investigation brought evidence that salt intake was in a positive relationship with systolic blood pressure and that children with higher blood pressure were more susceptible to develop hypertension in adulthood. The purpose of this paper was to determine total sodium chloride content in average daily meal (breakfast, dinner and supper) prepared for adolescents in boarding schools and young adults in student’s restaurants. In the meal time, samples of breakfast, dinner and supper, of 46 daily meals dedicated to adolescents and 63 daily meals dedicated to students were taken from boarding schools/students’ restaurants. Standardized laboratory methods were applied to determine proteins, fats, ash and water in order to calculate energy value of meal. Titrimetric method with AgNO3, and K2CrO4 as indicator, was applied in order to determine chloride ion and after that a content of NaCl was calculated as % NaCl. Descriptive statistical methods were applied in order to present average salt content in the whole and in 100g and in 100 kcal of average daily meal. Student’s t-test was applied to determine statistical differences of sodium chloride amount among meals. Energy value of the average adolescent’s and student’s daily meal was 2938.8 ± 457.3kcal (CV 15.6%) and 3338.4 ± 446.3kcal (CV 13.4%), respectively. Energy value of the average student’s daily meal was significantly higher (p<0.001). Energy density of the average adolescent’s and student’s meal was 130.0 ± 22.5 kcal/100g (CV 17.3%) and 136.8 ± 15.7 kcal/100g (CV 11.5%), respectively. Sodium chloride content in average daily meal for adolescents and students was 18.0 ± 3.3g (CV 18.4%) and 16.8 ± 3.7g (CV 22.0%). The difference was not statistically significant. Sodium chloride content in 100g of adolescent’s and student’s meals was 0.8 ± 0.1g (CV 18.4%) and 0.7 ± 0.1g (CV 21.3%), respectively. The difference was statistically significant. Sodium chloride content in 100kcal of the average adolescent’s and student’s meal was 0.6 ± 0.1g (CV 17.8%) and 0.5 ± 0.1g (CV 24.2%), respectively. The difference was statistically significant. Adolescents and young adults in Novi Sad that consume meals with 16-18g of salt are overloaded with sodium and it is reasonable to expect that some of them could not cope with sodium overload and might develop undesirable response to it.

Key words: salt, meals, adolescents, young adults

Introduction

The estimation of the World Health Organization showed that total burden due to cardiovascular diseases (CVD), expressed as DALY (disability adjusted life years lost) in developing, low-income and middle-income countries accounted for more than 80% of total DALYs lost worldwide. High blood pressure is recognized the most important risk factor and it accounts for 62% of stroke cases and 49% of coronary heart events (1). Epidemiological investigations brought overwhelming evidence that dietary salt intake within population was in a positive correlation with average blood pressure and prevalence of hypertension (2,3,4). Significant positive association was obser-
ved between sodium excretion and stroke, cardiovascular and all causes of death (5,6,7). Sodium/calorie intake ratio was directly associated with all causes and CVD mortality (8). High salt intake was recognized as risk factor for end stage of renal failure (9,10). It is also in a positive association with stomach cancer and osteoporosis in adults (11,12,13). Population based intervention studies showed that reduction of salt intake was followed with systolic and diastolic blood pressure depletion (14,15,16), stroke and chronic heart disease mortality rate reduction and with increased life expectancy within controlled population (16). Non-personal health interventions of salt reduction were recognized as cost effective methods for reduction of health care costs of chronic cardiovascular diseases (17,18,19). On the global level non-personal governmental actions on reducing salt content in processed food are cost effective ways to reduce chronic cardiovascular diseases burden measured as disability-adjusted life years / DALYs (20). Although a high blood pressure is not common in adolescents and young adults, it was found that salt intake of children and adolescents was in a positive relationship with systolic, or pulse or diastolic blood pressure (21,22,23). Youths with higher blood pressure were more susceptible to develop hypertension in adulthood (24). Data from investigations in developed countries indicated that the main source of salt for the general population (25, 26, 27) was processed food.

In the Republic of Serbia cardiovascular diseases are leading cause of death. They participate with 55.2% in the total death cases. Ischemic heart diseases are responsible for 150 889 DALYs. Cerebral and other vascular diseases are responsible for further 136 090 DALYs of the population (28). The latest national health survey indicated that a prevalence of hypertension (systolic blood pressure ≥140 mmHg and diastolic blood pressure ≥90 mmHg) in the Republic of Serbia was 46.5% among adults aged 18 year and more (29). In the Province of Vojvodina prevalence of hypertension (applied criteria for measured blood pressure were the same as in Serbia) among adults aged 45 years and more was 48.7% and in the city of Novi Sad it was 69.8% (30).

Countries that have been conducting national programs on salt reduction had started with providing data on salt intake of the population (31). Population based investigation on salt intake, concerning adults, or children and adolescents in the Republic of Serbia have not been performed. Our previous data indicated that average daily meal, breakfast, snack and dinner, in kindergarten in Novi Sad salt content was higher than children’s salt intake in developed countries and more than it is recommended for that age (21,32,33). In the city of Novi Sad there are two boarding schools and one student’s centre. The boarding schools prepare approximately 200-220 and the student’s centre near 3000 daily meals (breakfast, dinner and supper). We were interested to determine salt content in average daily meals prepared for adolescents and young adults/students.

**AIM**

The purpose of this paper was to determine total sodium chloride content in average daily meals dedicated to adolescents aged 15-18y in boarding schools and young adults/students aged 20-27y and to determine salt density of the controlled meals.

**Method**

Sampling: Trained samplers, during 2007 and 2008y took 46 daily meals dedicated to adolescents aged 15-18y in boarding schools and young adults/students aged 20-27y and to determine salt density of the controlled meals.
on until turned permanent brown-red. Calculation: 
\[ \% \text{NaCl} = \frac{\text{ml AgNO}_3 \times 0.05844 \times 5 \times 100}{\text{g tested}} \]

Standardized methods were applied in order to determine quantity of proteins, fats, ash and water. Obtained results were applied to calculate energy value (calories) of each daily meal. Energy density of the average daily meal was expressed as calories/100g ratio.

Sodium chloride content was presented by using descriptive statistical method including average ± SD and CV of sodium chloride per daily meal. Sodium chloride density was calculated as sodium chloride (g) per 100g of daily meal and sodium chloride (g) per 100kcal of each daily meal, as well. The Student’s t-test was applied to find out whether there were statistically significant differences of sodium chloride content, expressed in absolute number and as g /100g of daily meal and g/100kcal ratio.

**Results**

Obtained results showed that the adolescent’s and students’ average daily meal weighted 2285.3 ± 299.5g (CV 13.1%) and 2446.5 ± 271.3 (CV 11.1%), respectively. The average weight of the student’s average daily meal was statistically higher (p=0.003). Energy value of the average adolescent’s and student’s daily meal was 2938.8 ± 457.3kcal (CV 15.6%) and 3338.4 ± 446.3kcal (CV 13.4%), respectively. Energy value of the average student’s daily meal was statistically higher (p < 0.001). Energy density of the average adolescent’s and student’s meal was 130.0 ± 22.5 kcal/100g (CV 17.3%) and 136.8 ± 15.7 kcal/100g (CV 11.5%), respectively. The difference was not statistically significant (Table 1).

The average sodium chloride content in average daily meal for adolescents and students was 18.0 ± 3.3g (CV 18.4%) and 16.8 ± 3.7g (CV 22.0%), respectively. Sodium chloride density was significantly higher in adolescent’s daily meal compared to the student’s one, regardless the density of sodium chloride was expressed per 100g or per 100kcal (p<0.001) (Table 2.).

**Table 1. Energy value and energy density of average daily meals in boarding schools and students’ restaurants**

<table>
<thead>
<tr>
<th></th>
<th>Weight</th>
<th>Energy value</th>
<th>Energy density</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Students’ centre</strong></td>
<td>1230-3066 2446.5 271.3 11.1</td>
<td>1304.4-4103.7 3338.4 446.3 13.4</td>
<td>104.6-175.7 136.8 15.7 11.5</td>
</tr>
<tr>
<td><strong>Boarding schools</strong></td>
<td>1508-3178 2285.3 299.5 13.1</td>
<td>2038.2-4014.8 2938.8 457.3 15.6</td>
<td>85.5-182.9 130.0 22.5 17.3</td>
</tr>
</tbody>
</table>

**Table 2. Salt content and salt density of average daily meals in boarding schools and students’ restaurants**

<table>
<thead>
<tr>
<th></th>
<th>Salt content</th>
<th>Salt content in 100g</th>
<th>Salt content in 100kcal</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Students’ centre</strong></td>
<td>7.9-23.1 16.8 3.7 22.0</td>
<td>0.4-1.0 0.7 0.1 21.3</td>
<td>0.2-0.8 0.5 0.1 24.2</td>
</tr>
<tr>
<td><strong>Boarding schools</strong></td>
<td>9.7-25.6 18.0 3.3 18.4</td>
<td>0.4-1.1 0.8 0.1 16.4</td>
<td>0.3-0.9 0.6 0.1 17.8</td>
</tr>
</tbody>
</table>

\[ t = 3.026, \quad p = 0.003 \]
\[ t = 4.726, \quad p = 0.000 \]
\[ t = 1.890, \quad p = 0.061 \]
Discussion

High blood pressure has been indicated as a major risk factor for stroke, ischemic heart disease, hypertensive disease and other cardiovascular diseases and all causes of deaths (1,5,6,7,34). More than 80% of the high blood pressure attributed burden of diseases was recorded in low-income and middle-income countries in the Eastern Europe and Central Asia with a greater proportion of the burden in young age groups (35). From the public health point of view, it is important to elucidate modifiable risk factors within population and to implement intervention programs (36,37). The results came from community programs, that were conducted with participation of food industry and followed by the educational programs of the population, confirmed beneficial outcomes in reducing cardiovascular and stroke mortality rate (14,15,16). Although many studies suffer from methodological problems related to data collection on salt intake, the results suggest that higher sodium intake is related to higher blood pressure in children and adolescents (21,22).

There is increasing evidence that blood pressure of children, adolescents and young adults is in a positive relationship with sodium intake, especially when it is associated with the increased body mass index (21,22,23,38).

Data obtained by our investigation showed that average daily meal which includes three meals (breakfast, dinner and supper), dedicated to adolescents aged 15-19y and students aged 20-27y in boarding schools and student’s restaurants amounted 18.0 ± 3.3g and 16.8 ± 3.7g of salt, respectively and exceeded average salt intake of adolescents and young adults in developed countries (21,38). Detected amount of sodium in sodium chloride was not the whole one because the laboratory method, we applied in our investigation, was not able to identify all sodium presented in tested food samples. It detected only sodium that was bound to chlorine. Detected sodium chloride content in the controlled samples of the daily meal exceeds for more than three folds the amount of the established nutrient goal of the World Health Organization (36,37) and by more than two folds of the established achievable goals of the countries that have been conducting countrywide national programs (31). There is relatively little evidence of the salt sensitive proportion of the adolescents and young adults (39,40), but there is evidence that the salt sensitive proportion of the population is increasing with the age, body mass index and other associated diseases such are hypertension, diabetes mellitus and renal dysfunction (41,42,43).

For us, it was important to note that in majority of the studies (40,41,42,43,44), that investigated salt sensitivity among humans, sodium load (high salt intake) was lower or similar to the sodium content in the meals dedicated to adolescents and young adults in boarding schools and students’ restaurants in Novi Sad. These findings indicate that adolescents and young adults in Novi Sad that consume meals with 16-18g of salt are overloaded with sodium. It is reasonable to expect that some of them could not cope with sodium overload and might develop undesirable response to it. Our analyses showed that the average energy value of the controlled meals, although they were not energy dense (45) exceeded the latest WHO/FAO/UNU recommendation for energy intake of the adolescents girls and young adults of both gender (46). These observations suggest that the adolescents and young adults in Novi Sad who take high energy and salt dense meals are exposed to the unfavorable dietary pattern, i.e. diet that could lead to obesity, hypertension and other over nutrition related diseases (1,36,37). Our findings are in line with data suggested that in low-income and mild-income countries national and regional programs should be developed in order to support healthy start. Studies from developed counties clearly demonstrated beneficial effects from lifestyle modifying trials and programs (1,31,34,47,48,49).

Conclusion

Obtained results indicated that adolescents and young adults/students, throughout three meals received in boarding schools and students’ centre, had received salt in a quantity that exceeds internationally established population goal for average daily intake and population achievable goal. This amount also exceeds daily salt intake of adolescent and young adults in developed countries. Detected salt quantity showed that the target gro-
ups of adolescent and young adults are salt over-
loaded and thus it was reasonable to expect that
some of them would not be able to cope with it
especially those who were overweight, who have
positive family history of hypertension and other
cardiovascular risk factors. Further, more specific,
investigations are needed in order to provide data
relevant to highlight a magnitude of risk factors
within adolescent and young adult population
that could be responsible for high blood pressure
and related chronic diseases in adulthood in our
community. Beneficial effects of that kind of in-
vestigations and implemented programmes already
have been extensively evaluated.

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Performance of regional tuberculosis dispensaries in a province of Turkey in pre-DOTS era (1989-2002)

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Abstract

Background: In recent years, very few dispensary staff has been striving to apply directly observed therapy (DOT) elsewhere in Turkey, but the overwhelming majority of TB dispensaries still continue their usual practice today. Therefore, practice of any regional TB dispensary may mirror Turkey’s Tuberculosis Programme practice profile.

Method: Statistical Year Books of Sivas Province Health Department (from 1989 to 2002) are the main sources of data. The mid-year population numbers obtained from Statistical Year Books of Sivas Province Health Department were preferred for calculating annual incidences. Pearson’s correlation coefficients and, if data ordinal, Spearman’s correlation coefficients were used to determine correlations.

Results: There are three TB dispensaries in the Sivas Province. Total staff number at Sivas TB dispensaries decreased within years (r = -0.92, p < 0.001). TB incidence declined within years, also(r = -0.87, p < 0.0001). Chest X-ray examinations gradually decreased within years from 20,416 examinations in 1989 to 5856 examinations in 2002 (r = -0.75, p = 0.002). Annual microscopic examinations for acid-fast bacilli (AFB) declined within years with 1400 microscopy done in 1989 decreased to 445 examinations in 2002 (r=-0.62, p=0.018). Per each TB patient, the annual mean microscopy for AFB examination was 4.49 ± 1.47 and the mean chest radiography was 8.25±3.27 at local dispensaries in this fourteen-year period. The annual tuberculin skin test (TST) and Bacillus Calmette-Guerin (BCG) vaccinations per 100,000 population performed by local dispensaries did not statistically different within years (r = -0.45, p = 0.106 and, p = -0.15, p = 0.605, respectively).

Conclusion: TB incidence declined within years, but this situation seems to be not related with improving of dispensaries performance.

Key words: tuberculosis, dispensary, pre-DOTS era, application, performance

Introduction

The global burden of tuberculosis is still enormous. World Health Organization (WHO) Report 2006 on Global Tuberculosis Control pointed out that there were 8.9 million new cases of tuberculosis (TB) in 2004 (140/100 000 population), of which 3.9 million (62/100 000 population) were smear-positive. A total of 183 countries and territories implemented the Directly Observed Therapy Strategy (DOTS) during 2004. By the end of 2004, 83% of the world’s population lived in countries, or parts of countries covered by DOTS.1 Mainly funded by international organisations, National Tuberculosis Programmes (NTPS) of high-burden countries were relatively successful in implementing DOTS, in case detection and treatment success rates.1

Turkey, a European region country with approximately 70 million populations, with a widely distributed tuberculosis dispensary network,2 is lacked implementing DOTS in nation-wide yet. National Tuberculosis Programme (NTP) of Turkey reported to WHO that DOTS coverage was 2% in 2003, and 3% in 2004. There were 19 799 TB notified cases in Turkey in 2004, and 616 of them were under the supervision of DOTS.1
Tuberculosis dispensaries, first introduced in the 1920s, are peripheral units of NTP of Turkey. Although TB dispensaries are politically directed by TB Office of the Ministry of Health, their staff have been assigned to and supervised by Province Health Departments at regional levels. This dual management situation may cause lack of supervision of TB dispensaries applications and policies. In recent years, very few dispensary staff has been striving to apply directly observed therapy (DOT) elsewhere in Turkey, but the overwhelming majority of TB dispensaries still continue their usual practice today. Therefore, practice of any regional TB dispensary may mirror Turkey’s NTP practice profile.

On the other hand, a DOTS programme was implemented by our Province Health Department Communicable Diseases Section in the late 2003, we will able to compare DOTS performance with the pre-dots era applications in a few years later.

Materials and methods

Statistical Year Books of Sivas Province Health Department (from 1989 to 2002) are the main sources of data. All the available data related to TB dispensary applications have to be recorded into these year books. However, there were only the number of annual TB cases recorded; neither affected organs, nor patient gender or age were reported. In these written sources, the term “follow-up without medication” was used instead of the terms “cure” or “treatment completed” to mean that patient treatment was completed under the supervision of the dispensary.

As censuses in Turkey are applied every 5 years, and there has been a slight tendency of immigration in the region, the mid-year population numbers obtained from Statistical Year Books of Sivas Province Health Department were preferred for calculating annual incidences.

Statistics

Data were entered into an Excel Spreadsheet. SPSS (version 12.0) was used for statistical analyses. Data are expressed as mean ± SD. Pearson’s correlation coefficients and, if data ordinal, Spearman’s correlation coefficients were used to determine correlations. All p values are two sided, with p < 0.05 considered statistically significant.

Results

There are three TB dispensaries in Sivas province (~ 650,000 populations). Total staff number at Sivas TB dispensaries decreased within years. Province-wide health sector staff was 1645 persons in 1989, and gradually increased to 2530 persons in 2002. In contrast, dispensaries had 50 staff in 1989, and gradually declined to 37 persons in Sivas TB dispensaries in 2002 (r = -0.923, p<0.001). The number of the doctors working at TB dispensaries varied within years, with a minimum of three doctors in 1994 and, a maximum of ten doctors in 1996. During that time, dispensaries doctor/province-wide doctor ratios gradually declined within years (r = -0.73, p = 0.003). The annual mean population per each TB dispensary doctor was 99139 ± 36123 in these 14 study years.

Figure 1. Tuberculosis incidence per 100,000 population by dispensaries registries in Sivas Province between 1989 and 2002 (r = -0.868, p < 0.001).

Totally 3235 TB cases were registered at local dispensaries between 1989 and 2002, with a maximum of 357 cases in 1991 and a minimum of 137 cases in 1998 (Table 1). Both total TB cases and
TB incidences (per 100 000 population) as shown in Figure 1 declined within years ($r = -0.881$, $p<0.0001$, and $r = -0.868$, $p<0.0001$, respectively). There was a mean annual TB incidence of 35.5/100 000, with an annual reduction of 1.9%. Figure 1 indicates the changes in patient number registered in dispensaries within years. According to TB dispensaries registries, the TB incidence per 100 000 population decreased from 47.7 to 23.3 in the years 1989 and 2002 respectively (Table 1).

Table 1. Annual numbers, and, annual incidences (per 100 000 population) of tuberculosis cases and annual treatment completed cases registered at local dispensaries of Sivas Province in Turkey between 1989 and 2002.

<table>
<thead>
<tr>
<th>Year</th>
<th>Tuberculosis cases (n)</th>
<th>Incidence</th>
<th>Treatment completed (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1989</td>
<td>332</td>
<td>44.7</td>
<td>476</td>
</tr>
<tr>
<td>1990</td>
<td>307</td>
<td>44.4</td>
<td>475</td>
</tr>
<tr>
<td>1991</td>
<td>357</td>
<td>52.6</td>
<td>379</td>
</tr>
<tr>
<td>1992</td>
<td>255</td>
<td>38.4</td>
<td>324</td>
</tr>
<tr>
<td>1993</td>
<td>285</td>
<td>43.3</td>
<td>218</td>
</tr>
<tr>
<td>1994</td>
<td>269</td>
<td>41.9</td>
<td>218</td>
</tr>
<tr>
<td>1995</td>
<td>205</td>
<td>32.2</td>
<td>135</td>
</tr>
<tr>
<td>1996</td>
<td>200</td>
<td>31.3</td>
<td>198</td>
</tr>
<tr>
<td>1997</td>
<td>260</td>
<td>42.1</td>
<td>260</td>
</tr>
<tr>
<td>1998</td>
<td>137</td>
<td>22.2</td>
<td>177</td>
</tr>
<tr>
<td>1999</td>
<td>189</td>
<td>30.8</td>
<td>196</td>
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<tr>
<td>2000</td>
<td>141</td>
<td>22.8</td>
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</tr>
<tr>
<td>2001</td>
<td>152</td>
<td>24.5</td>
<td>137</td>
</tr>
<tr>
<td>2002</td>
<td>145</td>
<td>23.3</td>
<td>197</td>
</tr>
</tbody>
</table>

The annual TB incidence in our region correlates with Turkey’s national incidence (data not shown) between 1989 and 2002 ($r = 0.816$, $p<0.001$).

The highest number of patients examined at Sivas TB dispensaries (n = 26 537) was in 1991 while 2002 was the year with the least number of patients (n = 7 304) with a mean of 9,766 ± 8 451 for the 14 years period. The 14-year average of the annual patient number examined per 100 000 population is 2 237 ± 688 with a minimum of 1 174 and a maximum of 3 913. Naturally, there is a highly positive correlation between the number of the patients admitted to dispensaries per 100 000 population and those with TB notification per 100 000 population ($r = 0.737$, $p = 0.003$).

Annual microscopic examinations for acid-fast bacilli (AFB) declined within years with 1 400 microscopy done in 1989 decreased to 445 examinations in 2002. Annual microscopic AFB examination numbers per 100 000 population at local tuberculosis dispensaries between 1989 and 2002 are shown in Figure 2.

Annual chest X-ray examinations decreased within years from 20 416 examinations in 1989 to 5 856 examinations in 2002. Chest X-ray examinations per 100 000 population at TB dispensaries as shown in figure 3, gradually decreased within time ($r = -0.754$, $p = 0.002$).

Per each TB patient, the annual mean microscopy for AFB examination was 4.49 ± 1.47 and the mean chest radiography was 8.25 ± 3.27 at local dispensaries of Sivas in this fourteen-year period. In 1997, for example, only two microscopic examinations for AFB and, only three chest radiographies had been performed per each TB patient.

The mean chest radiography per AFB microscopy at Sivas TB dispensaries in these fourteen years was 12.6 ± 4.6 and it did not change within years ($r = -0.147$, $p = 0.615$). People who admitted to TB dispensaries were examined by chest radiography rather than AFB microscopy.

The annual microscopy for AFB per person examined at dispensaries during these 14 years is...
0.07 ± 0.022 while the mean chest radiography per person examined is 0.82 ± 0.24. The number of both microscopy (r = -0.132, p = 0.654) and chest radiography (r = 0.216, p = 0.459) per person examined at dispensaries has not changed within this 14 year-period as well.

Employed doctor and total staff number correlations with dispensaries’ applications in these 14 years were also evaluated. There were no significant correlations with doctor numbers and tuberculosis incidence, chemoprophylaxis, chest radiography and microscopy for AFB, or BCG vaccinations (data not shown). On the other hand, as total number of dispensaries personnel increased, chest radiographic examinations and microscopy for AFB numbers increased as well (r = 0.605, p = 0.022, and r = 0.640, p = 0.014, respectively).

The annual tuberculin skin test (TST) and Bacille Calmette-Guerin (BCG) vaccinations per 100 000 population performed by local dispensaries did not statistically different within years (r = -0.451, p = 0.106 and, p = -0.152, p = 0.605, respectively). The annual mean TST per 100 000 population was 729 ± 372 and the mean annual BCG vaccination per 100 000 population was 708 ± 330 in these fourteen years.

Annual contact tracing numbers throughout Sivas started to be mentioned in Statistical Year Books in 1995. According to the statistical information gathered from these books, mean contact tracing per patient was 3 ± 0.54 between 1995 and 2002. There was not any significant change in the number of annual contact tracing per patient registered from 1995 to 2002 (r = 0.218, p = 0.604). The average size of households is 5.0 in Sivas during this period.

Isoniazid chemoprophylaxis administered to 464 persons with latent tuberculosis infection (LTBI) throughout Sivas in 1989; however, only 64 persons with LTBI were commenced prophylaxis in the year 2002. Chemoprophylaxis administered to 1.34 patients per each registered TB patient in 1989 gradually declined, and in 2002, there were only 0.44 patient who commenced chemoprophylaxis (r = -0.603, p = 0.022). The contacts of the patients given chemoprophylaxis for LTBI per 100 000 population in the region between 1989 and 2002 are shown in Figure 4.
Discussion

The 2003 WHO Report on Global TB Control identified primary constraints preventing WHO targets for TB control from being achieved, of which lack of qualified staff was the main constraint. Staff of dispensaries of our region has decreased within years, from 50 people in 1989 to 37 people in 2002. Because staff have been chosen for dispensaries by Province Health Department (not by NTP officers), qualification of these personnel was not a subject of priority. In addition, there have been no studies about how many staff required for the central or peripheral units of NTP of Turkey.

This study clearly shows that TB incidence declined from 47.7 to 23.3 per 100,000 populations per year between 1989 and 2002, and this decline in the incidence significantly correlates with Turkey’s national incidence data for the same years. This mean annual reduction of 1.9% in TB incidences seems not to be related to the improvement of performance of TB dispensaries. While the number of the people applying to dispensaries decreased within years, annual chest radiographic and AFB microscopic evaluations declined as well. These findings suggest that the gradual decrease in official recordings of the patients with TB at local dispensaries' registry does not associate with any improvement in these institutions’ practice. This situation may be associated with the improvement in the living standards of the country or with lack of notification of patients who diagnosed other institutions or both. Ozsahin et al. reported that up to 50% of the patients with TB were not notified to local dispensaries by the diagnosing hospitals in our region. This may be a causal factor for the declining incidence of TB.

By the year 2004, tuberculosis control services were provided by 244 dispensaries which belong to the Ministry of Health, 31 dispensaries of which settled by voluntary organizations, 22 Chest Diseases Hospitals and 11 mobile tuberculosis groups in Turkey. These units examine approximately 2.5 million people each year and provide health care to 18,000 TB patients. Although some idealist doctors try to implement DOT in their regions, the overwhelming majority of the dispensaries all over the country have similar performance as in our regional dispensaries. Therefore, we think that results obtained from our regional dispensaries’ practices may reflect TB dispensary system of Turkey as a whole.

The first technical element of the WHO TB control strategy (DOTS) is case detection among symptomatic patients’ self-reporting to health services using sputum smear microscopy. As inexpensive and simple to perform, smear microscopy remains the cornerstone for the diagnosis of pulmonary TB. Many low-income countries TB units, with a passive case finding system, mostly without doctors, perform at least three sputum smear microscopy for acid-fast bacilli. However, per each registered TB patient, the annual mean microscopy for AFB examination was less than five examinations in our region’s dispensaries. Thus, approximately 10,000 persons admitted annually seem to be examined without microscopic evaluation. Our results suggest that smear microscopy was not a main diagnostic tool in our dispensaries, and this situation seems to get worse within years.

Patients with sputum smear-positive pulmonary TB should be monitored by sputum smear examination. These are the patients for whom bacteriological monitoring is possible. It is unnecessary, unreliable and waste of resources to monitor patients by chest radiography. For patients with sputum smear-negative pulmonary TB or extrapulmonary TB, clinical monitoring is the usual way of assessing the response to treatment. For smear-positive pulmonary patients, sputum smear should be performed at the end of the second month, during the fifth month and in the last month of the 6-month and 8-month treatment regimens. It seems that, at dispensaries of Sivas, the patient follow-up examination has been performed through chest radiography rather than microscopy. If only the previously diagnosed patients had been examined through microscopy, it seems that microscopy had been performed for almost none of the newly admitted patients. The numbers of the radiography per registered patient also make us think that the patients have not been controlled through chest radiography.

One of the main results of our study shows that there is no change in annual TST and BCG vaccinations within years, in addition to contact tracing.
and isoniazid chemoprophylaxis numbers were gradually declined from 1989 to 2002.

All these results mentioned above suggest that the practices at Sivas TB dispensaries seem not to be in accordance with the world-wide policy of WHO at least until the year 2002.

Unfortunately, some of the vital source of data, such as registered cases’ ages, genders, and affiliated organs (pulmonary or extra-pulmonary) were not included in Statistical Year Books of Sivas Province Health Department. Therefore, we could not analyze and discuss such issues, and we think that this is the main limitation of this present study.

Our results suggest that TB dispensaries of our region’s performances were not sufficient and getting worse within years in pre-DOTS era. On the other hand, a DOTS programme was implemented by our Province Health Department Communicable Diseases Section in the late 2003, we will able to compare DOTS performance with the pre-dots era applications in a few years later.

References


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Effects of Plateau Environment on Social Interaction

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3 Tianjin Medical University, China

Abstract

Objective: The paper explored the change of social interaction of young people exposed in plateau environment.

Methods: 214 young people living in Tibet Plateau for more than one year (plateau group) and 190 young people living in inland (Inland group) completed the survey. Social avoidance and distress were used as the indexes of social interaction, with perceived social support, interpersonal trust and self-esteem as influencing factors.

Results: Plateau group had higher scores on social avoidance, distress, interpersonal trust and self-esteem, and lower scores on perceived social support. In Plateau group, both perceived social support and self-esteem had significant negative betas on social avoidance, and perceived social support, interpersonal trust and self-esteem all had significant negative betas on distress. In Inland group, only self-esteem had significant beta on distress.

Conclusion: Effects of Plateau environment on social interaction and people’s mental health were discussed.

Key Words: plateau environment; self-esteem; perceived social support; social avoidance and distress; sociometer theory (SMT)

Introduction

Sitting at the center of the Tibet Plateau (91°06E and 29°36N) of 3,650 meters (1,1975 feet) elevation with 29 and 16.5 Celsius of the yearly highest and lowest temperature respectively (7.4 yearly average temperature), the high-altitude Lhasa city has low atmospheric pressure and showers over 3,000 hours every year distinguishing it as a “sunlit city” with intensified sun radiation and dry air. Moreover, the remote and outlying geographic location makes the city a sparsely populated place (about 400,000 inhabitants) with inconvenient communications. These factors can infect people both physically and psychologically.

On the other hand, People have a fundamental need to belong that motivates them to seek out social interactions with close others (Baumeister R. & Leary M., 1995). And interpersonal ties with other people serve various important functions. They provide emotional, instrumental, and informational support and can be a source of satisfaction and fulfillment (Denissen J., et al., 2008). Especially under harsh conditions, where communication is not so convenient, social interactions must adapt to the environment.

The paper investigated the social interactions (using social avoidance and distress as indexes) and related factors, including perceived social support, self-esteem, interpersonal trust, of young people living on the Plateau (Lhasa of Tibet, Qinghai-Tibet Plateau) for more than one year and young ones living in inland. The aim was through studying the differences between the two groups and the relations between these factors and social avoidance and distress to find out the potential influences of the Plateau environment on young people’s social interactions.
2. Methods

2.1. Sample and procedure

The study sample consisted of the plateau group including 214 people living and working in Lhasa, the capital of Tibet Autonomous Region for more than one year and the inland group with 190 people living in inland areas (9 provinces or cities around China). The two groups were all male people ranging from 16 to 23 years old (mean age 18.85 years, SD 1.02) for the Plateau group and from 16 to 22 years old (mean age 18.16 years, SD 1.32) for the inland group.

After excluding subjects who didn’t complete the questionnaires as required, the study sample was made up of 211 people (mean age 18.83 years, SD 1.01) for the Plateau group from 9 provinces or cities before they were in Lhasa, with 20.1% from Sichuan, 6.1% from Heilongjiang, 12.2% from Chongqing, 8.2% from Guizhou, 10.2% from Hunan, 8.2% from Fujian, 15.6% from Zhejiang, 11.2% from Shaanxi, 8.2% from Yunnan, and 184 people (mean age 18.03 years, SD 1.53) for the inland group, with 22.3% from Sichuan, 10.3% from Jilin, 20.2% from Hunan, 15.1% from Fujian, 11.4% from Zhejiang, 11.2% from Shaanxi, 9.5% from Kunming. Other demographic data had been listed in Table 1.

Table 1. The demographic data of the plateau group and the inland group

<table>
<thead>
<tr>
<th>Variable</th>
<th>Plateau group (n=211)</th>
<th>Inland group (n=184)</th>
</tr>
</thead>
<tbody>
<tr>
<td>age (mean±SD)</td>
<td>18.85±1.02 (ranged from 16 to 23)</td>
<td>18.03±1.53 (ranged from 16 to 22)</td>
</tr>
<tr>
<td>married</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>be in love</td>
<td>17.54% (37)</td>
<td>26.63% (49)</td>
</tr>
<tr>
<td>coming from rural areas</td>
<td>55.45% (117)</td>
<td>78.80% (145)</td>
</tr>
<tr>
<td>be in a one-parent family</td>
<td>6.16% (13)</td>
<td>11.96% (22)</td>
</tr>
<tr>
<td>be in a one-child family</td>
<td>28.10% (59)</td>
<td>32.61% (60)</td>
</tr>
</tbody>
</table>

Questionnaires were sent by post, and completed under the guidance of trained researchers or local research assistants. At first, the aim was introduced to the subjects, and letters of consent were signed by every subject. Then they were directed to complete the set of questionnaires anonymously. And their information was numerically coded to hide their identities.

2.2. Measurements

The set of questionnaires included the Perceived Social Support (PSSS), the Rosenberg Self-esteem Scale (RSES), Interpersonal Trust Scale (ITS), and the Social Avoidance and Distress Scale (SADS).

2.2.1. The Rosenberg Self-esteem Scale (RSES)

Self-esteem was assessed by the Rosenberg Self-esteem scale RSES (Rosenberg M., 1965), of which 10 items were used to evaluate one’s worthiness as a human. The RSES was designed for a 4-point scale from 1 (strongly disagree) to 4 (strongly agree), with the sum score ranging from 10 to 40, and the higher of the score meant the higher of self-esteem. Cronbach’s alpha was 0.80 and 0.81 for Plateau group and Inland group in this study respectively.

2.2.2. Interpersonal Trust Scale (ITS)

Interpersonal trust was measured using Interpersonal Trust Scale, developed by Rotter J. (1967), including 25 items, with 5-point scale from 1 (completely disagree) to 5 (completely agree). The sum of the scores ranged from 25 to 125 and the higher of the score meant the higher of self-esteem. It had been proven to be an effective tool to measure interpersonal trust. In prisoner’s dilemma games, people low in trust were more suspicious of peers (Schlencker B., Helm B., & Tedeschi J., 1973) and were perceived as less trustworthy themselves (Rotter B., 1967) relative to people high in trust. Cronbach’s alpha was 0.67 and 0.65 for Plateau group and Inland group in this study respectively.
2.2.3. Perceived Social Support Scale (PSSS)

The degree of perceived social support was assessed by the Perceived Social Support Scale (PSSS) developed by Zimet et al. (1988) which was devised as a 7-point scale (from very strongly disagree to very strongly agree). Having been validated and commonly used in Chinese populations (e.g. Chou K., 2000; Cheng S., Chan A., 2004; Yu D., Lee D., & Woo J., 2004), the PSSS was a 12-item measure of three aspects of social networks: family network, friends network and others network (Lubben J., 1988). Its score was obtained through adding all the scores of each item together. Cronbach’s alpha was 0.87 and 0.91 for Plateau group and Inland group in this study respectively.

2.2.4. Social Avoidance and Distress Scale (SADS)

Social Avoidance and Distress Scale (SADS) was used in this study as indexes of social interactions. The scale was developed by Watson and Friend in 1969. It mainly measured the tendency to avoid social interactions, and the bad feelings (like anxiety) during social interactions. It had 28 items, with 2 factors (social avoidance and distress), using 5-point scale from 1 (Strongly disagree) to 5 (Strongly agree). Scores of each factor range from 0 to 70, and higher scores meant more obvious tendency to avoid social interactions, or more serious distress. Cronbach’s alpha for social avoidance was 0.70 and 0.79 for Plateau group and Inland group in this study respectively. Cronbach’s alpha for distress was 0.68 and 0.83 for Plateau group and Inland group in this study respectively.

2.3. Statistical analysis

Descriptive analyses were performed for each scale for both groups, and based on which a series of independent sample t-tests were conducted to find out the differences between the two groups. Then multiple regressions were conducted using social avoidance and distress as dependant variable respectively and other variables as independent variables for both groups. All analyses were performed with Statistical Package for the Social Sciences (SPSS, version 14.0).

3. Results

3.1. Descriptive analysis and independent sample t-tests

Variables were computed based on each scale, including Perceived social support, Self-esteem, Interpersonal trust, Social avoidance and Distress. Each variable was analyzed and compared between the two groups. The results were shown in table 2. From these results, we could see that significant differences were found for all the variables studied. The scores of self-esteem, interpersonal trust, social avoidance and distress were significantly higher for plateau group, while the scores of perceived social support were significantly lower.

3.2. Multiple regression analyses

In order to study the influence of plateau environment on social interaction, multiple regression analyses were conducted. Social avoidance and distress were used as dependent variables respectively, and other variables were used as independent variables. The results were shown in table 3. From the
results, we could see that in different environment, the determining factors for social interactions were different. In Plateau group, both perceived social support and self-esteem had significant negative betas on social avoidance, and all the three variables studied had significant negative betas on distress. While in Inland group, none of the three variables had significant beta on social avoidance, and only self-esteem had significant beta on distress. Compared with Inland group, we could know that social interactions on plateau may have different mode. In this environment, perceived social support, interpersonal trust and self-esteem may be more important than in inland for social interaction.

4. Discussion

This study was designed to find out how Plateau environment would influence social interaction. From the descriptive analyses and comparisons of the two groups, we could find that Plateau group differed from Inland group in all the variables studied. Social interaction was more avoided and the distress to interact was more serious, with lower perceived social support for Plateau group. However, people’s interpersonal trust and self-esteem were higher in Plateau group. These results showed that Plateau environment had changed social interaction to some extent. And lower perceived social support may be because the population density was relatively smaller, and they were farther away from their families and friends.

And the results of multiple regressions were very interesting. Based on previous studies, perceived social support, self-esteem and interpersonal trust should be important factors for social interaction. But in this study, in the Inland group, all these three variables had non-significant coefficients on social avoidance, and only self-esteem had significant coefficient on distress. While in Plateau group, only interpersonal trust had non-significant coefficient on social avoidance, and all these variables had significant coefficients on distress. From these results, we could see that the Plateau environment not only had changed people’s tendency to interact with others, but also had changed the mode of social interactions. These results can be explained in the view of social exchange theory. For the Inland group there may be much more reasons for social interaction, common interests for example, and perceived social support, interpersonal trust, self-esteem may account for little variation. But on Plateau, social interaction is not so convenient, and reasons for social interaction are much less. Under this condition, they may expect more from social interaction, and are more easily to be disappointed. This may also be a reason for higher social avoidance and distress for plateau group. As a result, psychological factors, including perceived social support, interpersonal trust and self-esteem, become more important for social interaction. On this point, psychological intervention should be much more useful to adjust social interactions for Plateau group than Inland group.

According to Leary and Baumeisters’s (2000) sociometer theory (SMT), at low levels of social inclusion, “the sociometer evokes emotional distress as an alarm signal and motivates behaviors to gain, maintain, and restore relational appreciation”. And self-esteem serves as the sociometer. This may be the reason of lower self-esteem motivated higher distress for people in Inland group. On the other hand, people with higher self-esteem should like to communicate with others more. But in this study, the Plateau group had higher self-esteem and

| Table 3. Results of multiple regression analysis for two groups (beta) |
|---------------------------------|-----------------|-----------------|-----------------|-----------------|
|                                 | Social avoidance | Distress        |                  |                  |
|                                 | Plateau group    | Inland group    | Plateau group    | Inland group    |
| Perceived social support        | -0.181**         | -0.004          | -0.133*          | -0.004          |
| Interpersonal trust             | -0.107           | -0.134          | -0.184**         | -0.112          |
| Self-esteem                     | -0.364**         | -0.120          | -0.405**         | -0.163*         |
| R square                        | 0.222            | 0.028           | 0.253            | 0.034           |

*p<0.05, **p<0.01
higher social avoidance, which seemed to be paradoxical. This may be the other side of SMT, when social interaction become tough for objective conditions (such as Plateau environment), sociometer (self-esteem) may upgrade itself as so not to alarm. However, this is just a hypothesis needing further empirical study to support.

On the other hand, social interaction is the basic need of human beings. Factors influencing social interaction are also important to human’s health. Many studies (e.g. Cohen S. & Wills T., 1985; House J., Landis K. & Umberson D., 1988; Schwarzer R. & Leppin A., 1989) had confirmed that the availability of social support was associated with a reduced risk of mental and physical illnesses, even the reduced mortality. And self-esteem is an essential feature of mental health, positive self-esteem was supposed to be a protective factor in the field of health and social behavior (Mann, et al., 2004). From this perspective, the plateau environment had complicated influence on peoples’ mental health, with lower social support and higher self-esteem. And this effect should be further oriented in the future.

This study investigated the condition and special mode of social interaction on plateau environment, and found interesting results. But there were obvious limitations in this study. Firstly, all the results were derived on the basis of questionnaires, and there was no other strategy, which may cause common-method variation. Secondly, the number of subjects was relatively small, which had prevented the use of more advanced methods to analyze the data. On the basis of these results, future studies should pay more attention to using appropriate ways to regulate social interaction for people working and living on plateau.

References


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Risk factors of allergic rhinitis: a case-control study

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³ Institute of Social Medicine, Belgrade University School of Medicine, Serbia

Abstract

Objective: Allergic rhinitis is a major respiratory disorder and represents a global health concern. Its prevalence is increasing over the last decades and the reasons for this increase are not completely clear. The aim of this study was to investigate the factors associated with allergic rhinitis in the adult Serbian population.

Method: A case-control study of 100 outpatients with allergic rhinitis and 100 control subjects was conducted in Belgrade, Serbia in 2006. Cases and controls were matched by sex and age (± 5 years). A detailed questionnaire based on the latest research results in this field was used to obtain information about known risk factors. Univariate and multivariate logistic regression analyses were used for statistical analysis.

Results: The following factors were dependently associated with occurrence of allergic rhinitis: allergic asthma (Odds Ratio [OR], 3.00; 95% confidence interval [CI], 1.36-6.64) and atopic dermatitis (OR, 4.24; 95%CI, 1.35-13.31) among family members, allergic rhinitis (OR, 24.07; 95%CI, 3.15-183.89), allergic asthma (OR, 6.22; 95%CI, 1.34-28.87), infections of the airways (OR, 3.49; 95%CI, 1.82-6.72) and drug allergy (OR, 2.95; 95%CI, 1.01-8.61) in childhood, atopic dermatitis (OR, 3.02; 95%CI, 1.03-8.83), sinusitis (OR = 3.34; 95%CI, 1.52-7.35), and breastfeeding in the first months (OR, 2.86; 95%CI, 1.17-6.96). Asthma among family members was the only independent risk factor for allergic rhinitis (OR, 3.16; 95%CI, 1.04-9.59).

Conclusion: Our study indicates potentially important role of both genetic and environmental factors in the etiology of allergic rhinitis.

Key words: allergic rhinitis, case-control study, environmental factors, genetic factors, logistic regression analysis, risk factors.

Introduction

Allergic rhinitis is a symptomatic disorder of the nose induced by an immunoglobulin E (IgE) mediated inflammation of the nasal membranes in response to allergen exposure. Predominant symptoms are rhinorrhea, nasal obstruction, nasal itching and sneezing. Allergic rhinitis affecting between 10% to 40% of the global population and its prevalence is increasing both in children and adults, over the last decades (1). Due to its high and increasing prevalence, its impact on quality of life, the association with multiple comorbidities (asthma, sinusitis, conjunctivitis) and the considerable socioeconomic burden, allergic rhinitis is a major respiratory disorder and represents a global health concern (2). The reasons for this increase are not completely clear but there is accumulating evidence that both genetic and environmental factors play an important role (3). Some aspects of “western” lifestyle and environment are thought to be responsible. During the last decade of the 20th century, much attention was paid to the “hygiene hypothesis” as the most plausible working hypothesis to explain both temporal changes and the regional differences in allergic rhinitis preva-
ience, but significance of hereditary factors cannot be ignored. Exposure to environmental allergens is the most significant environmental factor in development and exacerbation of allergic rhinitis. Atmospheric pollution, changes in diet, antibiotic use, immunisations and patterns of infection in childhood, leading to changes in numbers of people with T-helper (Th)2, rather than Th1 immune responses, as well as number of people who produce IgE antibodies to inhaled allergens, also play an important role in the development of the allergic rhinitis (4). Another theory is that there has been a major change in the gene pool, predisposing more individuals to excessive IgE production and thus increased expression of allergic rhinitis (5).

In recent years, focus of our investigation has been on risk factors and health-related quality of life in allergic (atopic) diseases of the airways, primarily asthma (6,7) and rhinitis (8). The identification of risk factors is essential for the adaptation of preventive measures and optimization of rhinitis patient management.

The aim of this study was to assess the role of some suspected risk factors in development of allergic rhinitis in our environment.

**Patients and Methods**

**Patients**

This case-control study was conducted in 2006 year. The case group was composed of 100 adult allergic rhinitis patients who were consecutively recruited from the outpatient department of the Institute of Allergology and Immunology, Clinical Center of Serbia. All were clinically diagnosed as having allergic rhinitis on the basis of their medical history, clinical presentation (stuffy nose, runny nose, sneezing), skin prick testing with inhalant allergens and results of specific rhino provocation tests with allergens, following pertinent guidelines and recommendations (2).

All selected cases were interviewed – no one refused to participate. One control was chosen for each case. Controls (n = 100) were randomly selected outpatients from the other departments of the same Clinical Center. They were individually matched to cases by sex and age (±5 years). After an appropriate medical work-up, the subjects of the control group were diagnosed with hypertension (20), gastritis (12), gastroduodenitis (10), nephrolithiasis (15), and orthopedic trauma (43).

**Questionnaire**

All the subjects were interviewed by the same doctor using a detailed questionnaire based on the latest research results in this field. The questionnaire consisted of 61 items and included information about: (a) socio-demographic characteristics (age, sex, education, marital status, place of residence, birthplace, presence of air pollution in the place of residence); (b) associated upper respiratory illnesses: nonallergic rhinitis, sinusitis, nasal polyps; (c) associated allergic diseases: allergic asthma, atopic dermatitis (eczema), urticaria, food allergy, drug allergy; (d) history of already mentioned allergic diseases in childhood; (e) family history of allergic diseases; (f) history of respiratory tract infections /illnesses/ (pneumonia, bronchiolitis, bronchitis (wheeze)), (g) history of prematurity, birth weight, maternal age of birth, breastfeeding, family size, various harmful behavioral factors (cigarette smoking, smoking during pregnancy, housing conditions, pets).

Items about associated respiratory and/or allergic illnesses refer to clinical diagnosis made by a physician and not only based on history, signs and symptoms of the disease.

**Statistical analysis**

Univariate and multivariate logistic regression analyses were used for statistical analysis. The strength of the relationship between risk factors and allergic rhinitis was evaluated by calculating odds ratios (OR) and their 95% confidence intervals (CI) for all tested factors. Dependent variable was a “health status” (allergic rhinitis or absence of allergic rhinitis). All statistically significant variables from the univariate logistic regression analysis were put into the multivariate logistic regression model. Analysis was performed with the Statistical Package for the Social Sciences, SPSS, version 8.0 (SPSS Inc., Chicago, IL, USA), with significance set at $P<0.05$. 
Results

The study included 100 patients with allergic rhinitis and 100 controls (57 males and 43 females), matched according to sex and age (± 5 years). The mean age was 33.79±12.44 years in allergic rhinitis group and 33.78±12.66 years in the control group. There were not significant differences between cases and controls in educational level or in place of residence (Table 1).

Table 1. Socio-demographic characteristics of cases and controls

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Cases (n = 100)</th>
<th>Controls (n = 100)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years (mean±SD)</td>
<td>33.79±12.44</td>
<td>33.78±12.66</td>
</tr>
<tr>
<td>Sex (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>57</td>
<td>57</td>
</tr>
<tr>
<td>Females</td>
<td>43</td>
<td>43</td>
</tr>
<tr>
<td>Educational level (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-8</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>8-12</td>
<td>55</td>
<td>56</td>
</tr>
<tr>
<td>&gt;12</td>
<td>40</td>
<td>39</td>
</tr>
<tr>
<td>Place of residence (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rural</td>
<td>13</td>
<td>16</td>
</tr>
<tr>
<td>Urban</td>
<td>87</td>
<td>84</td>
</tr>
</tbody>
</table>

According to univariate logistic regression analysis (Table 2), air pollution in the place of residence, drug allergy, atopic dermatitis, sinusitis, respiratory infections in childhood, allergic asthma in childhood, allergic rhinitis in childhood, drug allergy in childhood, asthma among family members, allergic rhinitis among family members, atopic dermatitis among family members, and breastfeeding in the first months were significantly associated with allergic rhinitis.

In order to estimate an independent non-confounded effect of the potential risk factors, multivariate conditional logistic regression analysis was used. All statistically significant variables from univariate analysis were entered into the model. Significantly increased risk of allergic rhinitis was associated only with asthma among family members (OR, 3.16; 95%CI, 1.04-9.59; P = 0.042) (Table 3).

Table 2. Factors related to allergic rhinitis – univariate logistic regression analysis

<table>
<thead>
<tr>
<th>Variable</th>
<th>B*</th>
<th>SE†</th>
<th>P</th>
<th>OR‡</th>
<th>95% CI§</th>
</tr>
</thead>
<tbody>
<tr>
<td>Air pollution near place of residence</td>
<td>1.15</td>
<td>0.31</td>
<td>0.000</td>
<td>3.17</td>
<td>1.72-5.85</td>
</tr>
<tr>
<td>Drug allergy</td>
<td>0.84</td>
<td>0.40</td>
<td>0.036</td>
<td>2.32</td>
<td>1.05-5.08</td>
</tr>
<tr>
<td>Atopic dermatitis</td>
<td>1.10</td>
<td>0.55</td>
<td>0.044</td>
<td>3.02</td>
<td>1.03-8.83</td>
</tr>
<tr>
<td>Sinusitis</td>
<td>1.21</td>
<td>0.40</td>
<td>0.003</td>
<td>3.34</td>
<td>1.52-7.35</td>
</tr>
<tr>
<td>Respiratory infections in childhood</td>
<td>1.25</td>
<td>0.33</td>
<td>0.000</td>
<td>3.49</td>
<td>1.82-6.72</td>
</tr>
<tr>
<td>Allergic asthma in childhood</td>
<td>1.83</td>
<td>0.78</td>
<td>0.020</td>
<td>6.22</td>
<td>1.34-28.87</td>
</tr>
<tr>
<td>Allergic rhinitis in childhood</td>
<td>3.18</td>
<td>1.04</td>
<td>0.002</td>
<td>24.07</td>
<td>3.15-183.89</td>
</tr>
<tr>
<td>Drug allergy in childhood</td>
<td>1.08</td>
<td>0.55</td>
<td>0.048</td>
<td>2.95</td>
<td>1.01-8.61</td>
</tr>
<tr>
<td>Asthma among family members</td>
<td>1.09</td>
<td>0.41</td>
<td>0.007</td>
<td>3.00</td>
<td>1.36-6.64</td>
</tr>
<tr>
<td>Allergic rhinitis among family members</td>
<td>1.74</td>
<td>0.65</td>
<td>0.007</td>
<td>5.71</td>
<td>1.59-20.39</td>
</tr>
<tr>
<td>Atopic dermatitis among family members</td>
<td>1.44</td>
<td>0.58</td>
<td>0.013</td>
<td>4.24</td>
<td>1.35-13.31</td>
</tr>
<tr>
<td>Breastfeeding in the first months</td>
<td>1.05</td>
<td>0.45</td>
<td>0.021</td>
<td>2.86</td>
<td>1.17-6.96</td>
</tr>
</tbody>
</table>

*Coefficient, †Standard Error, ‡Odds Ratio, §Confidence Interval.

Table 3. Factors related to allergic rhinitis – multivariate logistic regression analysis

<table>
<thead>
<tr>
<th>Variable</th>
<th>B*</th>
<th>SE†</th>
<th>P</th>
<th>OR‡</th>
<th>95% CI§</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthma among family members</td>
<td>1.15</td>
<td>0.57</td>
<td>0.042</td>
<td>3.16</td>
<td>1.04-9.59</td>
</tr>
<tr>
<td>Constant</td>
<td>-2.075</td>
<td>0.67</td>
<td>0.002</td>
<td>0.13</td>
<td></td>
</tr>
</tbody>
</table>

*Coefficient, †Standard Error, ‡Odds Ratio, §Confidence Interval.
Discussion

Allergic rhinitis represents a global health problem. Although often trivialised by patients and doctors allergic rhinitis is a significant cause of morbidity, in addition to its substantial economic impact (5). Much effort has been made to identify risk factors for the development of allergic rhinitis (4,9). It is likely that there is a multilevel interaction between genetic and environmental factors in the etiology of allergic rhinitis (3). Our study indicates potentially important role of allergic rhinitis, allergic asthma and atopic dermatitis among family members, allergic rhinitis, allergic asthma, infections of the airways and drug allergy in childhood, atopic dermatitis, sinusitis, air pollution and breastfeeding in the first months as dependent factors which increase the risk of allergic rhinitis. Asthma among family members was the only independent risk factor for allergic rhinitis.

Allergic rhinitis is most common atopic disease with strong links to asthma. Epidemiological studies have consistently shown that allergic rhinitis and asthma often co-exist in the same patients, suggesting the concept of “one airway, one disease” (2,10-12). According to our results, there was a strong association between allergic rhinitis and allergic asthma in childhood. Also, our study has shown that individuals with diagnosis of allergic rhinitis in childhood are about 24 times more likely to have allergic rhinitis as adults than negative controls.

Allergic rhinitis and asthma are frequently associated. It was shown that allergic rhinitis correlated to, and constituted a risk factor for the occurrence and severity of asthma (2). Approximately 80% of asthmatics have rhinitis and somewhere between 25% and 50% of patients with rhinitis have associated asthma (13). In patients with both disorders, rhinitis appears first in 45% of the cases (14). Recent studies show that the deposition of allergen into the lower respiratory tract leads to increased inflammation of the upper respiratory tract, even if the patients are only suffering from allergic rhinitis (15). It is now recognized that asthma and persistent allergic rhinitis do not constitute distinct disease categories but in fact represent the final common pathway of closely related pathological processes in the upper, lower or both parts of the respiratory tract (2,16).

Bugiani et al. (12) concluded that the risk of asthma in subjects with allergic rhinitis was significantly higher than the risk in subjects without allergic rhinitis, and that bronchial asthma and allergic rhinitis, when associated, seemed to share the same risk factors as allergic rhinitis alone, while asthma without allergic rhinitis seemed to be a different condition, at least with respect to some relevant risk factors.

A study that examined risk factors of onset and remission of allergic rhinitis and asthma in Swedish adults (17) showed that the onset of asthma was highly associated with allergic rhinitis among atopics (OR, 5.70), but also tended to be related to non-atopics (OR, 3.50). In the Copenhagen Allergy Study (18), more than 99% of subjects with allergic asthma also had allergic rhinitis.

According to hygiene hypothesis larger family size, exposure to respiratory infections, microbial exposure, and exposure to other bacterial components such as endotoxin have a protective effect against the development of allergic rhinitis and other allergic diseases (19). The hygiene hypothesis has been proposed as a possible explanation for the doubling of the incidence of allergic rhinitis in the past 20 years (20). Several cohort studies have demonstrated that the prevalence of allergic rhinitis is correlated with an increased number of older siblings (21), and with increased family size (22). The rationale of the protective effect of a large family is that older siblings transmit respiratory infections to younger siblings.

However, not all studies have found an inverse association between infections and allergic rhinitis. Recent study of Tamay et al (9) has shown that frequent respiratory infections in childhood significantly increase risk for allergic rhinitis (OR, 1.36). Our results are in concordance with this finding (OR, 3.49).

Different studies in North America (23), Europe (24) and South Australia (25) have shown that the prevalence of atopy (defined as positive skin tests to common aeroallergens) and allergic rhinitis is higher in urban than in rural areas. Recently, it has been found that farmers’ children have less allergic rhinitis than other children, suggesting therefore that lifestyle in the countryside could protect children from the development of allergy (26). In the present study place of residence of the majority of subjects with allergic rhinitis was urban.
Our study was shown that air pollution near place of residence increase risk of allergic rhinitis. Recent findings suggest that exposure to outdoor air pollutants may increase the risk of allergic rhinitis in children (27-29). In a Taiwanese study (30) long-term exposure to outdoor air pollutants increases the risk of allergic rhinitis. In a British study the occurrence of general practice consultations due to allergic rhinitis was related to short term exposure to sulfur dioxide (SO2) and ozone (O3). The strongest association was found for daily levels during 3 to 4 days prior to consultation (27). Air pollution was significant environmental factor of allergic rhinitis in Singapore study (31). Traffic related air pollution may increase the risk of allergic development and exacerbate symptoms in particular susceptible subgroups (32). The study of von Mutius et al (24) has shown that air pollution is associated with increased rhinitis symptoms but is not necessarily associated with an increased incidence of allergic rhinitis or allergen sensitization.

The relationships between allergic rhinitis and chronic sinusitis are close and complex. They are often a continuum of disease (33). This relationship can be demonstrated not only in terms of anatomy, physiology and epidemiology, but also experimentally, by studying the sinus involvement following nasal allergen provocations and pathophysiologically, by phenotyping and comparing the inflammation present in both diseases. Results of such studies have confirmed the fundamental role of nasal inflammation in general and allergic inflammation in particular in the genesis of sinusitis (34). Sinusitis can increase risk for allergic rhinitis (OR, 1.29) (10). According to our results sinusitis was risk factor for allergic rhinitis (OR, 3.34), but not an independent one.

Atopic dermatitis frequently is the first manifestation of an atopic diathesis, which occurs in genetically predisposed individuals and also includes allergic rhinitis and asthma. Up to 80% of children with atopic dermatitis eventually develop allergic rhinitis later in childhood (35). In the present study subjects with atopic dermatitis were more frequently diagnosed as allergic rhinitis (OR, 3.02).

A genetic component in allergic rhinitis as well as in other allergic diseases has been shown and the best established risk factor for allergic rhinitis is a family history of allergy, especially allergic rhinitis (36). Adults with a family history of asthma or rhinitis have a 3 to 4 fold risk of development asthma and a 2 to 6 fold risk of developing rhinitis, compared with adults with no family history (37). An increase risk of children developing allergic rhinitis was found when either parent had a positive history, and the risk is highest if both parents are affected (38,39). The risk of the second child developing allergic rhinitis when either parent or the eldest child, or both, had allergic rhinitis was found to increase in study of Lee et all (40). The German case-control study had determined that the correlation of allergic rhinitis between siblings is significantly higher than that between parent and child (41). In twin studies, concordance rates of allergic rhinitis and serum IgE levels in monozygotic twins are quite similar in twins raised apart, suggesting a strong familial/genetic component (39). Atopic individuals, with family history of rhinitis, first born children and immigrants are predisposed to develop allergic rhinitis (5). The risk of allergic rhinitis was also increased in a child with positive parental history of any atopic diseases (40).

In our study, family history of allergic rhinitis as well as history of asthma and atopic dermatitis are important risk factors of allergic rhinitis. Individuals who had family members affected with asthma had significantly higher risk of contracting the allergic rhinitis (OR, 3.16).

The effect of breastfeeding on the development of allergic rhinitis and other atopic conditions has been assessed in many studies but remains controversial with some researchers showing a protective effect of breastfeeding (42,43) and others showing no association (44,45) or even a positive association (46). In our study breastfeeding was the predisposing factor for allergic rhinitis, but not independent one.

Aspirin and other non-steroidal anti-inflammatory drugs commonly induce rhinitis and asthma. In a population-based random sample, aspirin intolerance was more frequent among subjects with allergic rhinitis than among those without (2.6% vs. 0.3%, \(P<0.01\)) (47). Drug allergy and drug allergy in childhood were risk factors for allergic rhinitis in our study.

Our results support the hypothesis that allergic rhinitis is a multifactorial disease related to
genetic and various environmental influences. It was shown that familial atopic background (allergic rhinitis, allergic asthma and atopic dermatitis among family members) have the important role in genesis of allergic rhinitis. According to our results, asthma among family members was the only independent risk factor for allergic rhinitis.

Recognizing the risk factors is important for the diagnosis and prevention of the disease. Patients with symptoms of allergic rhinitis should be evaluated for asthma. Allergic rhinitis patient have an increased risk of developing asthma and may form a suitable population for secondary intervention (early recognition and treatment of allergic rhinitis) to interrupt the “allergic march” in respiratory diseases, i.e. progression of allergic rhinitis to bronchial asthma, improve quality of life, and may also reduce the overall cost of care.

Family predisposition of allergy should be considered as simply and the most cheapest predictive risk factor for allergy development.

Further studies are required to evaluate the precise role of the environment. It would also be interesting to compare these results with those obtained in a population of asthmatic patient.

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A Qualitative Evaluation of Nurses’ Perception towards the Role of Pharmacist in Healthcare Setup in Pakistan

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Abstract

This study aims to explore the nurses’ perception toward the role of pharmacist in the health care setup. A qualitative study design was adopted. Face to face interviews were conducted using a semi-structure interview guide. A total of twelve nurses were the part of study. All the interviews were transcribed verbatim and thematically analyzed for its content. The main focus of interviews were on: 1) Perception regarding pharmacists’ role; 2) Importance of pharmacists in health setting; 3) Seeking help from pharmacists; 4) Pharmacist - Nurses Collaboration. Findings demonstrated that some nurse has shared a thought that pharmacists have a vital role in the success of any healthcare system. However, in their opinion, pharmacists just provide medicine and having a kind of managerial job in hospital. When respondents were asked about their collaboration in patient care, some of the respondents showed positive perception and emphasized on the importance of the availability of pharmacists. They were willing to collaborate because it would definitely benefit the patients. Moreover respondents stressed that the pharmacists should be available around the clock for consultation. Although nurses considered pharmacists as drug expert who know more about medicines as compared to other healthcare professionals, they were more likely to believe that pharmacists’ involvement would be an intrusion into their affairs. Pharmacists’ services are focusing towards management of pharmacies rather than patient care. A possible reason behind this behavior may be the minimal level of interaction among the two professions due to the unavailability of pharmacists.

Key words: Perception, Pakistan, Nurses, Pharmacist, Health care system;

Introduction

For the last two decades a sudden increase in the demand for health care services is experienced worldwide (Sitzia, 2001). In response to this call the demand of health care professionals also has increased too many folds. Nowadays an average health care setup facing new challenges in the form of limited financial resources, rising healthcare cost, increasing health demand and heightened public expectations(Hagbaghery et al., 2004). A collaborative relationships among the multiple disciplinary health care professional will be an ideal strategy to cope with these challenges and use their expertise to improve the patient care as per consumers expectations (Alan. J et al., 2006). Moreover, collaborative care by the health care providers has the potential to improve patient care, enhance patient safety and reduce work load issues that cause burnout among healthcare professionals (Oandasan et al., 2006). It is cited that in the health care setup where pharmacist has collaboration in direct patient care has higher rate of positive outcomes (Dranitsaris et al., 2001,
Hanlon et al., 1996, Tsuyuki et al., 2002). Main focus of previous work was on the collaboration between pharmacist and the doctor (Adepu and Nagavi 2006; Nathan, A. and C.A. Sutters 1993). However, there is merely any effort that highlights the nurses and pharmacists interaction.

In developing countries especially in Pakistan, health seeking behavior and determinants of the use of health services is an important concern(Khowaja, 2009). Increase in the population is poor quality of life; pollution, improper diet and the low health literacy are the main challenges to provide effective health care to inhabitants (Babar, 2006). Moreover, the healthcare system in Pakistan has been confronted with problems of inequity, scarcity of resources, inefficient and untrained human resources, gender insensitivity and structural mismanagement (Babar, 2006). These issues are alarming for Ministry of Health Pakistan to take some positive steps to cope the shortage of human resource in health sector to provide effective health care to the community (Azhar et al., 2009). In Pakistani health care setup previously there was shortage of medical doctors only but with the initiative for the Punjab government to hire pharmacist as an essential member of the health care team has increased the demand of qualified pharmacist as well. On other hand if we see the paramedical staff then Nurses are the largest group serving health care system in Pakistan (WHO, 2002-2008). The role of nurses in primary care has developed rapidly (Hollis, 2005) and even some of the drug related issues are handled by the nursing staff or one can assume that there is a good collaborative working relationship of nurses with physicians in Pakistani health care setup (San Martin-Rodriguez et al., 2005, Ogbinmi and Adebamowo., 2006). However, in current scenario the pharmacist demand in health care system in increasing, it is one of the future priorities of Ministry of Health Pakistan to incorporate the role pharmacist in Pakistani health care system. In other words pharmacist will collaborate with the physicians and nursing staff to provide affective care to the patients. Keeping in view this motivation, this study aims to explore the nurses’ perception toward the role of pharmacist in the health care setup.

Methods

Face to face interviews were conducted using a semi-structure interview guide. Qualitative approach was used to gain understanding on this issue, as it allows a flexible exploration of respondents’ experiences (Berg, 2004).

Study Location

This study was conducted among the nursing staff offering their services in health care units in Lahore. Lahore is one the third most populous city of Pakistan with the estimated population of 10 million approximately (NIOP, 2007). 18 public and 38 private hospitals at present serve in the city(Wikipedia, 2009). The time frame of this study was from April 2007 until June 2007.

Study Design

Face to face interviews were conducted using a semi-structured interview guide, developed after extensive literature review was used for the interview. All the respondents were approached using their contact (Berg 2004). Through purposive sampling method, key informants were interviewed until saturation point was reached(Roy et al., 2007). Each interview lasted approximately 15 to 25 minutes. All the interviews were audio taped and transcribed verbatim. The transcripts were repeatedly and thematically analyzed line by line for its content(Mohamed et al., 2005). The main focus of interviews was on the nurse perception towards the role of pharmacists and their willingness to collaborate with pharmacists. Furthermore, information was also gathered regarding their experience working with pharmacists. Probing questions were used where necessary and respondents were given freedom to express their views.

Ethical considerations

The study protocol was approved by the institutional research ethics committee school of pharmaceutical science Universiti Sains Malaysia.
Furthermore a written consent was obtained from the participants prior to the interview. It was assure to all the respondents that there personal information will be kept confidential.

**Results**

A total of 12 respondents were identified through contacts and interviewed. All the respondents participated in this study were female with a working experience in nursing profession more than eight years. In terms of age 4(33.3%) of the respondents were aged less than thirty years. However, 5(42.6%) of respondents were from age group thirty to forty years and one fourth were aged over forty. The Thematic content analysis of the interviews yielded four major themes; perception regarding pharmacists’ role, availability of pharmacists, seeking help from pharmacists and pharmacists-nurses collaboration. Of these twelve nurses only ten reported that pharmacist available at their hospital.

**Theme one: Perception regarding pharmacists’ role**

Nurses in Pakistan’s healthcare system have the opinion that the pharmacists’ role was limited to one who provides medicines and being the drug expert. Majority stated that;

Yes, we know about a pharmacist, the medicines supplied to ward and hospital are provided by Pharmacists. They are directly in contact with the suppliers and provide medicines which are required.

However very few shared a thought that;

*Pharmacist is the one having a good knowledge about medicine, it is the responsibility of pharmacist to check thoroughly about medicine, either the prescribed medicine is available at the store or not. If it is available then who is the manufacturer, is it the same name mentioned by the prescriber or it is the same drug with different name. Pharmacist is the one to make final decision about the use of medicine because they know more about the benefits and side effects as compared to other member of healthcare team.*

**Theme Two: Importance of pharmacists in healthcare setting**

Regarding the importance of pharmacists in healthcare setting, all the interviewees agreed that with the presence of pharmacist in the health care setup we can provide better health care to the patients.

*Nurse one: Pharmacist is important member of health care team, if he doesn’t provide medicine in time how can patient recover.*

*Nurse two: Pharmacists are the drug experts and seller who are trained properly.*

**Theme three: Seeking help from pharmacists**

The theme three is one of the core elements of this study that evaluates the nurse attitude toward help seeking from the pharmacist. A negative attitude was found among the nurse regarding the help seeking from pharmacist regarding the patient care.

*Nurse one: among the health care professional our relation is limited to doctors only and after doctors we concern about the patient. Pharmacists are quite separate their job nature is different from the doctors and ours.*

*Nurse Two: We have nothing to do with Pharmacist. We have our own duty and they have their own. They come and check registers and medicines. We have to work within the wards. In foreign countries it happens that you can call pharmacist if needed but, here in our country we get medicines on weekly basis.*

**Theme four: Nurses attitudes toward Pharmacist - Nurses collaboration**

Overall attitude was positive toward the Pharmacist - Nurses collaboration. Details are described as follow;

*Nurse five: Yes, we are willing to work in collaboration with pharmacist; they come and check what medicines are being used. They also check that the medicines which are being given to the patients are proper or not.*

*Nurse six: Yes, we will work with them in collaboration if they are available, this alliance would be definitely benefit for the patients.*
Nurse seven: Yes, it will be great if Pharmacist is the part of healthcare setting. The services provided by the pharmacist should be 24 hours; this will help the health care team to get pharmacist consultation at any time.

Discussion

This was a qualitative study that highlighted the nurses’ perception and attitude toward pharmacists in Pakistani health care setup. Pharmacists in developing countries are still underutilized and under estimated for their professional skills. Moreover, their role as healthcare professionals is not deemed necessary by other healthcare provider. The findings of this study highlight a negative perception among nurse toward the capabilities of the pharmacist. It was revealed that majority has visualized the role of pharmacists as a drug provider and those who stay in contact with the suppliers for the availability of the medicine in the hospital. Although very few has considered pharmacists as drug expert who know more about medicines as compared to other healthcare team. However, still many perceive consider pharmacist role in the hospital for the managerial job at the main pharmacy (Azhar et al., 2009). This can be one of the possible factor that lying hindrance for the pharmacist to prove their capabilities in the patient care (Azhar et al., 2009).

If we see the health care setup at the developed countries the presence of pharmacist is essential in any health care team. Their importance was highlighted by almost all the interviewees and this was consistent with studies done in several countries which reported that pharmacists could make a great contribution to the provision of the primary health care, especially in developing countries (Smith, 2004, Jesson and Bissell, 2006) and that their role varies in different parts of the world. Some dealt with preparation and supply of medicines while some focus on sharing pharmaceutical expertise and knowledge with doctors, nurses and patients(Gilbert, 2001). Whilst questioning the respondents about the presence of pharmacists at the hospitals, more than half were unaware about the existence of pharmacists in their hospital. The main reason was the unavailability, which was the common issue discussed in number of studies (Goel et al., 1996, FIP, 1998, FIP, 1997). Lack of human resources creates a significant difference between the health services availability. In many cases this was due to the fact that the number of pharmacists was less than required (Goel et al., 1996, FIP, 1998, FIP, 1997), or we can say that the numbers of post allocated for the pharmacist in Pakistan are less then the demand. In this case Ministry of Health Pakistan can play a vital role by taking some initiative to increase the number of post of pharmacist in government and private health care setup. Such initiatives will also help in presenting the role of pharmacist in better not only in terms of pharmacy management but also in the patient and community care. In this way the negative attitude toward the pharmacist among the health care professional can also be rectified as majority of the nurses they were not willing to seeking help from pharmacists in patient care. They have negative perception toward the role of pharmacist; they did not consider pharmacists as members of the health care team who can be involved in patient care. Their opinion regarding pharmacists was just to provide medicines and take care of their managerial job. The lack of interactions between the two professions and scarcity of pharmacist in the health care setup can be a possible reason for this behavior. These findings are some what consistent to the findings of Gillbert (1997) that report almost same attitude among the nurses toward help seeking form pharmacist.

However, surprisingly a very positive attitude was observed towards pharmacist-nurse collaboration. The respondents shared a thought that pharmacists’ involvement is essential component to attain affective patient care. They understood that working together will improve patient outcomes. This finding complies with the findings of Makowsky et al, (2009) that reports the willingness by health care professionals to work together as a team. Moreover, nearly all agreed that collaboration with pharmacists can only be fulfilled if they were available in the hospital. These finding highlight that the availability of pharmacists is one of the major issue in developing countries especially in Pakistan (Azhar et al., 2009).
Conclusion

Overall a negative perception was found toward the role of pharmacist in health care setup. Pharmacist was identified as a drug expert and his skill were only confounded only to the issues concerning pharmacy management. A possible factor for this behavior may be, Nurses believe that by incorporating the role of pharmacist in patient care may decrees their worth and can result intrusion into their duties. Other factors responsible for this behavior are the common belief in Pakistan’s healthcare setting that only doctors and nurses’ alliance can fulfill all the requirement of the patients. In a same way nurses in Pakistan visualized the role of pharmacists as a drug provider. Last but not the least the main cause behind this behavior may be was the minimal interaction between the two professions which are because of the less number of pharmacists that practice in patient care in Pakistan.

Recommendation

Findings of this study highlight the need of more methodological strong studies that further focus on the identification of the factors responsible for this negative behavior among the nurses in Pakistan health care system. Furthermore, ministry of health should take initiative to increase the number of pharmacist in Pakistani health care setup. Such initiatives will be helpful in creating an environment for affective patient care and will be helpful in positive modification of the nurses’ attitude toward the role of pharmacist.

Competing interests

The authors declare that they have no competing interests.

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An epidemiological study of physical and mental health of rescuing soldiers in 5.12 Wenchuan earthquake

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Abstract

Introduction: A powerful earthquake struck Wenchuan in China on 12 May 2008. The physical and mental health of rescuing soldiers was investigated in 5.12 powerful earthquake in Wenchuan.

Methods: The analysis of descriptive epidemiology was made in 1187 rescuing soldiers in the areas of Wenchuan county and Dujiangyan city. By the questionnaire survey method, the content involved the body general condition as well as the skin mucous membrane system, the respiratory system, the digesting system, the urinary system, the nervous system symptom and the psychological and mental health.

Results: The diseases in dermatological, psychological and respiratory systems were predominant, and the incidence was 50.35%, 48.80% and 37.93%, respectively. The diseases were testified to be lower in the incidence of digestive, neurological and urinary system, and the incidence rate was 29.14%, 21.93% and 5.08%, respectively.

Conclusion: The psychological and mental health of rescuing soldiers who experienced the earthquake disaster was harmed in various degrees, and the corresponding measures should be made in the medication and mental intervention.

Key words: epidemiology, Wenchuan earthquake, rescuing soldiers, physical and mental health

Introduction

A violent earthquake may bring about the most devastating disasters that cause mass casualties. The severe bodily and psychological injuries in the survivors pose the most difficult problems with regards to emergency aid and treatment after the catastrophe.¹ ² ³ Major disasters can be followed by an increase in incidence and outbreaks of infectious diseases ⁴ ⁵ and a strong link exits between the extent of damage caused by catastrophic earthquakes and an increase in morbidity rates for acute illness.⁶

At 14:28:01.42 (Beijing time) on May 12, 2008 “Wenchuan” had the powerful earthquakes with a magnitude of 8.0 on the Richter scale in the province of Sichuan of China. The epicenter of the massive earthquake was located in Wenchuan, Sichuan. A report from the Chinese Ministry of Civil Affairs stated that the death toll from this devastating earthquake rose to 69,196, 374,176 people were injured and 18,381 people were missing within a seriously devastated area of 100,000 km². Hundreds and thousands of buildings, including hospitals and health-care centers were destroyed. Almost all the roads in western Sichuan were blocked. The estimation of the economic loss was higher than US $140 billion, making the earthquake the costliest natural disaster in Chinese history by far.
The People’s Liberation Army rapidly reached, rescuing the life from the ruins, processing massive victim remains, searching crashed aircraft and transporting the grains to the isolated mountainous area and played the very important role in the earthquake relief work process. The serious earthquake caused mass casualties, bringing about the physical and mental illness in the survivors and rescuers. Previous studies have suggested that major disasters can be followed by an increase in the incidence of complex injuries and outbreaks of infectious diseases in victims.7,8 The earthquake will also have the very tremendous influence to the disaster relief personnel’s physical and mental health. The previous research paid great attention the disaster relief personnel’s psychological question. 9, 10, 11, 12

The epidemic studies to the relief personnel diseases were little reported. 13, 14, 15

In order to understand earthquake relief work officers and soldiers’ psychology and health situation, our Beijing Military Region General hospital “Hua Yawei the earthquake relief work medical team” had carried on the sample investigation of relief army officers and soldiers in the earthquake areas of Wenchuan and the Dujiangyan county and identified the types of illness, which will provide the basis for the concerned departments to draw up the related measures.

Subjects and Methods

Subjects: Investigation subjects were the rescue army officers and soldiers in 5.12 serious earthquake in Wenchuan. We distributed 1187 copies of questionnaires one month after the earthquake, reclaimed 1187 copies of questionnaires.

Methods: The method was the overall general survey and the time was two months after the disaster. By the questionnaire survey method, the content involved the body general condition as well as the skin mucous membrane system, the respiratory system, the digesting system, the urinary system, the nervous system symptom and the stress disorder symptom. All investigators accepted unified training, using the unified quantification investigation standard. The personnel included: (1) one person was totally in charge of spot investigation and the quality control. He was responsible to distribute individual ID number for the surveyor and to carry on the quality inspection of the returned survey forms. (2) eight persons were responsible for the questionnaire survey specifically.

Statistical analysis: After all questionnaire completed, the data entry was carried on. One staff entered the data 2 times using the Excel software and another staff carried on the data checkup. The categorical variables are presented as percentages. A statistical significance was deemed present when the p-value was equal to or less than 0.01. All statistical calculations were performed using the SPSS, version 11.0, software for Windows.

Results

Demographics: There were 1187 army officers and soldiers participating in the investigation. Of these, 1173 were male and 14 were female (range: 17 years to 35 years, average age 22.09 years). Of the patients, 28 were younger than 18 years, 1100 were aged between 18 and 30 years and 59 were older than 30 years (Table. 1). They mainly undertook the duties of dealing with project emergency, searching and rescuing the disaster victims, shipping the casualty and searching the crashed aircraft.

Table 1. Demographic characteristics of rescuing soldiers in earthquake areas. Variables category number rate (%)

<table>
<thead>
<tr>
<th>Variables category</th>
<th>number</th>
<th>rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>male</td>
<td>1173</td>
<td>98.80</td>
</tr>
<tr>
<td>female</td>
<td>14</td>
<td>0.18</td>
</tr>
<tr>
<td>age range</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤18 years old</td>
<td>28</td>
<td>0.36</td>
</tr>
<tr>
<td>18-30 years old</td>
<td>1100</td>
<td>92.67</td>
</tr>
<tr>
<td>≥30 years old</td>
<td>59</td>
<td>4.97</td>
</tr>
</tbody>
</table>

According to the survey result, diseases were classified according to the body system. The incidence rate ranging from high to low was that of skin disease, the psychological illness, the respiratory disease, digestive tract disease, the nervous system disease and the urinary disease, respectively. The corresponding disease incidence rate was 50.35%, 48.80%, 37.93%, 29.14%, 21.93% and 5.08%, respectively (Table 2). The incidence rates of skin disease, the psychological illness, respiratory disease were higher than those of digestive tract disease, the nervous system disease and the urologic disease (p<0.01)
The survey results showed that the cardinal symptoms of skin and mucous membrane system were skin rashes such as papule nettle rash and eczema, and the fungus infectious athlete’s foot in the army officers and soldiers (Table 3). The incidence rate of was 31.92% (362/1134) and 22.57% (256/1134), respectively. The main performances of psychological illness were irritability-restlessness, the vigilance, sadness, testiness, intensity and so on (Table 4). The corresponding disease incidence rate was 12.48% (78/625) 10.24% (64/625) 10.08% (63/625) 9.60% (60/625) and 9.12% (57/625). 45 cases suffered from depression (7.20%), whereas 6.56% had anxiety (n=41)

The results showed that cardinal symptoms of respiratory system were the cough, the expectoration, the hemoptysis, the nasal discharge, the dyspnea and so on (Table 5). The corresponding disease incidence rate was 13.72% (162/1181) 17.70% (209/1181) 17.87% (211/1181) 3.30% (39/1181) 14.48% (171/1181) 7.45% (88/1181) and 12.96% (153/1181), respectively.
tion and nasal discharge (Table 5) and the incidence rate was 17.70% (209/1181) 17.87% (211/1181) and 14.48% (171/1181), respectively. The serious respiratory symptoms such as hemoptysis and dyspnea were rare, and the incidence rate was 3.3% (39/1181), 7.45% (88/1181), respectively.

The cardinal symptoms of digestive tract symptom were gastroenteritis with the symptoms of abdominal pain and diarrhea (Table 6). 15.63% (n=184) had abdominal pain and 10.62% (125/1177) suffered diarrhea.

The main performances of nervous system were headache, dizziness, insomnia and vertigo (Table 7), the incidence rate respectively was 10.92% (128/1172), 10.92% (128/1172), 9.89% (116/1172) and 7.42% (87/1172), respectively.

### Discussion

Serious natural disaster had great influence on physical and mental health of disaster victims and relief staffs. It is necessary to investigate and analyze the changes and know the rule and the reason, which will contribute to the recovery and treatment of victims, and have great significance to relief work.

Our survey showed that the incidence rates of skin disease and the psychological illness were the highest in the earthquake relief work process officers and soldiers. Skin diseases' main manifestations were papule nettle rash, eczema, dermatitis and fungus infectious athlete's foot. During the Chi-Chi earthquake of Taiwan the most commonly illnesses in disaster refugees were acute respiratory infection (50.1%), musculoskeletal pain (17.4%), trauma (12.5%), acute gastroenteritis(7.2%), and skin rash (7.1%). The incidence rates of diseases in relief staffs were different from those in disaster refugees. The trauma was the common disease in refugees while not in relief staffs. Han reported that the diseases were found mainly in psychological symptoms (62.16%) and respiratory system (51.78%) in the inhabitants in “Wenchuan earthquake“, which were similar to our results.

The reasons were as follows: the climate of earthquake disaster area was moist, sultry and suitable for mosquito growth and reproduction. After the disaster, the destructed building, the bad lodging environment and the bad sanitary condition were advantageous to the occurring of skin disease. Because the army officers and soldiers lived together in the tents set up roadside, the incidence rate of allergic disease (papule nettle rash) caused by mosquito biting was higher, and the incidence rates of athlete’s foot, the ringworm of the body and eczema and dermatitis’s disease caused by fungal infections were also quite higher. In addition, it was the reason of higher incidence rate of

<table>
<thead>
<tr>
<th>Table 6. Distribution of symptoms of digestive system</th>
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<tbody>
<tr>
<td><strong>Symptom</strong></td>
</tr>
<tr>
<td>-----------------</td>
</tr>
<tr>
<td>Stomachache</td>
</tr>
<tr>
<td>Vomiting</td>
</tr>
<tr>
<td>Abdominal distension</td>
</tr>
<tr>
<td>Anepithymia</td>
</tr>
<tr>
<td>Constipation</td>
</tr>
<tr>
<td>Diarrhea</td>
</tr>
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</table>

*Note: The subject having one symptom was calculated 1 person-time.*

<table>
<thead>
<tr>
<th>Table 7. Distribution of symptoms of nervous system</th>
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</thead>
<tbody>
<tr>
<td><strong>Symptom</strong></td>
</tr>
<tr>
<td>-----------------</td>
</tr>
<tr>
<td>Headache</td>
</tr>
<tr>
<td>Dizziness</td>
</tr>
<tr>
<td>Insomnia</td>
</tr>
<tr>
<td>Vertigo</td>
</tr>
</tbody>
</table>

*Note: The subject having one symptom was calculated 1 person-time.*
skin disease during the early time of disaster relief that the corresponding medicines were quite deficient and treats were not prompt.

The investigation showed that earthquake relief work officers and soldiers had the varying degree’s psychological illness and the main performances were agitation, the vigilance, sadness, intensity and so on.

The reasons were as follows:
1. The major part of army soldiers were born in the 1980s, and their psychology growth had not been mature. Their former living experiences were quite simple, and had not withstood the quite obvious psychological discipline. The casualties this big earthquake created were huge. The disaster relief scene was frigid, which was an obvious direct-viewing psychological impact on relief soldiers, and their psychological bearing capacity was insufficient.
2. Usual trains lacked the pointed psychological training and the psychological education, and self-adjustment was insufficient under the emergency mode;
3. After the earthquake occurred, the psychological medicine workers were relatively deficient, and psychological unblocking measures weak. The above factors can cause the psychological illness of relief army officers and soldiers. The incidence rates of psychological illnesses such as depression and anxiety were lower than that of the disaster victims. On the one hand because the very severe earthquake scene and the family member lose caused the enormous damage at heart, and the psychological wound was serious. On the other hand because disaster victims cannot estimate the future life condition, they easily had obviously sorrowful, despondent, anxious moods. Moreover the society and the government’ positive propaganda, the care and the salute to rescue groups were helpful to enhance confidence, increase the value feeling, the sense of honor, and improve officers’ and soldiers’ condition at heart in a large degree.

In addition, we discovered that respiratory symptoms were mainly common cold performances such as cough, expectorating, pharyngalgia and nasal discharge. The reasons were as follows:
1. The earthquake relief work load was heavy physical ability consumes in a big way and the body was weary.
2. The seismic region environment was disorderly and the air pollution was heavy.
3. Do not adapt to the moist sultry climate and climate changes after the disaster such as the high temperature and rains.
4. The living in the open country, the centralized personnel and impeded ventilates created respiratory disease’s dissemination easily. All above factors caused the increase of probability of the respiratory infections, but the serious breath diseases of hemoptysis, the scant of breath were seen seldom.

The digestive tract symptoms were mainly abdominal pain, diarrhea, distension of the abdomen, poor appetite and so on. The reasons were as follows: The food habit changed suddenly and the living conditions rapid changed, causing the function disorder of the stomach and intestines. The intense psychological stimulation caused the digestive stress response. After earthquake the country and the local government took the advantageous preventive measures such as strengthening the protection and the control of tap water, preventing the water source pollution. Using of the bottled water and paying attention to the health and disinfection, the serious intestinal infectious diseases were unpopular and the incidence rates of the digestive disease were lower. In view of the above survey results and the army reality, we suggest that we may strengthen the intensity of training and take the preventive action as following:
1. We should improve the army officers’ and soldiers’ daily life condition under emergency situation as far as possible and amend the emergency equipment including the clothing, the diet and the drugs. In this survey that the incidence rate of skin disease is extremely high in the army officers and soldiers, because soldiers cannot take a bath regularly, cannot change the clothes and lack the corresponding medicine. Similarly the respiratory diseases with higher incidence rate were related with weary body and the...
dropped body resistance. Therefore the improvement of wartime living conditions and jury rig are imperative.

2. It is very important to pay great attention to the mental hygiene construction in army officers and soldiers usually, adopt the practical efficacious device and the measure to carry on the scientific psychological exercise and improve the mental hygiene quality. During the emergency we should strengthen psychological counseling and the opening, rich and optimize the methods to reduce the pressure fast. The concerned department must detail some psychological workers thorough disaster area and the army basic unit, carrying on specialized psychological unblocking to the soldiers and the disaster victims. The daily medical worker must grasp some mental hygiene general knowledge, while on duty discovering promptly and carrying on essential psychological unblocking and the treatment to the patients. 16

3. We should usually strengthen the pointed adaptation training in the adverse circumstance, trying to find out effective, suitable wartime demand rule of thumb and enhancing the adaptive ness to the adverse circumstance.17 We should further strengthen individual and the environmental sanitation management under the emergency mode. It is necessary that eliminating the vectors of mosquito, fly, mouse and preventing infectious diseases’ popularity.

4. We must reasonably equip and assign the medical service resources and safeguard medical service way is unobstructed. It must be avoided that the lack of medical service resources with the waste coexisted in different area

References


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Lessons from an IV Drug abuser: Reform the blood safety surveillance measures

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Abstract

An IV drug abuser donated his blood to check his HIV status for free. He concealed his past drug abuse, but appropriately chose the Confidential Unit Exclusion (CUE) option. Since the screening for transfusion transmissible infections tested negative, he tried to donate blood for a second time following a consultation session. This time, he declared his past drug behavior and was permanently rejected from further blood donation. Apart from the factors on the donor side, the health interview, donor notification, and post-CUE consultation procedures should also be sufficient for making such donors feel safe about stating their past history of risky behaviors.

Case presentation

This report details how a blood center learned from an IV drug abuser of the need to improve the blood safety surveillance efficacy at the donor interview, consultation, and Confidential Unit Exclusion (CUE) system levels. A young married man in his mid 30s with a university degree, living in an urban area of Mashhad and working as a governmental employee, volunteered to donate blood in April 2007. The donor was determined to be emotionally stable during the health interview session. After successfully completing the health interview and prior to blood donation, he chose the CUE option, designating that his blood should not be used for transfusion. Following the successful donation, his blood tested negative for routine screening tests. Due to the lack of post-CUE consultation and donor notification system for self-rejected donors, no feedback was collected from the donor. Three months later, the same donor contacted the blood center to ask about the donor testing results. Since any information regarding blood donors and their donation is kept confidential and the donor identity had to be verified in a face-to-face manner, he was referred to the consultation department.

At the consultation session, he indicated that an unsafe sex practice seven months prior to the donation was the main reason for his decision to choose CUE. The consultant was a female physician who had not been especially trained for counseling the blood donors infected with common transfusion transmissible infections; moreover, no psychologist was present for the consultation. Based on the routine screening test results, the physician informed the donor of his eligibility to donate blood one year after the last unsafe sex experience. Nine months later, in June 2008, the donor volunteered to donate his blood for a second time. He declared his IV drug abuse as the real reason for choosing the CUE option in his previous donation; consequently, the donor was permanently rejected from blood donation.
Discussion

The donor serves as an overt example of those who volunteer to donate blood just to check their HIV status for free [1]. In the Mashhad blood center, as in other regional blood centers under the Iranian Blood Transfusion Organization, the task of screening and interviewing donors is done by physicians who have the required knowledge of blood safety and transfusion medicine and have been specially trained for counseling and interviewing blood donors. Based on the data from the digital databank of Mashhad Blood Center, 3.54% of all cases of permanent deferral of blood donation in the most recent two years were IV drug abusers. In addition, unpublished data from the Vice Chancellor of the treatment office of Mashhad University of Medical Sciences indicate that 24% of the customers of withdrawal clinics for opiate addiction treatment are IV drug abusers.

The donor in question was also an example of those who properly choose the CUE option. The application of the CUE system began following a 1986 FDA recommendation about providing the opportunity for self-exclusion for donors who think their blood in not safe for blood transfusion [2]. The history of introducing CUE at the Mashhad blood center dates back to the 1990s.

A good reason why the donor concealed his past history of IV drug abuse would be the mistrust of the blood center’s privacy policy regarding the confidentiality of his private information. This is especially significant when sharing information regarding the infection or drug addiction with others, which may threaten the social position or job of donors. In addition, people sometimes volunteer to donate blood in groups. In such situations, the donor may feel pressured by others in the group to donate blood despite concerns of probable rejection by the physician during the health interview session because of a past history of high risk behaviors [3, 4]. A physician of the same sex might provide better communication to a donor to convince him or her to declare the past history of drug abuse, unsafe sex, or other common causes of donor rejection. Indeed, three months after the initial donation, the donor in question failed to correctly state the real reason of his CUE during the consultation session. A standard consultation with a physician and a psychologist who are especially trained to counsel donors infected with common transfusion transmissible infections would be appropriate for convincing such donors not to conceal their past history of risky behaviors.

The good news from this particular donor was that he properly chose the CUE option during the first blood donation and ultimately stated his drug abuse, which resulted in being permanently rejected for blood donation. Maybe the factors that were evident in the donor (e.g., living in an urban area, possessing a university degree, and having a governmental job) are predictors of donors’ understanding and appropriate use of CUE. The bad news could be his concealment of the drug abuse in the second blood donation, which could have subsequently increased the rate of “Remained Risk of Transfusion Transmissible Infections”.

Conclusion

The significance of this case was that it demonstrated the need to pay more attention to the factors affecting outcomes of both health interviews with blood donors and consultations with infected blood donors. It is also essential to provide an atmosphere in which donors—especially first-time donors who are not still familiar with blood centers—realize that the center’s employees respect their privacy and confidentiality. A post-CUE consultation should be a routine procedure as well as employing trained physicians and psychologists in consultation department, which has proved to be helpful. Additional noteworthiness of the case was that the in-depth analysis of it shed light on future research. Based on the experience of this case, several hypotheses were developed regarding the factors associated with the appropriate use of CUE.
References


2. Department of Health and Human Services, Food and Drug Administration: Additional recommendation for reading further the number of units of blood and plasma donated for transfusion or for further manufacture by persons at increased risk of HTLV-3/LAV infection. Memorandum to all registered blood establishments, October 30, 1986.


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Dexamethasone / human chorionic gonadotrophin (hCG) and dexamethasone / nafarelin as a valid diagnostic tests in reproductive aged women with polycystic ovarian syndrome (PCOS)

DEKSAMETASON /HUMANI HORIONSKI GONADOTROPIN (HCG) AND DEKSAMETASON/NAFARELIN SU VALIDNI DIJAGNOSTIČKI TESTOVI U REPRODUKCIJSKOJ DOBI ŽENE SA POLICISTIČNIM OVARIJSKIM SINDROMOM (PCOS)

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2 University Clinical Center Tuzla, Internal clinic, department of Endocrinology, Bosnia and Herzegovina.

Abstract

Introduction. Hyperandrogenism is a functional, diagnostic and therapeutic problem of women in reproductive age. The aim of this study was to determine the validity of dexamethasone-human chorion gonadotrophin (DEXA/hCG) and dexamethasone-nafarelin (DEXA/N) testing in the differential hyperandrogenism diagnosis in differentiating polycystic ovary syndrome (PCOS) from other forms of hyperandrogenism.

Subjects and methods. Prospective study included 30 women of reproductive age with PCOS, selected by diagnostic Rotterdam criteria (group A) and 12 women of reproductive age who are not PCOS (group B). Subgroup A1 (n = 15) and B1 (n = 6) were treated with DEXA/hCG test, subgroups A2 (n = 15) and B2 (n = 6) were treated with DEXA/N test. All respondents had the same parameters: cortisol, dehydroepiandrosterone sulphate (DHEAS), total testosterone, SHBG, free androgen index (FAI) and 17-hydroxyprogesterone (17-OHP) basal, during and after testing.

Results: The suppression with dexamethasone during (DEXA /hCG) test in subgroups A1 and B1, the fourth day was followed by a significant decline in average values (p<0.05) DHEAS, testosterone, SHBG, free androgen index (FAI) and 17-hydroxyprogesterone (17-OHP) basal, during and after testing. In DEXA/N after the suppression test in subgroups A2 and B2 there was a significant decline.
in average values of (p< 0.05) DHEAS, testosterone, SHBG, FAI and 17-OHP on the fourth day of the test when compared to the basal value. After the injection of nafarelin ampoules of 100 ug in subgroup A2 there was a significant increase in the value of 17-OHP (p<0.001), greater than 7 nmol/l, while the significant increase in subgroup B2 (p<0.01) was 5 nmol /l in relation to the value before injection of nafarelin. Average value of 17-OHP in the DEXA /N test was significantly higher (p<0.001) when compared to the average value of 17-OHP in the DEXA /hCG test in subjects with PCOS.

**Conclusion:** The results of this study showed that DEXA /hCG and DEXA/N are valid tests for the diagnosis of PCOS, but the nafarelin test is more significant.

**Key words:** PCOS, dexamethasone/hCG test, dexamethasone/nafarelin test.

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**Sažetak**

**Uvod.** Hiperandrogenizam je veliki funkcionalni, dijagnostički i terapeutski problem u reproduktivnoj dobi žene.

**Cilj** ove studije bio je da se utvrdi validnost dexamethason/humani horionski gonadotropin (DEXA/hCG) i dexamethason/nafarelin (DEXA/N) testova u diferencijalnoj dijagnozi hiperandrogenemije u razlikovanju policističnog ovarijskog sindroma (PCOS) od drugih oblika hiperandrogenizma.

**Ispitanici i metode.** Prospektivnom studijom obuhvaćeno je 30 žena reproduktivne dobi sa PCOS, odabrani po Rotterdam dijagnostičkim kriterijima (grupa A) i 12 žena reproduktivne dobi koje nemaju PCOS (grupa B). Podgrupa A1 (n=15) i B1 (n=6) su tretirane DEXA/hCG testom, podgrupe A2 (n=15) i B2 (n=6) su tretirane DEXA/N testom. Svim ispitanicama su određeni isti parametri: kortizol, dehidroepiandrosteron sulfat (DHEAS), ukupni testosteron, SHBG, slobodni androgeni indeks (FAI) i 17-hidroksiprogesteron (17-OHP) bazalno, u toku i nakon testiranja.

**Rezultati:** Nakon supresije dexamethasonom tokom (DEXA/hCG) testa u podgrupama A1 i B1, četvrtog dana uslijedio je signifikantan pad srednjih vrijednosti (p<0.05) DHEAS, testoste-

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**Introduction**

Clinical hyperandrogenism (hirsutism, acne, alopecia, seborhea, menstrual disorder, infertility) is a problem in reproductive age women with androgen hypersecretion. Androgens can stimulate the ovaries, adrenal glands, or both together, or arise from peripheral conversion of androstenedione. Androgen found in the following breakdown diseases: androgen active tumors, non-classical congenital adrenal hyperplasia (CAH), hyperandrogenism with insulin resistance and acanthosis nigricans (HAIARAN), idiopathic hirsutism (IH), hyperandrogenemia with hirsutism in PCOS. About 82% of the total hyperandrogenism is result of PCOS (1) The various forms of hyperandrogenism, use functional endocrine tests for their diagnosis. Low doses of dexamethasone suppressive test (48h/2mg LDDST) is a method to distinguish between screening tumor and functional hiperandrogenism (2). Role of adrenal gland
in PCOS is known, because the abnormal regulation of the cytochrome P450c17-alpha, cause abnormal function of enzymes in the ovary and adrenal glands in synthesis of androgen 17-OHP (3). Disregulation of adrenocortical cytochrome P450c17-alpha causes the increase of 17-OHP after ACTH stimulation. Hyperandrogenemia in about 40-60% of women has elevated 17-OHP response to ACTH stimulation (4). DHEAS is in 95% synthesized in the adrenal cortex, but is often elevated in PCOS for more than 50% (5). Also, women with PCOS have elevated 17-OHP after GnRH stimulation (6). Good hormonal response to GnRH agonists injected nafarelin proved to be a good diagnostic test in testing shafts hypothalamus-pituitary-gonads. Numerous studies showed that the response to other GnRH agonists were similar to response to nafarelin (7,8,9,10). Significant difference in response was found after the test of nafarelin and leuproplid of 10ug/kg, except that the same doses of nafarelin gave 10 times stronger response (11). Good growth of 17-OHP values after injection of 5000 IU HCG showed a good diagnostic test for the diagnosis of PCOS. (12) The aim of this study was to determine the validity of the functional tests DEXA/hCG and DEXA/N for the differential diagnosis in functional ovarian hyperandrogenism (FOH).

Subjects and methods.

Prospective study included 30 women of reproductive age under suspicion of PCOS, selected by Rotterdam criteria (13), 18-35 years old, with signs of hyperandrogenism, menstrual disorders and infertility. The study covers treatment of infertile patients during the period from 2007th to 2009th. Excluded from the study were patients who had NCAH, hyperprolactinemia, Sy Cushing, androgen active ovarian tumors and adrenal glands. Patients with PCOS were divided into two subgroups: 15 were tested with DEXA/hCG test (group A1), 15 was tested with DEXA/N test (group B1). The control group consisted of 12 healthy women of reproductive age between 18-35 years of age, of which six were treated with DEXA/hCG test (subgroup A2) and six of them with DEXA/N test (subgroup B2). Respondents with PCOS and those in the control group had the same parameters. With DEXA/hCG test in high follicular phase of the menstrual cycle, we analyzed the basal levels of hormones and hormone levels during the fourth day of therapy with dexamethasone (cortisol, DHEAS, testosterone, SHBG, 17-OHP). The subjects were treated daily with 4x1 tablets of 0.5 mg of dexamethasone (dexametazon,Krka, Novo Mesto ,Slovenia) during the five days. On the fourth day of testing, we analyzed the levels of hormones, then injected 5000 IU of hCG (Chorionom, IBSA,Lugano, EU)ni them, and the fifth day of the test the level of 17-0Hp were determined.

Dexamethasone-Nafarelin test

Same procedure was then carried out, as in-DEXA/hCG test, with the 100 ug of Nafarelin, instead of hCG.

Definition: Hirsutism is defined based on the Ferriman-Gallwey (FG) score greater than 8 (14), ovulatory dysfunction was defined by less than 8 menstrual cycles per year or luteal progesterone less than 9.54 nmol / l, menstrual cycle dysfunction more than 34 days and less than 21 days (15). Metabolic syndrome is defined by the recommendation of International Diabetes Federation (IDF) (16). Biochemical hyperandrogenism is defined if the total testosterone is greater than 2.08 nmmol / L, DHEAS greater than 7.8 umol / L. If the total testosterone (UT) is greater than 7.2 nmol / L and greater than DHEAS 20.8 umol / l there was doubt on the existence of active androgenic tumors, and elevated serum 17-OHP over 9.1 nmmol / L and elevated peak higher after ACTH of 30 .3 nmol / L is considered NCAH (17). HOMA-IR greater than 2.16 and QUICKI less 0.34 than they were a sign of insulin resistance (IR) and reduced insulin sensitivity, (IS), counted by the formulas (18). Free androgen index (FAI) was counted by the formula = (total testosterone (nmmol) x 100 / SHBG (nmol / L) (19). Transvaginal color Doppler (TVCD) criterion was: more than 12 follicles in the ovary, the size of 2-9 ml, ovarian volume greater than 10 ml, increased ovary Stroma (formula = p / 6 (DB1xDB2xDB3) (21).

Laboratory assays: Taking blood for determination of insulin and fasting glucose. Insulin
(µIU / ml) was determined by RIA (direct radioimmunoassay) on Wallec automatic counter (Wizard) Turku Finald company. INSI-CKIT Irma was used, firm DiaSorin, Italy. Insulin sensitivity was calculated by formula: HOMA-IR = fasting insulin (µIU / ml) x fasting glucose (mmol / L) / 22.5, higher finding greater than 2.16. QUICK = 1/log fasting inzulinan (µIU / ml) + log fasting glucose (mg / dl). DHEAS, 17-OHP, total T, 17-OHP, SHBG, as determined by RIA (direct radioimmunoassay) on Wallec automatic counter (Wizard) Turku Finald company. The original IRMA kits for individual hormone IMMUNOTHEC a Beckman Coulter Company, France were used. Oestadiole, Pg, FSH, LH, prolactin, testosterone were determined by the method of the apparatus Fluorimmunoaoassay Wallace, DELFIA FLUROMETER. The original DELFIA KITS for individual hormone Turku, Finald were used. Glucose in the hospital conditions is measured by enzym colorimetrics method (Glucose GOG-PAP) on the unit VP Super System, diagnosis Division, USA. Estimation of free testosterone was calculated by the formula FAI = total testosterone (nmol/L) x100/SHBG (nmol / L) (ref. ≤ 3) (15).

**Statistical analysis:** Collected data were entered in a specially created database on personnal computer. Statistical processing is carried out under

<table>
<thead>
<tr>
<th>Table 1. Clinical and basal hormonal characteristics of polycystic ovary syndrome (PCOS) and control subjects</th>
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<tbody>
<tr>
<td><strong>Parameter</strong></td>
</tr>
<tr>
<td>Age</td>
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<tr>
<td>Age of menarche</td>
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<tr>
<td>BMI (kg/m²)</td>
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<tr>
<td>Vaist circumference (cm)</td>
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<tr>
<td>Obesity (%)</td>
</tr>
<tr>
<td>Metabolic Syndrome (%)</td>
</tr>
<tr>
<td>Acne/ seborrhoea (%)</td>
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<tr>
<td>Hirsute (%) F-G score</td>
</tr>
<tr>
<td>Infertile (%)</td>
</tr>
<tr>
<td>PCOM , 10 ml (%)</td>
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<tr>
<td>Insulin fasting (µU/mL)</td>
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<tr>
<td>Insulin 120 min. OGTT(µU/mL)</td>
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<tr>
<td>Glucose fasting ( mmol/L)</td>
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<tr>
<td>Glucose in 120 min. OGTT</td>
</tr>
<tr>
<td>HOMA-IR (ref. &lt;2.16)</td>
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<tr>
<td>QUICKI (ref. &gt; 0.34)</td>
</tr>
<tr>
<td>LH/FSH ratio</td>
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<tr>
<td>Estradiol (pmol/L)</td>
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<tr>
<td>Pg –luteal (nmol/L)</td>
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<tr>
<td>Prolactin (ng/ml)</td>
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<tr>
<td>Total testosterone (nmol/L)</td>
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<tr>
<td>SHBG (nmol/L)</td>
</tr>
<tr>
<td>FAI (range 0-3)</td>
</tr>
<tr>
<td>DEHEAS (nmol/L)</td>
</tr>
<tr>
<td>17-OHP (nmol/L)</td>
</tr>
</tbody>
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Note: :Parametri su izraženi kao srednja vrijednost ± SD, kao median (99% confidence interval), FAI= free androgen indx, HOMA =homeostasis model assessment, QUICKI=quantitative insulin sensitivity index, DHEAS-dehydroapiandrosterone sulphate, OHP-17 hydroxy progesterone, SHBG-sex hormone-binding hormone, LH=luteinizing hormone, FSH=follicle stimulating hormone. Significant values (*) p<0.05 for PCOS vs. control, NS=no significant
Results

Comparison between PCOS group vs. control group (Table 1).

When comparing women with PCOS and control groups, the first had significantly higher BMI (p < 0.03), the waist circumference (OS) (p < 0.001), and greater representation of the metabolic syndrome (p < 0.05), PCOM (p < 0.004), fasting insulin (p < 0.03), 2h after OGTT insulin (p < 0.007), HOMA-IR (p < 0.003) and significantly lower QUICK index (p < 0.05). Women with PCOS had significantly high hirsutism prevalence (p < 0.05), and a higher rate of infertility (p < 0.001) in comparison to healthy control group. Total testosterone (p < 0.03) and FAI (p < 0.001) were significantly higher, whereas SHBG (p < 0.006) was significantly lower in women with PCOS when compared to control group. Women with PCOS had significantly elevated LH / FSH ratio (p < 0.04), low luteal Pg (p < 0.001) and lower follicular oestradiol (p < 0.006) in comparison to the control group of healthy women.

After the suppression of DEXA /hCG test in women with PCOS there was a significant drop in cortisol (p < 0.01), DHEAS (p < 0.01), testosterone (p < 0.05), FAI (p < 0.01), 17-OHP (p < 0.05) in comparison to basal values before therapy with dexamethasone and a significant increase in 17-OHP (p < 0.001) in the HCG test, greater than 7 nmol / L compared to the value prior to HCG (Table 2). After the suppression of DEXA /hCG test in healthy women there was a significant drop in cortisol (p < 0.01), DHEAS (p < 0.01), testosterone (p < 0.01), FAI (p < 0.05), 17-OHP (p < 0.05), when compared to the basal values before dexamethasone therapy and significant increase in 17-OHP (p < 0.01) in the HCG test, less than 5 nmol / L in relation to the value prior to HCG. (Table 2)

After the suppression of DEXA / N test in women with PCOS there was a significant drop in cortisol (p < 0.01), DHEAS (p < 0.01), testosterone (p < 0.01), FAI (p < 0.01) when compared to the basal dexamethasone values before therapy and a significant increase in 17-OHP (p < 0.001) in the nafarelin test, higher than 7 nmol / L when compared to values before nafarelin therapy(Table 3). After the suppression of DEXA / N test in healthy women there was a significant drop in cortisol (p < 0.01).

**TABLE 2. Dexamethasone /human chorionic gonadotrophin (hCG) test**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Before Dexamethasone</th>
<th>After Dexamethasone</th>
<th>HCG test</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PCOS CONT.</td>
<td>PCOS CONT.</td>
<td>PCOS CONT.</td>
</tr>
<tr>
<td>Cortisol (nmol/L)</td>
<td>412±150</td>
<td>414±</td>
<td>&lt;50 0b</td>
</tr>
<tr>
<td>DHEAS (µmol/L)</td>
<td>9,3±4,2</td>
<td>7,6±</td>
<td>3,2±1,20b</td>
</tr>
<tr>
<td>UT (nmol/L)</td>
<td>2,9±</td>
<td>1,9±</td>
<td>1,4±0,5a</td>
</tr>
<tr>
<td>FAI (nmol/L)</td>
<td>9,1±3,6</td>
<td>2,1±1,4</td>
<td>4,6±0,80b</td>
</tr>
<tr>
<td>SHBG (nmol/L)</td>
<td>31±5,2</td>
<td>64±38</td>
<td>33±4,2</td>
</tr>
<tr>
<td>17-OHP (nmol/L)</td>
<td>5,42±0,32</td>
<td>4,70±0,32</td>
<td>2,14±0,340a</td>
</tr>
</tbody>
</table>

aP<0,05; bP<0,01; cP<0,001; PCOS ◊ Dexamethasone before vs.after; Control Δ Dexamethasone before vs.after: PCOS ◊ hCG before vs.after; control Δ hCG before vs.after, DHEAS dehydroepiandrosterone; UT, ukupni testosteron; FAI, free androgen indeks; SHBG, seks hormone-binding globulin; 17-OHP, 17-hydroxyprogesterone.
DHEAS (p< 0.01), 17-OHP (p< 0.01) testosterone (p< 0.01), FAI (p< 0.01) when compared to the basal values before dexamethasone therapy and significant increase in 17-OHP (p< 0.01) in the nafarelin test, less than 5 nmol / l in relation to the value before nafarelin (Table3).

Average value of 17-OHP in DEXA / N test was significantly higher (p< 0.001) compared to the average value of 17-OHP in DEXA /hCG test in women with PCOS, while the control group did not have any significant difference in the value of 17-OHP (NS). In comparison to the control group, value 17-OHP in women with PCOS was significantly higher in DEXA / N (p < 0.001) and DEXA /hCG test (p< 0.01) (Figure 1).

<table>
<thead>
<tr>
<th>PARAMETRI</th>
<th>Before dexamethasone</th>
<th>After dexamethasone</th>
<th>NAFARELIN</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PCOS</td>
<td>CONT.</td>
<td>PCOS</td>
</tr>
<tr>
<td>Cortisol (nmol/L)</td>
<td>410±120</td>
<td>398±120</td>
<td>&lt;50 0b</td>
</tr>
<tr>
<td>DHEAS (µmol/L)</td>
<td>10,1±3,6</td>
<td>7,2±1,6</td>
<td>3,1±1,40b</td>
</tr>
<tr>
<td>UT (nmol/L)</td>
<td>3,1±0,13</td>
<td>1,36±0,15</td>
<td>1,3±0,60a</td>
</tr>
<tr>
<td>FAI (nmol/L)</td>
<td>9,4±4,2</td>
<td>2±2,2</td>
<td>4,1±0,9b</td>
</tr>
<tr>
<td>SHBG (nmol/L)</td>
<td>32±4,3</td>
<td>62±48</td>
<td>34±3,1</td>
</tr>
<tr>
<td>17-OHP (nmol/L)</td>
<td>5,62±0,2</td>
<td>4,60±0,38</td>
<td>2,1±0,30b</td>
</tr>
</tbody>
</table>

*D<0,05; **P<0,01; †P<0,01; PCOS ‡ Dexamethasone before vs.after; Control Δ Dexamethasone before vs.after; PCOS ◊ nafarelin before vs.after; Control † nafarelin before vs.after;

DHEAS dehydroepiandrosterone; UT, totali testosteron; FAI, free androgen indeks; SHBG, sex hormone-binding globulin;

17-OHP, 17-hydroxyprogesterone.

**Discussion**

Hyperandrogenism is a functional problem in women of reproductive age, manifested through hirsutism, acne / seborrhoea, oligo-anovulatory disorders, obesity, infertility. Approximately 85% of the total hyperandrogenism belongs to PCOS.

(1). Low dose of dexamethasone suppressive test (2mg/48h LDDST) is the possibility to differentiate the functional tumor hyperandrogenism. Good suppression of cortisol, with values of less than 50 nmol / l excludes cancer, ovarian cancer and adenoma of adrenal gland. If suppression of UT is less than 40% of basal values, the suppression of cortisol greater than 50 nmol / L, this indicates the existence of malignant ovarian secretory tumors and adrenal glands that secrete androgens.

LDDST shows 100% sensitivity and 88% specificity in identifying patients with androgen secreting tumors. Suppression of cortisol less than 50 nmol / l, with suppression of testosterone less than 40% of basal value indicates the existence of a benign ovarian tumors and adrenal cortex. Good suppression of cortisol levels (less than 50 nmol / l) and DHEAS, with the weak suppression of testosterone, requires additional nafarelin or hCG test, to be separated from other forms of PCOS FOH (2). The results of this study showed that DEXA / hCG and DEXA / N are valid tests in distinguishing PCOS from other forms of FOH. 17-OHP in-
crease in both the test above 7 nmol/l confirmed the diagnosis of PCOS. Adrenal gland under the control of ACTH has an important role in the pathogenesis of PCOS. Cytochrome P450c17-alpha is a key enzyme in steroidogenesis androgens in the ovary and adrenal gland. Abnormal regulation of cytochrome P450c17-alpha in the ovary and adrenal glands causes a rise in 17-OHP, a forerunner of the synthesis of cortisol and other androgens (3,4).

Rosenfield et al. indicate that abnormal regulation of cytochrome P450c17-alpha causes a hyperandrogenism originated from the ovary and adrenal cortex (22). Approximately 40-60% of women with hyperandrogenemia have excessive adrenal androgen response to ACTH stimulation (3). Androgen DHEAS is encouraging 95% of adrenal glands in healthy women, but in women with PCOS the origin of 50% DHEAS is ovarian (5).

Therefore, it is necessary to supress the function of adrenal glands with dexamethasone, and then GnRH agonist and hCG stimulates steroidogenesis in the ovaries and increase 17-OHP after stimulation of ovarian origin. Women with PCOS have elevated 17-OHP response to nafarelin stimulation with GnRH agonist (6,23). Results of other studies have showed similar results, obtained with different values, depending on the GnRH agonist used, with and without using dexamethasone test. Sahin et al. indicates that the 17-OHP response after ACTH was significantly higher in women with PCOS when compared to control group (3). Fulghesu et al. indicate that women with PCOS with increased ovarian stroma cancer have an increased response to LH, 17-OHP, testosterone, androstenedione and after stimulation with GnRH agonist nafarelin when compared to a control group of healthy women and women with PCOS with normal ovarian stroma (24).

Levrant et al. indicate that the increase in 17-OHP was significant in dexamethasone and nafarelin and HCG test in comparison to a control group of healthy women, and HCG test can be used as a diagnostic test for FOH (12). In conclusion, the combined five-day DEXA /hCG and DEXA / N tests were significant in the differentiation of tumor hyperandrogenism FOH, and are also significant in distinguishing PCOS from other forms of FOH.

References


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Results of treatment of simple unstable uncomplicated lower leg shaft fractures treated operatively and nonoperatively

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² Department for physiotherapy, Clinic for orthopaedic and traumatology, University and Clinical Centre, Bosnia and Herzegovina
³ Department of Cardiology, General Hospital “Prim.dr Abdulah Nakaš”, Bosnia and Herzegovina

Abstract

For the purpose of this research, 60 patients were observed with simple unstable uncomplicated fracture of lower leg, divided into two groups: group treated nonoperatively and group treated operatively subdivided on subgroup of patients treated with compression plate and screw and subgroup of patients treated with intramedullary nails and secure screws. After eight months period the results of major complication (neurovascularary complications, non union, osteomyelitis, amputation) and deformities (varus-valgus, antecurvatum-recurvatum, shortening, rotation) were measured and compared. The differences between the groups in all parametries were not significant what leads to conclusion that nonoperative treatment of this fractures should not be abandoned.

Introduction

Lower leg bones are the most frequently injured among the other bone injuries. According to data of National Centre for Health statistic in USA, 492000 fractures of tibia, fibula and ankle joint were reported per year.¹

Therefore it would be advisable that doctrine about the treatment of this fracture is harmonized. But, the therapy of fractures of this region, besides the femoral neck fractures, are still the object of the most conflicting opinions.²

Tibia is, because of its location, very exposed to injuries, mostly because that one third of its surface is located subcutaneously. In addition to, the blood supply is more uncertain than the other bones which are surrounded with muscles. The ankle is, as the knee joint, a ginglymus type of joint and there is no capability for accommodation on rotatory deformations after fracture of tibia. So, the special care is necessary during reduction of the fracture i.e correction of such deformities. Delayed union, non union and infections are relatively often complications of the lower leg bones.²

What is the optimal treatment of the simple unstable uncomplicated lower leg fracture?

Maybe, the best answer on this questions gave Nicol who emphasises importance of good judgement in treatment of this fracture: “Every fracture is particularly problem and decision to treat it with internal osteosynthesis or nonoperatively should be done by particularly judgement of benefits and risks of all methods and particularly circumstances of every case. This is the invitation for the best judgement but that is more difficult to acquire than virtuosity in the operation room.”¹

Today, the majority of authors who are occupied with this problems agree that doing with classification is necessary to describe very precisely anatomic location, pattern of fracture line, associated injury of fibula, position and number of fragments and amount of soft tissue damage.¹,²,³,⁴,⁵
Very detailed classification system was suggested by AO ASIF group Muller and all. (1990) and, with amendment, accepted by Orthopedic Trauma Association (OTA).

Tibial shaft fractures, according to this classification are divided into:

A simple
B with wedge fragment
C complex

Further, simple tibial shaft fracture are divided:
A/1 spiral
A/2 oblique
A/3 transverse

Patients and methods

Patients

In this research was included 60 patients with lower leg fractures, treated on Clinic for orthopaedic and traumatology of Clinic Centre in Sarajevo, in period from 2001 to 2004 operatively and nonoperatively:
- 20 patients was treated with skeletal traction through tibial tuberosity, upper knee cast immobilisation, than with Patella Tendon Bearing (PTB) cast according Sarmiento
- 20 patients were treated with rigid osteosynthesis with plates and screws
- 20 patients were treated with intramedullary nail and secure screws

This research was included:
- patients of different ages, both gender, with lower leg shaft fractures: simple, unstable, uncomplicated
- the patients without signs of cardiac, pulmonary, hepatal, renal or other insufficiency or other conditions that could been interfered on fracture healing
This research was excluded next conditions:
- uncooperated patients which were not keeping adequate postoperative regime
- patients which were not appeared at first or control examinations

The result of treatment were estimated after eight months of starting treatment based on anamnesis, clinical examination and radiogram of lower leg with knee and ankle joint.

**Method of research**

At admission of every patient on Clinic for orthopaedic and traumatology, anamnesis, clinical exam, standard laborotary analyses, chest radiogram, lower leg radiogram with ankle and knee joint in two directions, ECG and exam by internist were done.

Patients included in this research were divided into two groups:

- a) group of patients treated nonoperatively (skeletal traction, upper knee cast, PTB cast according Sarmiento... 20 patients
- b) group of patients treated operatively:
  - rigid osteosynthesis with compressive plates and screws...20 patients
  - intramedullary nail and secure screws... 20 patients

The goal of this research was to measure and to compare finally results of nonoperative and operative treatment of the patients with simple unstable uncomplicated lower leg shaft fracture using the parameters from this table:

From the Table 1. in this research, when treatment of the patients with simple, unstable, uncomplicated lower leg shaft fracture were finished, the results of major complications (nonunion, osteitis, amputation and neurovascular disorders) and deformities (varus-valgus, antecurvatum-recurvatum, shortening and rotation) were measured and compared.

**Table 1.** (Johner R, Whrus O.): Classification of tibial shaft fractures and correlation results

<table>
<thead>
<tr>
<th></th>
<th>Excellent</th>
<th>Good</th>
<th>Fair</th>
<th>Poor</th>
</tr>
</thead>
<tbody>
<tr>
<td>non union osteitis, amputation</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>yes</td>
</tr>
<tr>
<td>neurovascular disorders</td>
<td>no</td>
<td>minimal</td>
<td>moderate</td>
<td>serious</td>
</tr>
<tr>
<td>deformity:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>varus/valgus</td>
<td>no</td>
<td>2-5</td>
<td>6-10</td>
<td>over 10</td>
</tr>
<tr>
<td>antecurvatum/recurvatum</td>
<td>0-5</td>
<td>6-10</td>
<td>11-20</td>
<td>over20</td>
</tr>
<tr>
<td>rotation</td>
<td>0-5</td>
<td>6-10</td>
<td>11-20</td>
<td>over 20</td>
</tr>
<tr>
<td>shortening</td>
<td>0-5mm</td>
<td>6-10mm</td>
<td>11-20mm</td>
<td>over 20 mm</td>
</tr>
</tbody>
</table>

**Table 2.** Table of frequencies neurovascular disturbances

<table>
<thead>
<tr>
<th>Neurovascular disturbances</th>
<th>Excellent</th>
<th>Good</th>
<th>Fair</th>
<th>Poor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients treated with transosseall extension-upper knee cast -PTB cast according Sarmiento</td>
<td>20</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Patients treated i.e.operated with intramedullary nail and secure screws</td>
<td>20</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Patients treated i.e.operated with DC plate and screws</td>
<td>20</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

\[df=(3-1)x(4-1)=2x3=6; \ a=0.03; \ \chi^2a=12.6; \ \chi^2=0\]

Theoretical value of \(\chi^2\) testa in this case is 12.6. Empirical value is 0. There are no significant differences between the groups.
Statistic processing of finally results

The results were processed by hi - square test with degree of freedom 6.

Result of research

![Graph 1. Graphic representation frequencies of neurovascular disorders](image1)

![Graph 2. Graphic representation frequencies of nonunion, osteitis and amputation](image2)

Table 3. Table of frequencies nonunion, osteitis and amputation after treatment, $\chi^2=0.001$

<table>
<thead>
<tr>
<th></th>
<th>Excellent</th>
<th>Good</th>
<th>Fair</th>
<th>Poor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonunion</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>yes</td>
</tr>
<tr>
<td>Osteitis</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>yes</td>
</tr>
<tr>
<td>Amputation (major complication)</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>yes</td>
</tr>
<tr>
<td>Patients treated with transosseal extension-upper knee cast -PTB cast according Sarmiento</td>
<td>20</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Patients treated i.e.operated with intramedullary nail and secure screws</td>
<td>19</td>
<td>0</td>
<td>0</td>
<td>1 (osteitis)</td>
</tr>
<tr>
<td>Patients treated i.e.operated with DC plate and screws</td>
<td>19</td>
<td>0</td>
<td>0</td>
<td>1 (nonunion)</td>
</tr>
</tbody>
</table>

Table 4. Table of frequencies varus-valgus deformities after treatment, $\chi^2=0.125$

<table>
<thead>
<tr>
<th></th>
<th>Excellent</th>
<th>Good</th>
<th>Fair</th>
<th>Poor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deformity Varus-valgus</td>
<td>none</td>
<td>2-5 degree</td>
<td>6-10 degree</td>
<td>over 10 degree</td>
</tr>
<tr>
<td>Patients treated with transosseal extension-upper knee cast -PTB cast according Sarmiento</td>
<td>16</td>
<td>4</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Patients treated i.e.operated with intramendullary nail and secure screws</td>
<td>19</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Patients treated i.e.operated with DC plate and screws</td>
<td>19</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Theoretical value is 12.6. Empirical value is 0.001 that means the differences between the groups are not significant.

Theoretical value is 12.6. Empirical value is 0.125 that means the differences between the groups are not significant.
Table 5. Table of frequencies antecurvatum-recurvatum deformities, $\chi^2=0,251$

<table>
<thead>
<tr>
<th>Deformity</th>
<th>Excellent</th>
<th>Good</th>
<th>Fair</th>
<th>Poor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antecurvatum-recurvatum</td>
<td>0-5 degree</td>
<td>6-10 degree</td>
<td>11-20 degree</td>
<td>over 20 degree</td>
</tr>
<tr>
<td>Patients treated with transosseall extension-upper knee cast -PTB cast according Sarmiento</td>
<td>16</td>
<td>4</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Patients treated i.e.operated with intramedullary nail and secure screws</td>
<td>20</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Patients treated i.e.operated with DC plate and screws</td>
<td>20</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Theoretical value is 12,6.
Empirical value is 0,251 that means the differences between the groups are not significant.

Table 6. Table of frequencies deformity rotation of fragments, $\chi^2=0$

<table>
<thead>
<tr>
<th>Deformity</th>
<th>Excellent</th>
<th>Good</th>
<th>Fair</th>
<th>Poor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rotation of fragments</td>
<td>0-5 degree</td>
<td>6-10 degree</td>
<td>11-20 degree</td>
<td>over 20 degree</td>
</tr>
<tr>
<td>Patients treated with transosseall extension-upper knee cast -PTB cast according Sarmiento</td>
<td>20</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Patients treated i.e.operated with intramedullary nail and secure screws</td>
<td>20</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Patients treated i.e.operated with DC plate and screws</td>
<td>20</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Theoretical value is 12,6.
Empirical value is 0 that means the differences between the groups are not significant.
Discussion

There were no neurovascular disturbances in group nonoperatively neither operatively treated patients in this research (Table 2, graph 1). Sarmiento (7,8) reports few cases (1-4) nonoperatively treated patients but in series of 231 - 761 patients. Muller(5), Tausch(9), Roman(10) report 2-6 cases of neurovascular disturbancies operatively treated patients but in series of over 300 patients. In literature, neurovascular complications are more often in operated patients.

There are no statistically significant differences in neurovascular disturbances between operatively and nonoperatively treated patients in this research.

In the group of operatively treated patients, in this research were two cases of major complications: one case of osteomyelitis and one case of nonunion (Graph 2, Table 3).

In the group of nonoperatively treated patients there are no cases of nonunion, osteomyelitis and amputation. In the research of Matusu (10), Karaharu et al. (11), Jensen (12), te Mulla (5) the cases of nonunion and osteomyelitis were reported (6-21) but in series of 123-286 operatively treated patients. In researches of Sarmiento (7,8) in series over than 700 patients there are no nonunion and osteomyelitis of nonoperatively treated patients. There are no significant differences between operatively and nonoperatively treated patients. In literature the number of frequencies of nonunion and osteomyelitis are more numerically in groups of operatively treated patients what was shown in this research too.

Although, number of frequencies of varus - valgus deformities is more numerical in group of nonoperatively treated patients that differences are not significant between the groups in this research. In researches of Infanger(9) and Matusu (10) percentage of angular deformities are less numerous in groups of operatively treated patients. In these researches authors suggested operative treatment i.e. intramedullary fixation.

There are no statistically significant differences frequencies of antecurvatum- recurvatum deformity between the groups operatively and nonoperatively treated patients in this research although the frequencies of these deformities are more numerous in the group of nonoperatively treated patients (Table 5, graph 4). There are a lot of researches with suggestion for operative treatment because of less number of angular deformities frequencies (9, 10, 11, 12). In researches of Dehne, Nicol and Sarmiento with suggestion for nonoperative treatment. These authors admit more numerous frequencies of angular deformities and shortening deformities but comparing other important parameters they still suggest nonoperative treatment.

Neither one patients in this research had rotation deformity in both groups so there are no significant differences between the groups (Table 6, graph 5).

There are no significant differences frequencies of shortening deformities between groups although frequencies of shortening deformities are more numerous in the groups of nonoperatively treated patients. Empirical value of hi-square test is 0,073 but theoretical value is 12,6, so there are no significant differences between the groups (Table 7, graph 6).

<table>
<thead>
<tr>
<th>Deformity shortening</th>
<th>Excellent</th>
<th>Good</th>
<th>Fair</th>
<th>Poor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients treated with transosseal extension-upper knee cast-PTB cast according Sarmiento</td>
<td>17</td>
<td>3</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Patients treated i.e. operated with intramedullary nail and secure screws</td>
<td>19</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Patients treated i.e. operated with DC plate and screws</td>
<td>20</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Table 7. Table of frequencies deformity of shortening after treatment, $\chi^2=0.073$

<table>
<thead>
<tr>
<th>Deformity</th>
<th>Excellent</th>
<th>Good</th>
<th>Fair</th>
<th>Poor</th>
</tr>
</thead>
<tbody>
<tr>
<td>shortening</td>
<td>0-5 mm</td>
<td>6-10 mm</td>
<td>11-20 mm</td>
<td>over 20 mm</td>
</tr>
</tbody>
</table>

Theoretical value is 12.6.

Empirical value is 0.073 that means the differences between the groups are not significant.
Sarmiento\(^{7,8}\) reports average length of shortening of 10 mm in series over 400 nonoperatively patients so the length of shortening in this research is less than 10 mm. In the researches of Muller, Van Linden et al\(^{5,11,12}\) the operative treatment is preferable.

**Conclusion**

There are no statistical differences between operatively and nonoperatively treated group of patients with simple unstable uncomplicated lower leg shaft fracture. This research leads to conclusion that nonoperative method with skeletal traction than with upper knee cast and finally with Patella Tendon Bearing cast according Sarmiento should not be abundant in the treatment of simple unstable uncomplicated lower leg shaft fracture because, according to the results, there are no significant differences between this groups and operatively treated group but there are no operative risks.

**References**


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Abstract

**AIM** of this research is to show the importance of mycobacteriological examination of bronchoalveolar lavage (BAL) in diagnostic of pulmonary tuberculosis.

**Material and methods:** Retrospective study was carried out to show the number of patients suspected to be ill with pulmonary tuberculosis (TB) whose bronchoalveolar lavage (BAL) samples were examined in Mycobacteriological laboratory of Clinic for Pulmonary diseases and TB “Podhrastovi” in a six-year period (2003 - 2008.) and it was compared Mycobacterium tuberculosis (BK- Bacillus Koch –BK) positivity of BAL with sputum examination findings: microscopic (smear) and cultural.

**Results:** In six-year period (2003. - 2008.) BAL was done in 115 patients suspected to be ill with pulmonary TB. In 33,04 % of them BAL was microscopically and in all of them (100%) cultural Mycobacterium tuberculosis (Bacillus Koch –BK) positive. In the same patients sputum examination findings were microscopically (smear) Mycobacterium tuberculosis (Bacillus Koch –BK) positive in 16,52 % and cultural positive in 75,65 % cases.

**Conclusion:** By this research it has been shown the importance of bronchoalveolar lavage in obtaining a sample of a better quality for finding Mycobacterium tuberculosis (Bacillus Koch) in respiratory system and its value in diagnostic of pulmonary tuberculosis.

**Key words:** Mycobacterium tuberculosis, sputum, BAL.
Sažetak

**Cilj:** pokazati značaj mikobakteriološkog ispitivanja bronhoalveolarnog lavata u dijagnostici plućne tuberkuloze.

**Materijal i metode:** Ovo je retrospektivna analiza broja pacijenata koji su bili suspektni da boluju od plućne tuberkuloze (TBC) čiji su uzorci bronhoalveolarne lavaže (BAL) ispitivani u Mikobakteriološkom laboratoriju Klinike za plućne bolesti i TBC “ Podhrastovi” u šestogodišnjem periodu (od 2003.- 2008.) i upoređivana je pozitivnost na *Mycobacterium tuberculosis* (Bacillus Koch- BK) sa nalazima ispitivanja sputuma : mikroskopski ( razmaz) i u kulturi.

**Rezultati:** U šestogodišnjem periodu (2003-2008.) urađen je BAL kod 115 pacijenata sumnjivih da boluju od plućne tuberkuloze. Kod njih 33,04 % BAL je bio mikroskopski i kod svih (100%) kulturelno pozitivan na *Mycobacterium tuberculosis* (Bacillus Koch- BK). Kod istih pacijenata ispitivanja sputuma su bila *Mycobacterium tuberculosis* (Bacillus Koch- BK ) mikroskopski ( razmaz) pozitivna u 16, 52%, a u kulturi u 75,65 % slučajeva.

**Zaključak:** Ovim istraživanjem je pokazan značaj bronhoalveolarne lavaže u dobijanju uzorka većeg kvaliteta za otkrivanje *Mycobacterium tuberculosis* (Bacillus Koch) u respiratornom sistemu i njen značaj u dijagnostici plućne tuberkuloze.

**Ključne riječi:** *Mycobacterium tuberculosis*, BAL, Sputum

**AIM**

**Aim** of this research is to show the importance of mycobacteriological examination of bronchoalveolar lavage (BAL) in diagnostic of pulmonary tuberculosis.

**Material and methods**

This is the retrospective analysis of the number of patients suspected to be ill with pulmonary TB whose bronchoalveolar lavage samples were examined in Mycobacteriological laboratory of Clinic for Pulmonary diseases and TB “ Podhrastovi” in a six-year period (2003. -2008.) and it was compared *Mycobacterium tuberculosis* (Bacillus Koch-BK) positivity of BAL with sputum examination findings: microscopic and cultural.

**Results**

Results are shown on the Table 1., Table 2., and Graphic1.

**Table 1.** Mycobacteriological examination of BALs per year sputum examination in the same cases suspected of pulmonary TB

<table>
<thead>
<tr>
<th>Year</th>
<th>Number of Year</th>
<th>BAL (BK) Smear</th>
<th>BAL (BK) Cultural</th>
<th>Sputum (BK) Smear</th>
<th>Sputum (BK) Cultural</th>
</tr>
</thead>
<tbody>
<tr>
<td>2003</td>
<td>15</td>
<td>4</td>
<td>15</td>
<td>1</td>
<td>8</td>
</tr>
<tr>
<td>2004</td>
<td>17</td>
<td>1</td>
<td>1</td>
<td>16</td>
<td>15</td>
</tr>
<tr>
<td>2005</td>
<td>22</td>
<td>1</td>
<td>1</td>
<td>15</td>
<td>15</td>
</tr>
<tr>
<td>2006</td>
<td>11</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>11</td>
</tr>
<tr>
<td>2007</td>
<td>21</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>11</td>
</tr>
<tr>
<td>2008</td>
<td>33</td>
<td>10</td>
<td>23</td>
<td>6</td>
<td>17</td>
</tr>
<tr>
<td>Total</td>
<td>115</td>
<td>38</td>
<td>115</td>
<td>19</td>
<td>87</td>
</tr>
</tbody>
</table>

**Graphic 1.** Mycobacteriological examination of BALs per year and sputum examination in the same cases suspected of pulmonary TB

Introduction

The most important step in diagnostic of pulmonary tuberculosis is the finding of *Mycobacterium tuberculosis* in sputum, either by microscopic examination or by sputum cultivation (1,2,3). Although all clinical and chest x-ray parameters indicate pulmonary tuberculosis, sputum finding is often smear and cultural *Mycobacterium tuberculosis* (Bacillus Koch-BK) negative(1). Bronchoalveolar lavage is endoscopic method in which, by fiber-optic bronchoscopy, lower airways are washed by instillation and aspiration of isotonic salt solution, and so obtained material is examined in the same way as sputum.
In 2003, we did 15 BAL. 4 (26.67%) of them were microscopically positive, but all 15 were culturally positive. Sputum examination: 2 microscopically (13.33%), and 8 (53.33%) culturally positive. In 2004, we did 17 BAL. One was microscopically (5.88%), and all were culturally positive. Sputum examination: 3 microscopically (17.65%), and 15 (88.24%) culturally positive. In 2005, we did 22 BAL. One was microscopically (4.54%), and all were culturally positive. Sputum examination: 4 were microscopically (18.18%), and 16 (72.73%) culturally positive. In 2006, we did 11 BAL. 3 were microscopically (27.27%), and all were culturally positive. Sputum examination: 1 microscopically (9.09%), and all were culturally positive. In 2007, we did 27 BAL. 19 were microscopically (70.37%), but all of them were culturally positive. Sputum examination: 3 microscopically (11.11%), and 20 (74.07%) culturally positive. In 2008, we did 23 BAL. 10 were microscopically (43.48%), and all of them were culturally positive. Sputum examination: 6 microscopically (26.09%) and 17 (73.91%) culturally positive. In all 115 patients in 6-year period BAL was microscopically positive in 33.04% and culturally positive in 100%. With sputum examination there were 16.52% microscopically and 75.65% culturally positive Mycobacterium tuberculosis (Bacillus Koch-BK) positivity.

The higher level of positivity was in samples obtained by BAL either microscopically or by cultural examination.

### Table 2: Comparison in mycobacteriological positivity between BALs and sputum examination in per cents

<table>
<thead>
<tr>
<th>Year</th>
<th>Number per year</th>
<th>BAL BK+ microsc. (smear) %</th>
<th>BAL BK+ cultural %</th>
<th>SPUTUM BK+ microsc. (smear) %</th>
<th>SPUTUM BK+ cultural %</th>
</tr>
</thead>
<tbody>
<tr>
<td>2003</td>
<td>15</td>
<td>26.67</td>
<td>100</td>
<td>13.33</td>
<td>53.33</td>
</tr>
<tr>
<td>2004</td>
<td>17</td>
<td>5.88</td>
<td>100</td>
<td>17.65</td>
<td>88.24</td>
</tr>
<tr>
<td>2005</td>
<td>22</td>
<td>4.54</td>
<td>100</td>
<td>18.18</td>
<td>72.73</td>
</tr>
<tr>
<td>2006</td>
<td>11</td>
<td>27.27</td>
<td>100</td>
<td>9.09</td>
<td>100</td>
</tr>
<tr>
<td>2007</td>
<td>27</td>
<td>70.37</td>
<td>100</td>
<td>11.11</td>
<td>74.07</td>
</tr>
<tr>
<td>2008</td>
<td>23</td>
<td>43.48</td>
<td>100</td>
<td>26.09</td>
<td>73.91</td>
</tr>
<tr>
<td>Total</td>
<td>115</td>
<td>33.04</td>
<td>100</td>
<td>16.52</td>
<td>75.65</td>
</tr>
</tbody>
</table>

### Discussion

In Clinic for pulmonary diseases and TB “Podhrastovi” we do mycobacteriological examination of BAL in each case of pulmonary disease which is suspected to be pulmonary TB, but it is smear or cultural Mycobacterium tuberculosis (Bacillus Koch-BK) negative, or in other suspicious cases where there is doubt is it pulmonary TB or other pulmonary disease with similar chest x-ray or clinical findings, whether there is association of pulmonary TB and other pulmonary disease first of all lung cancer. This retrospective examination shows a greater number of Mycobacterium tuberculosis positivity of BAL in comparison with sputum examination. Ranasinghe C.D. (4) in Shri Lanka shows the results of prospective study of smear-negative pulmonary TB using BAL in 281 individuals with pulmonary TB suspected clinically or on chest radiography and 23, 1% of smear-negative individuals had microscopically BK positive BAL. Safianovska A. and al. (5) did BAL in 642 patients in Warsaw, Poland during 7 years (1999.-to 2006.) with different chest x-ray and in 61 of them the Mycobacterium tuberculosis was isolated; in 24 of them isolated mycobacteria were clinical significant: Mycobacterium tuberculosis in 17 and Mycobacterium kansasi in 7 cases. Triller N. and al. (6) in 1469 patients who were underwent bronchoscopy examination in 2006. year with 40 of them pulmonary TB was suspected and in 6 of them Mycobacterium tuberculosis was isolated in culture of bronchial
wishing. They suggest that bronchoscopy in suspected pulmonary TB should be performed only in high suspicious patients where sputum smear examination before bronchoscopy is negative.

**Conclusion**

By this research it has been shown the importance of bronchoalveolar lavage in obtaining a sample of a better quality for finding *Mycobacterium tuberculosis* in respiratory system and its value in diagnostic of pulmonary tuberculosis.

**References**


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The influences of traumatic brain injuries in largeness of fussion convergency

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Ophthalmology Clinic, Clinical Centar University of Sarajevo, Bosnia and Herzegovina

Abstract

Traumatic brain injuries had a main reason to deppend upon with deficit of motor fusion. We aim to investigated weather the patients with traumatic brain injuries had deficit motoric fusion. The study of populations contains 50 patients with many sujectively problems because can not explain objectivly analyses. Deficit of motoric fusion indicated that disturbances had to be motoric and following disability of patients to hold superposition of view to fixation object. In our study the influences of traumatic brain injuries in largeness of fusion convergence was significantly higher after 6 months of the medical treatment p<0.01, t=0.914 and r= 0.881 and Hi² t-test 6.81. The explanations about difficulties of near vision after traumatic brain injuries the visual disturbances must to observed in all simptomatology’s because that it is only conduct for check really diagnosis and control of visul motor system.

Key words: traumatic brain injuries, motor fuzija.

Introduction

Traumatic brain injuries using vibration waves, stroke power and without visible damage causing differences cerebral disorders and between those disorder fusion convergence. In physiological condition fusional convergence develop disparities pictures at the retina. The disparities causing fusion mechanism those showed as convergence. The pictures of the objects started on temporal side both retina because the object saw like double at the near. Corrected reflex of fusion convergence and double vision disappear.

AIM

We aim to investigated weather the patients with traumatic brain injuries had deficit motoric fusion.
Materials and method

Our research was based on 50 patients with traumatic brain injuries at the Ophthalmology Clinic, Clinical University Sarajevo. All the patients were sent to this clinic from 2000 to 2003. The group of patients was between from 10 to 40 years old. The study group had traumatic brain injuries and subjectively disturbances at the near vision. The authors have tried to do comparative study and compare results those with of other fifty patients with similar problems who’s had not traumatic brain injuries. Following the study authors was done in both groups of patients: anamnesis, determining vision acuity in near and far vision monocular and binocularly, examination of the anterior and retinal segment, skiascopy, eye motility and oculomotor balance of external eye muscles, cover-uncover test, measuring angle with prisms, neurological examination, brain computer tomography (CT) and statistic examination.

Results

In this study examination 50 patients with traumatic brain injuries, 40 (80 %) were males and 10 (20%) females.

Table 1. Vision capabilities of our patient on near vision

<table>
<thead>
<tr>
<th>Near vision</th>
<th>Binocular</th>
<th>Number of patients</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>VOU reading J1 at the distance of 75 cm</td>
<td>27</td>
<td></td>
<td>54 %</td>
</tr>
<tr>
<td>VOU reading J1 at the distance of 40 cm</td>
<td>14</td>
<td></td>
<td>28 %</td>
</tr>
<tr>
<td>VOU Reading J1 at the distance of 35 cm</td>
<td>9</td>
<td></td>
<td>18 %</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td>50</td>
<td></td>
<td>100 %</td>
</tr>
</tbody>
</table>

Table 2. Size angle of exophory measurement with prisms dioptres before treatment

<table>
<thead>
<tr>
<th>Ortophory at the far</th>
<th>Number of patients</th>
<th>%</th>
<th>Size angle in prisms dioptres (pd)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Egsophory at the near</td>
<td>9</td>
<td>18 %</td>
<td>2 - 4 Pd</td>
</tr>
<tr>
<td></td>
<td>15</td>
<td>30 %</td>
<td>4 - 6 Pd</td>
</tr>
<tr>
<td></td>
<td>26</td>
<td>52 %</td>
<td>6 - 8 Pd</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td>50</td>
<td>100 %</td>
<td></td>
</tr>
</tbody>
</table>

Table 3. Middle values of convergent fusion before treatment

<table>
<thead>
<tr>
<th>Size of fusion (pd)</th>
<th>Number of patients</th>
<th>%</th>
<th>S. D.</th>
<th>Hi² t-test</th>
</tr>
</thead>
<tbody>
<tr>
<td>To 2 Pd</td>
<td>25</td>
<td>50 %</td>
<td>14. 61</td>
<td>9. 61</td>
</tr>
<tr>
<td>Unstable between 0-6 Pd</td>
<td>15</td>
<td>30 %</td>
<td>18. 6</td>
<td>11. 22</td>
</tr>
<tr>
<td>To 12 Pd</td>
<td>10</td>
<td>20 %</td>
<td>14. 18</td>
<td>6. 84</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td>50</td>
<td>100 %</td>
<td>17. 11</td>
<td>9. 41</td>
</tr>
</tbody>
</table>

Table 4. Values of convergent fusion 2 months after treatment

<table>
<thead>
<tr>
<th>Size of fusion (pd)</th>
<th>Number of patients</th>
<th>%</th>
<th>S. D.</th>
<th>Hi² t-test</th>
</tr>
</thead>
<tbody>
<tr>
<td>unstable from 0 to 6 Pd</td>
<td>13</td>
<td>26 %</td>
<td>18. 41</td>
<td>8. 11</td>
</tr>
<tr>
<td>to 10 Pd</td>
<td>15</td>
<td>30 %</td>
<td>18. 6</td>
<td>9. 02</td>
</tr>
<tr>
<td>to 18 Pd</td>
<td>10</td>
<td>20 %</td>
<td>14. 18</td>
<td>7. 84</td>
</tr>
<tr>
<td>Unstable from 1 to 2 (without of improvement)</td>
<td>12</td>
<td>24 %</td>
<td>18. 86</td>
<td>9. 12</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td>50</td>
<td>100 %</td>
<td>16. 44</td>
<td>12. 1</td>
</tr>
</tbody>
</table>
The results of examination anterior and retinal segments were normal. The examination of eye motility finding orthophory at the far and exophory at the near. Size angle of exophory measurement with prisms dioptries.

**Discussion**

The authors have worked sample 50 patients with traumatic brain injuries who’s have subjectively disturbances at the near vision. The convergent fusion after 2 months of medical treatment of the total number where convergent fusion shows the values 10 patients (20 %) where convergent fusion shows the value 18 Pd, were S. D. 14.18 and $H_i^2$ t-test 7.84, 15 patients (30%) where convergent fusion shows the value 10 Pd where standard deviation shows the value 18.6 and $H_i^2$ t-test 9.02, 13 patients (26 %) where convergent fusion shows the unstable value from 0 to 6 Pd where standard deviation shows the value 18.41 and $H_i^2$ t-test 8.11, 12 patients (24 %) where unstable values from 1 to 2 without improvement standard deviation shows value 18.6 and $H_i^2$ t-test 9.12.

The value of convergent fusion after 6 months medical treatment of the total number of 50 patients. We had 15 patients (30 %) shows values from 0 to 16 Pd, S. D. shows values 18.6 and $H_i^2$ t-test 7.22., 9 patients (18 %) shows stabal values from0 to 10 Pd, S. D. shows values 17.61 and $H_i^2$ t-test 5.41., 10 patients (20 %) shows values of convergent fusion from 0 to 22 Pd, S. D. shows values 14.18 and $H_i^2$ t-test 6.84., 8 patients (16 %) shows stabal values of convergent fusion from 0 to 4 Pd, S. D. shows values 16.41 and $H_i^2$ t-test 5.18 and 8 patients (16 %) shows values of convergent fusion about 1 Pd, S. D. shows values 15.01 and $H_i^2$ t-test 5.18.

Base acquired data patient’s shows signification improvement of near vision in relation of statistic values of convergent fusion before treatment that we had $H_i^2$ t-test 9.41., after 2 months of the medical treatment $H_i^2$ t-test 12.10 and best statistic data we had after 6 months of the medical treatment $p<0.01$, $t=0.914$ and $r=0.881$ and $H_i^2$ t-test 6.81.

We had compared our data with data of other authors. Gianutsos R. (1) and Rizzo M. (2, 3) shows that 50% of patients with traumatic brain injuries had visual systematic changes, like as disturbances of central visual at near vision without of disturbances of visual motor balance. This authors in their study of 314 patients showed that the 70 % of patients had parafoveolar fixations of -5º and less. Kerkhoff and co-authors (4, 5) shows that the visual disturbances after trauma brain injuries had disability of visual system made differences between normal objects at the differences brighten so that more of objects appeared like as static’s or moves objects.

Many effects of the disturbances fusion and visual motor changes are very important for longtime work at near. Kerkoff G. (6, 7, 8). The disturbances of visual motor fusion after traumatic brain injuries, the patients had blurred and doubled visual acuity and sometimes had to lose ability of recognize known objects at the mesopic and scotopic brighten Zihl J (9, 10, 11, 12), Kerkoff G (13, 14, 15, 16, 17), some of them wonted stronger brightness at the near work. All of this subjectively disturbances had our patients. That the authors can to explained this disturbances, we had to remind some of the events in physiological visual acuity at near, when we had to unit three cerebral fenomens: accommodation, convergence and myosis whose had to use clear foveolar binoculars visual acuity at the nears objects. When this physiological process changed, than both of eye had to

---

**Table 5. Values of convergent fusion 6 months after treatment**

<table>
<thead>
<tr>
<th>Size of fusion (pd)</th>
<th>Number of patients</th>
<th>%</th>
<th>S. D.</th>
<th>$H_i^2$ t-test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stabile from 0 to 10 Pd</td>
<td>9</td>
<td>50 %</td>
<td>17.61</td>
<td>5.41</td>
</tr>
<tr>
<td>Stabile from 0 to 4 Pd about 1 Pd</td>
<td>8</td>
<td></td>
<td>16.41</td>
<td>5.13</td>
</tr>
<tr>
<td>From 0 to 16 Pd</td>
<td>15</td>
<td>30 %</td>
<td>18.6</td>
<td>7.22</td>
</tr>
<tr>
<td>From 0 to 22 Pd</td>
<td>10</td>
<td>20 %</td>
<td>14.18</td>
<td>6.84</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>50</strong></td>
<td><strong>100 %</strong></td>
<td><strong>21.44</strong></td>
<td><strong>6.81</strong></td>
</tr>
</tbody>
</table>
limited accommodation, less convergence or without of convergent and we had not myosis. After deficiency of fusion convergence the patients with traumatic brain injuries had exophoria at the near vision. First authors who’s had to write that this disturbance of visual near acuity after traumatic brain injuries with his study of small number patients was Jaensch (18). Some of them patients with dysfunction of motility had to be diagnostics like as paralytic squint and whose had to diplopies and had not harmonize with objectively analysis of visual motility.

The patients with traumatic brain injuries had disturbances of visual motor fusions and disturbances of fusions convergence had to lead in exophories at the near vision. The posttraumatic insufficiency of fusion convergence had to difficult prognosis at the near vision but in long times these symptoms to disappear or became tolerable after medical treatment.

**Conclusion**

- The study with 50 patients was conducted at the Ophthalmology Clinic, Clinical University Center in Sarajevo. All of the patients had to mentioned problems at the near vision and fast tired.
- The brain CT and neurological examination was normal.
- After following and consideration examine the authors had to find defect of visual motor fusion that’s had to hard diagnostics as a clinical units.
- The explanations about difficulties of near vision after traumatic brain injuries the visual disturbances must to observed in all simptomatology’s because that it is only conduct for check really diagnosis and control of visual motor system.
- All patient shows increased after prismatic adaptation treatment for long time all those different visual responds.
References


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Bioavailability of antioxidants from tea infusions with honey addition

BIORASPOLOŽIVOST ANTIOKSIDANASA IZ RASTVORA ČAJA SA DODATKOM MEDA

Aldina Kesic, Zorica Hodzic, Aida Crnkic, Mirzeta Saletevic, Benjamin Catovic

University in Tuzla, Faculty of Science, Department of Chemistry, Bosnia and Herzegovina

Abstract

It is often assumed that antioxidant nutrients contribute to the protection afforded by fruits, vegetables, red wine, tea and honey against diseases of aging. In this study the antioxidant activities of fourteen tea samples and three types of Bosnian honey were evaluated. Total antioxidant activity was determined using Ferric Reducing Ability of Plasma (FRAP) assay. Antioxidant activities of evaluated tea varied from 1276 -11710 µM/L, and honey diluted samples from 182,5 – 4612,5 µM/L. Honey contains more antioxidants and minerals than sugar (the darker, the more). In this research we would like to establish benefits of adding honey instead of sugar in tea. Our results strongly suggest that honey addition in tea plays important role in their antioxidant activity. These role depend on botanical origin of honey.

Key words: Antioxidant activity, FRAP, tea, honey.

Introduction

Antioxidant components are microconstituents present in the diet that can delay or inhibit lipid oxidation, by inhibiting the initiation or propagation of oxidizing chain reactions, and are also involved in scavenging free radicals (1).

Free radical reactions occur in the human body as well as in food systems. Reactive oxygen and nitrogen radical species (ROS/RNS) are an integral part of normal physiology. The over-production of these reactive species due to oxidative stress can cause damage to biomolecules and cause cellular injury and death, which may lead to various chronic diseases such cancers, cardio- and cerebrovascular diseases (2,3).

In addition, naturally occurring antioxidants, when consumed, can also act as nutraceuticals

Sažetak

Česte su predpostavke da antioksidansi sadržani u voću, povrću, crvenom vinu, čaju i medu učestvuju u zaštitni organizma od bolesti i starenja. U ovom istraživanju izmjerena je antioksidacijska aktivnost četrnaest uzoraka čaja i petnaest uzoraka meda, koji su svrstani u tri različite vrste. Svi uzorci porijeklom su iz Bosne i Hercegovine. Mjerenje ukupne antioksidacijske aktivnosti uzoraka čaja i meda vršeno je spektrofotometrijskom FRAP (Ferric Reducing Ability of Plasma) metodom. Ukupna antioksidacijska aktivnost čaja kreće se od 1276 do 11710 µM/L, a uzoraka rastvora meda od 182,5 do 4612,5 µM/L. Sadržaj antioksidanasa i minerala u rastvoru meda veći je nego njihov sadržaj u rastvoru šećera. Tamniji uzorci meda imaju veću antioksidacijsku aktivnost u odnosu na svjetlje uzorke. Analize vršene u ovom istraživanju dokazuju prednost dodatka meda umjesto šećera u čaj. Rezultati dobijeni ovim istraživanjem ukazuju na činjenicu da se dodatkom meda u čaj značajno povećava njegova antioksidacijska aktivnost. Antioksidacijska aktivnost meda zavisi od njegovog botaničkog porijekla.

Ključne riječi: Antioksidacijska aktivnost, FRAP, čaj, med.
which can help protect one from oxidative damage in the body (4,5). In western medicine, the balance between antioxidation and oxidation is believed to be a critical concept maintaining a healthy biological system (6,7,8).

Tea is one of the most commonly consumed beverages in the world (9). The chemical composition of tea leaves consists of: tanning substances, flavonols, proteins and amino-acids enzymes, aroma substances, vitamins, minerals and trace elements (10). It is of interest to investigate the antioxidant properties of medicinal plant extracts especially those traditionally used in folk medicine.

Honey is a remarkable product from the hive prepared by honeybees from the nectar and other sugary substances derived from many plants. (11) All over the world, honey is considered a part of traditional medicine. (12). Honey contains a variety of phytochemicals (as well as other substances such as organic acids, vitamins and enzymes) that may serve as sources of dietary antioxidants (13). The amount and type of these antioxidant compounds depends largely upon the floral source/variety of the honey (13).

Honey has been reported to be effective in the healing of wounds and burns (14) and as an antimicrobial agent (15) and in providing gastric protection against acute and chronic gastric lesions (15).

The aim of the present study was to compare antioxidant activity levels in the extracts different types of tea and honey, from the north-east area of Bosnia and Hercegovina. Total antioxidant activity has been determined using ferric reducing ability of plasma assay - FRAP (16).

Methods and materials

All chemicals and reagents were of analytical grade and were purchased from: Fluka-Switzerland: (2,4,6-tri[2- pyridyl]-s-triazine) and Semikem-Sarajevo: (chloric acid; ferrous sulphate heptahydrate; ferric chloride hexahydrate; sodium acetate trihydrate; acetic acid). Spectrophotometric measurements were performed by Cecil CE 2021 UV-VIS spectrophotometer.

Samples of tea and honey were prepared according to a standard protocol. To 1 g of plant material was added 200 mL deionised water (temperature of added water was 98 °C), and left to stay 15 min, without additional heating. The extracts were filtered and the liquid portions were analyzed for their antioxidant activity.

To 5g of honey was added 20 mL deionised water. Honey solution quantitative added in volumetric tasks (50 mL) and fill with deionised water. Liquid portions of 200 µL were analyzed for their antioxidant activity.

FRAP assay measures the change in absorbance at 593 nm owing to the formation of blue colored FeII-tripyridyltriazine compound from colorless oxidized FeIII form by the action of electron donating antioxidants. Standard curve was prepared using different concentrations (100-1000 µmol/L) FeSO4·7H2O. All solutions were used on the day of preparation. In the FRAP assay the antioxidant efficiency of the antioxidant under the test was calculated with reference to the reaction signal given by an FeII-solution of known concentration, this representing a one electron exchange reaction. The results were expressed in µmol FeII/L of extract. Data presented are average of three replications.

Results

Antioxidant activities of evaluated diluted honey samples varied from 182,5 – 4612,5 µM/L. Antioxidant activities of evaluated tea varied from 1276 -11710 µM/L.

Figure 1. Influence of adding different botanical origin honey in tea

Figure 1. shows an influence of adding honey with different botanical origin in examined types of tea. It is understood that forest honey, whic...
contains the most antioxidants has the biggest impact on the antioxidative tea activity. The least impact on the antioxidative tea activity has acacia honey, because it has the least content of antioxidants.

Honey antioxidant activity values show concentration within 182,5 µM/L and 4612,5 µM/L. Average antioxidant activity of forest honey is 4426,25 µM/L, meadow 1517,727 µM/L and acacia 880 µM/L.
When we studied the effect of honey botanical origin on antioxidant activity, it was found that the highest antioxidant activity shows forest honey samples. In contrast, acacia honey samples show the lowest antioxidant activity (Fig. 2).

These data show a relationship between botanical origin of honey and their antioxidant activity.

Discussion

The results of the 4 researches show that medicinal plants are a very rich source of antioxidants. In this work, antioxidant activity was measured in the extracts of medicinal plants that were prepared as teas. Based on the values of antioxidant activity, we have classified medicinal plants in four groups. Extract Melissa folium has very high FRAP (>10 mM/L); high FRAP (8 - 10 mM/L) n = 4; good FRAP (5 – 8 mM/L) n = 3; low FRAP (1-5 mM/L) n = 7. The researches of antioxidative activity in medicinal plants show very high value in extract Melissa officinalis L (17,18,l9,20). It is also proved high antioxidative activity in plants from Labiatae family (21).

Honey has a phytochemical profile which includes polyphenols and other substances that can act as antioxidants. Antioxidants perform the role of eliminating free radicals, which are reactive compounds in the body. Free radicals are created through the normal process of metabolism and contribute to many serious diseases.

Investigations of Slovenian honey show that antioxidant activity was the lowest in the brightest acacia and lime honeys and the highest in darker honeys, namely fir, spruce and forest (22). These results are in correlation with ours. Our results show that antioxidant activity was the lowest in the brightest acacia honeys and the highest in darker forest honey. The color of the analyzed honey samples in this study was very variable and ranged from pale yellow to dark brown.

Some investigations in USA show that antioxidant activity of honey is 0.2 to 0.7 mmol FRAP/100 g. These investigations confirm that honey shows higher antioxidant activity than refined sugar (23). The results of antioxidant activity of honey obtained by using FRAP method are showed in Table 2.

According to their reducing ability/antioxidant power, 15 honey samples can be divided into three groups: a) low FRAP (<1 mM/L), n = 4; b) good FRAP (1-2 mM/L) n = 6; high FRAP (>2 mM/L) n = 5.

Figure 1 shows an influence of adding honey with different botanical origin in examined types of tea. It is understood that forest honey, which contains the most antioxidants, has the biggest impact on the antioxidative tea activity. The least impact on the antioxidative tea activity has acacia honey, because it has the least content of antioxidants.

Taken together, our results strongly suggest that honey addition in tea plays an important role in their antioxidant activity. These roles depend on botanical origin of honey.

In this research we would like to establish benefits of adding honey instead of sugar in tea. Sugar is the quintessential source of energy and most foods, when digested, are metabolized by the body as basic sugar (glucose). It is a major source of calories in the diet. The body will save the excess energy in sugar as fat. While some stored fat is necessary, too much is undesirable and pose several health concerns especially for diabetics. Sugar also supports the growth of the bacteria that causes tooth decay.

A healthier alternative is honey. Honey is one of the oldest sweeteners used by man and was highly valued by ancient Egyptians for its medicinal and healing properties.

Honey contains more antioxidants and minerals than sugar (the darker, the more). Unlike table sugar, it is made up of inverted sugars. This makes it an ideal “instant energy” source. Regular sugar is made up of sucrose. Honey is made up of varying proportions of fructose and glucose, which means it’s much sweeter.

Acknowledgment

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References


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Abstract

This study has proved differences in aspects of metabolic syndrome (MS) among sexes, as well connection between MS and neuropathies. The aim of our research was to compare blood sugar levels before and after GTT as well as neurophysiological parameters of n.medianus and n.ulnaris in persons of both sexes with newly discovered MS. All subjects were dermatologically examined. The analysis comprised of 36 subjects of both sexes each with found MS. Men’s age was in average 52.75±7.5 (40-65), women 52.1±7.7 (38-67). Average blood sugar level in women was 5.86±0.87 (4.5-8) mmol/L and in men a little higher (p=0.0969), or 6.19±0.8 (4.7-8) mmol/L. Average values of blood sugar after 120 minutes were not significantly different (p=0.7052), or 5.41±1.63 (3.3-9.7) mmol/L in women, and 5.27±1.52 (2.7-9.8) mmol/L in males. Motoric velocity medians were higher in women for n.medianus sin and n.ulnaris sin (p=0.0081) and n.ulnaris dex (p=0.0293), while terminal motoric latency medians were significantly longer for n.ulnaris sin (p=0.0349) and n.ulnaris dex (p=0.011). There were no significant differences in sensory conduction velocities of n.medianus and n.ulnaris among groups, but the amplitude of the highest peak f sensory response was higher for n.medianus sin and n.ulnaris sin (p=0.0009) in females. The results point to the fact that there are differences in neurophysiological parameters for the examined nerves between sexes, meaning the nerve structures during MS are more prominent in men. There are no significant differences in skin changes between sexes. There was no significant difference among blood sugar value, sensory symptoms of neuropathy and examined skin pigmented lesions (p=0.8564). Also, there were no significant difference between blood sugar value and skin types (p= 0.81).
Sazetak

Ova studija je pokazala aspekte metaboličkog sindroma (MS), spolnu zastupljenost, udruženost MS i neuropatija, povezanost MS i pigmentnih promjena na koži, kao i tipovima kože. Cilja studije je bio da se istraži nivo glukoze prije i poslije GTT testa, kao i neurofiziološke parametre nervus medianus i nervus ulnaris kod osoba oba spola sa otkrivenim MS. Analizom je obuhvaćeno 36 ispitanika oba spola sa utvrđenim MS. Starosna dob muškaraca je bila 52.75±7.5 (40-65), a kod žena 52.1±7.7 (38-67). Prosječna vrijednost šecera u krvi kod ženskih ispitanika iznosila je 5.86±0.87 (4.5-8) mmol/L, a kod muskih ispitanika nesto viša (p=0.0969), ili 6.19±0.8 (4.7-8) mmol/L. Nakon 120 minuta nije ustanovljena sigurna razlika u prosječno vrijednost šecera u krvi između muških 5.27±1.52 (2.7-9.8) mmol/L i ženskih ispitanika 5.41±1.63 (3.3-9.7) mmol/L (p=0.7052). Motorička provodljivost n. medianus l.sin. i n. ulnaris l.sin. je bila visoka kod žena (p=0.008) i n. ulnaris l. dex. (p=0.0293), dok je je terminalna motorička latencija bila signifikantno duža za n. ulnaris- sin (p=0.0349) i ulnaris dex (p=0.011). Nije ustanovljena signifikantna razlika u senzornoj konduktivnoj provodljivosti n. medianusa i n. ulnaris sa unutar grupe, ali je najviši pik amplitude senzornog odgovora ustanovljen kod žena na n. medianus sin. (p=0.0269) i n. ulnaris dex. (p=0.011). Rezultati pokazuju da postoje signifikantna razlike između polova nakon analize neurofizioloških parametara, sa većom zastupljenosću kod muškaraca sa MS. Nije ustanovljena signifikantna razlika u promjenama na koži između ispitanika oba spola. Nije utvrđena signifikantna razlika između vrijednosti šecera u krvi, simptoma senzorne neuropatije i ispitivanih pigmentnih promjena na koži (p=0.8564). Takođe, nije ustanovljena signifikantna razlika između vrijednosti šecera u krvi i tipova kože (p=0.81).

Ključne riječi: Metabolički sindrom (MS), Glikemija, GTT, Elektrofiziologija, N. medianus, N. ulnaris, Kožne promjene

Key words: Metabolic syndrome (MS), Blood sugar level, GTT, Electroneurography, N. medianus, N. ulnaris, Skin changes

Introduction

The first component of metabolic syndrome (MS) is central obesity, defined by waist length, combined with at least two of four elements: elevated triglycerides (TGL), lowered HDL cholesterol, elevated blood pressure and elevated blood sugar on an empty stomach.

There is evidence that incidence of MS and distribution of its components in men and women differ. Research of the working population in Spain and France show the prevalence of MS 11.5% in men and 4.1% in women, with tendency of growth in older age, which actually varies in different categories of professional activity (1).

Among adults in Turkey, MS was found present in 26.9% subjects, 31.3% women and 21.7% men (2). The data that in persons with acute ischemic syndromes MS is found in 70.2% women and 52.6% men shows the possible consequences of this syndrome (3).

From the very adolescence, accumulation of intra-abdominal fat tissue can cause the onset of MS, including metabolic and inflammatory components, which has a more serious effect on blood pressure in men, which can than be added to magnification of sympathetic activity noticed also only in men (4). Obesity is in strong connection with MS, a no obesity has a stronger association with the risk of insulin resistancy in women (5).

There is an inverse connection of adiponectin in plasma and insulin resistance. Subclinical inflammation is present in MS with proved differences in levels and expression of different sensitive biomarkers of inflammation between sexes. In, for example, non-diabetic population, smoking is related to the fall in the level of adiponectin, rise in high-sensitivity C-reactive protein (hs-CRP) and higher level of interleukin-1 receptor antagonist (IL-1Ra) in women (6,7,8).

In persons with acute ischaemic syndromes and MS, men had a more frequent rise in TGL concentration, and women fall of HDL concentration (3). As a confirmation of genetic predisposition in women, there is a rise in the risk for low HDL-C, dyslipidaemia and MS, which is combined with alleles of the gene apolipoprotein A5 (APOA5), more precisely, APOA5 SNPS (9).
So, according to a study in Sweden, women with MS had a higher Body Mass Index (BMI) and the level C-reactive protein, and stood a higher chance of fulfilling the waist length criteria, and the syndrome was more prevalent and characterized by obesity, and law-level inflammation (10).

In the pathogenesis of MS there is a great interest about the role of free radicals oxidation stress. Research in Japan has shown cellular anti-oxidants enzymes such as glutathion peroxidase 1 (GPX1), play the central role in the control of reactive oxigen species, and GPX1 polzmorphism (Pro198Leu) is combined with MS in men, but not in women (11).

MS is in fact often present in patients with neuropathy, and also impaired glucose intolerance (IGT), as well as normal glucose tolerance (NGT) compared to the prevalence within general population (12). It is well known that the polz-neuropathy of longer nerves is common complication of diabetes mellitus. However, intermittent hyper-gicamia or insuliune resistance combined with prediabetes could be sufficinet to damage distal parts of nerves. Preferent damage of small non-myelized nerves is suggested by the existence of prominent neuropathic pain, predominant sensors damage and early autonomous dysfunction (13).

Studies confirm certain differences in aspects of MS between sexes, as well as connection of MS and neuropathies, but relatively small number of them is concerned with this syndrome and differences of electroneurographic parameters between the sexes. Therefore, the aim of our research is to attempt to at least partly shed light on this problem.

**Aim of research**

In persons with newly discovered MS (both sexes) we will compare the levels of blood sugar on empty stomach and after GTT, pigment skin changes, as well as neurophysiological parameters of n.medians and n.ulnaris.

**Materials and methods**

Analysis encompassed 36 subject of each sex, with newly-discovered MS. Men were aged in average 52.75±7.5 (40 – 65), and women 52.1±7.7 (38 – 67). 11 female subjects and 9 male subjects had sensory symptoms of neuropathy in the hand. All patients with MS were tested for blood glucose levels and oral glucose tolerance test (OGTT) was performed. Skin and visible mucous were examined. Pigmented skin changes were tested by dermatoskopy (Visiomed sistem).

Neurophysiological testing was conducted in room temperature, and ‘physiological’ skin temperature with female subjects in the lying position. Neurographic parameters were measured with the machine EMNG Medelec Synergy (EMG and EP Systems – Oxford Instruments, 2004). Superficial stimulatory registration bipolar electrodes were used (so called, large touch-proof). Sensory conductor velocity n.medianus and n.ulnaris was measured by stimulation of the wrist and registration on index and little fingers, between the first and second interphalangial joint. Terminal motoric latency was measured by stimulating the wrist and registration on thenar and hypothenar, more precisely 6cm proximally from the registration electrode on the stomach, m.abductor pollicis brevis for n.medianus and m.adductor digiti minimi for n.ulnaris. Proximal measurement for both nerves was conducted in the segment just above the elbow. During electroneurographic processing (ENG) sensory nerve conductivity velocity (from the stimulating artefact to primary deviation of the isoelectric line) was analyzed, with an amplitude of the sensory nerve action potential (SNAP); terminal motoric latency of n. medianus and n.ulnaris on both sides, with the highest amplitude of compound muscle action potential (CMAP), measured from the location of the primary deviation from the isoelectric line upon stimulatory artefact up to the final return of the needle to the isoelectric line. While determining motoric and sensory response, stimulation was performed until the CMAP and SNAP amplitudes ceased to grow. The levels of blood sugar and glucose tolerance after 120 minutes were showed as median with standard deviation, and during the statistical analysis of differences between sexes T-test and HiSquare test were used. During the statistical analysis of neurophysiological parameters, were estimated values of median and non-paremeter Man Whitney U test, and differences were valued as significant for p<0.005.
Results and discussion

The average blood sugar value in women was 5.86±0.87 (4.5-8.0) mmol/L, and in men the value was not significantly higher (p=0.0969), that is, 6.19±0.8 (4.7 – 8 mmol/L). Majority of 27 female subjects and 20 male subjects had the blood sugar values within standard (3.9 – 6.1 mmol/L), while values above this were shown in 9 women and 16 men, which was a significantly different distribution among sexes (p=0.0189).

The average blood sugar levels after 120 minutes during OGTT test were not significantly different (p=0.7052), 5.41±1.63 (3.3 – 9.7) mmol/L in women and 5.27±1.52 (2.7 – 9.8) mmol/L in men. 23 persons of each sex had blood sugar values within standard, 8 females and 9 males had above that, and 5 females and 4 males had lowered values, so there was no important difference in the distribution of these values among groups (p=0.8348).

Skin examination showed 22 patients with skin type Fitzpatrick 2, 12 patients with skin type Fitzpatrick 3, and two patients with Fitzpatrick 4. There were ten patients with seborrhoic warts, six patients with compound naevi (Visiomed score - between 2 and 4) , and 3 patients (female) with lentigines and melasma. In one patient we found naevus dysplasticus (Visiomed score 8.4). There was no significant difference among blood sugar value, sensory symptoms of neuropathy and examined skin pigmented lesions (p=0.8564). Also, there was no significant difference between blood sugar value and skin types (p= 0.81).

Parameters of motoric and sensory electroneurographic analysis of n.medianus and n.ulnaris in male and female subjects with MS are shown in tables 1-4. Motoric condactory velocity medians usually have higher values in women, terminal motoric latencies are lower.

Statistical analysis has shown that motoric velocity medians of n.medianus sin n.ulnaris sin and n.ulnaris dex are significantly higher in women while terminal motoric latency medians of both n.ulnaris in women are longer (Table 5). CMAP surfaces acquired upon proximal and distant stimulation did not show important differences among sexes (Table 6).

There were no significant differences in sensory conduction velocities of n.mwsianus and n.ulnaris among the groups. However, the amplitude of the highest peak of the sensory response was significantly higher in n.medianus sin and n.ulnaris sin in females (Table 7). One patient did not show sensory response of n.medianus sin and one in n.medianus dex.

Table 1. Parameters of motoric neurographic analysis od n.medianus and n.ulnaris in 36 female subjects with metabolic syndrome.

<table>
<thead>
<tr>
<th>Motoric velocity (m/s)</th>
<th>Mediana</th>
<th>Percentile (25-75)</th>
<th>Min.</th>
<th>Max.</th>
</tr>
</thead>
<tbody>
<tr>
<td>n.medianus sin.</td>
<td>57,95</td>
<td>55,6-61,35</td>
<td>51,6</td>
<td>66,8</td>
</tr>
<tr>
<td>n.medianus dex.</td>
<td>57,2</td>
<td>53,75-59,7</td>
<td>49</td>
<td>65,3</td>
</tr>
<tr>
<td>n.ulnaris sin.</td>
<td>53,2</td>
<td>51-55,1</td>
<td>46,6</td>
<td>63,2</td>
</tr>
<tr>
<td>n.ulnaris dex.</td>
<td>55,85</td>
<td>53,65-58,025</td>
<td>50</td>
<td>63,4</td>
</tr>
</tbody>
</table>

Table 2. Parameters of sensory neurographic analysis od n.medianus and n.ulnaris in 36 female subjects with metabolic syndrome.

<table>
<thead>
<tr>
<th>Motoric latency (msec)</th>
<th>Mediana</th>
<th>Percentile (25-75)</th>
<th>Min.</th>
<th>Max.</th>
</tr>
</thead>
<tbody>
<tr>
<td>n.medianus sin.</td>
<td>3,4</td>
<td>3,15-3,675</td>
<td>2,6</td>
<td>4,9</td>
</tr>
<tr>
<td>n.medianus dex.</td>
<td>3,275</td>
<td>2,85-3,66</td>
<td>2,6</td>
<td>5,8</td>
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<tr>
<td></td>
<td>cmapper I</td>
<td>cmapper II</td>
<td></td>
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<td>-----------</td>
<td></td>
<td></td>
</tr>
<tr>
<td>medianus sin.</td>
<td>20,7</td>
<td>18,9</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>14,925-24,825</td>
<td>15,05-23,2</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>8</td>
<td>6,3</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>40,2</td>
<td>38,6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>medianus dex.</td>
<td>19,5</td>
<td>18</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>16,5-32,325</td>
<td>14-28,525</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>6,9</td>
<td>5,8</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>40,8</td>
<td>42,9</td>
<td></td>
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</tr>
<tr>
<td>ulnaris sin.</td>
<td>14,2</td>
<td>13,45</td>
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<tr>
<td></td>
<td>10,95-19,65</td>
<td>10,175-16,025</td>
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<td></td>
<td>5,2</td>
<td>3,7</td>
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<tr>
<td></td>
<td>37,1</td>
<td>35,7</td>
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<td>ulnaris dex.</td>
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<tr>
<td></td>
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<td>10,175-16,025</td>
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</tr>
<tr>
<td></td>
<td>4,1</td>
<td>4,9</td>
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<td></td>
</tr>
<tr>
<td></td>
<td>25,8</td>
<td>5,2</td>
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</tbody>
</table>

**Table 2. Parameters of motoric neurographic analysis of n.medianus and n.ulnaris in 36 male subjects with metabolic syndrome**

**Motoric velocity (m/s)**

<table>
<thead>
<tr>
<th></th>
<th>cmapper I</th>
<th>cmapper II</th>
</tr>
</thead>
<tbody>
<tr>
<td>medianus sin.</td>
<td>54,6</td>
<td>52,8</td>
</tr>
<tr>
<td></td>
<td>51,325-58,825</td>
<td>50,7-56,7</td>
</tr>
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<td></td>
<td>44</td>
<td>46,8</td>
</tr>
<tr>
<td></td>
<td>62,9</td>
<td>61,5</td>
</tr>
<tr>
<td>medianus dex.</td>
<td>55,6</td>
<td>3,55</td>
</tr>
<tr>
<td></td>
<td>52,05-58</td>
<td>3,35-3,912</td>
</tr>
<tr>
<td></td>
<td>34</td>
<td>2,85</td>
</tr>
<tr>
<td></td>
<td>62,4</td>
<td>4,9</td>
</tr>
<tr>
<td>ulnaris sin.</td>
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<td>3,525</td>
</tr>
<tr>
<td></td>
<td>48,05-53,975</td>
<td>3,2375-3,825</td>
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<td></td>
<td>32,4</td>
<td>2,6</td>
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<tr>
<td></td>
<td>61,3</td>
<td>5,2</td>
</tr>
<tr>
<td>ulnaris dex.</td>
<td>52,8</td>
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<tr>
<td></td>
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</tbody>
</table>
### Table 3. Parameters of sensory neurographic analysis of n.medianus and n.ulnaris in 36 female subjects with metabolic syndrome

<table>
<thead>
<tr>
<th></th>
<th>Median</th>
<th>Percentile (25-75)</th>
<th>Min.</th>
<th>Max.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sensory velocity (m/s)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n.medianus sin.</td>
<td>49,45</td>
<td>45,975-53,8</td>
<td>0</td>
<td>57,7</td>
</tr>
<tr>
<td>n.medianus dex.</td>
<td>49,1</td>
<td>43,675-52,225</td>
<td>0</td>
<td>58,9</td>
</tr>
<tr>
<td><strong>CMAP I (mV)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n.medianus sin.</td>
<td>21,5</td>
<td>17,3-28,475</td>
<td>6</td>
<td>43,9</td>
</tr>
<tr>
<td>n.medianus dex.</td>
<td>23,1</td>
<td>16,475-30,9</td>
<td>6,6</td>
<td>47,6</td>
</tr>
<tr>
<td><strong>CMAPII (mV)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n.medianus sin.</td>
<td>19,9</td>
<td>16,15-27,675</td>
<td>6,5</td>
<td>38,4</td>
</tr>
<tr>
<td>n.medianus dex.</td>
<td>21,15</td>
<td>14,5-28,075</td>
<td>3,7</td>
<td>46,8</td>
</tr>
<tr>
<td><strong>Amplitude SNAP (µV)</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>n.medianus sin.</td>
<td>49,05</td>
<td>46,475-51,025</td>
<td>41,5</td>
<td>56,2</td>
</tr>
<tr>
<td>n.medianus dex.</td>
<td>14,65</td>
<td>10,675-20,05</td>
<td>0</td>
<td>49,7</td>
</tr>
</tbody>
</table>

CMAP: complex muscle action potential:
CMAP I upon distal stimulation;
CMAP II upon proxima stimulation
Table 4. Parameters of sensory neurographic analysis of n.medianus and n.ulnaris in 36 male subjects with metabolic syndrome

<table>
<thead>
<tr>
<th>Sensory velocity (m/s)</th>
<th>n.medianus sin</th>
<th>n.ulnaris sin</th>
<th>n.medianus dex</th>
<th>n.ulnaris dex</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mediana</td>
<td>49,55</td>
<td>48,1</td>
<td>11,65</td>
<td>13,4</td>
</tr>
<tr>
<td>Percentile (25-75)</td>
<td>45,525-52,975</td>
<td>44,625-50,35</td>
<td>8,15-17,15</td>
<td>8,075-21,2</td>
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<tr>
<td>Min.</td>
<td>37,1</td>
<td>19,8</td>
<td>4,7</td>
<td>4,3</td>
</tr>
<tr>
<td>Max.</td>
<td>62,2</td>
<td>55</td>
<td>30</td>
<td>33,9</td>
</tr>
<tr>
<td>SD: standard deviation;</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Min.: minimal;</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Max.: maximal;</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SNAP: sensory nerve action potential</td>
<td></td>
<td></td>
<td></td>
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</tbody>
</table>
Table 6. Significance of differences in CMAP surfaces of n.medianus and n.ulnaris in male and female subjects with MS

<table>
<thead>
<tr>
<th>MOTORIC NERVE</th>
<th>CMAP</th>
<th>p...</th>
<th>n.medianus sin</th>
<th>I</th>
<th>0,2437</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<td></td>
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<td></td>
<td></td>
<td>II</td>
<td>0,3384</td>
</tr>
<tr>
<td></td>
<td></td>
<td>n. medianus dex.</td>
<td>I</td>
<td>0,7018</td>
<td></td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>II</td>
<td>0,4305</td>
</tr>
<tr>
<td></td>
<td></td>
<td>n. ulnaris sin.</td>
<td>I</td>
<td>0,0989</td>
<td></td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>II</td>
<td>0,1712</td>
</tr>
<tr>
<td></td>
<td></td>
<td>n. ulnaris dex.</td>
<td>I</td>
<td>0,2648</td>
<td></td>
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</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>II</td>
<td>0,4404</td>
</tr>
</tbody>
</table>

**Table 7. Differences in sensory conductory velocities and amplitude SNAP of n.medianus and n.ulnaris in male and female subjects with MS**

<table>
<thead>
<tr>
<th>SENSORY NERVE</th>
<th>PARAMETER</th>
<th>p...</th>
<th>n.medianus sin</th>
<th>Velocity</th>
<th>0,9865</th>
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<tr>
<td></td>
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<td></td>
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</tr>
<tr>
<td></td>
<td></td>
<td>Amplitude SNAP</td>
<td>0,0269</td>
<td>n. medianus dex.</td>
<td>Velocity</td>
</tr>
<tr>
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<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Amplitude SNAP</td>
<td>0,1122</td>
<td>n.ulnaris sin.</td>
<td>Velocity</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Amplitude SNAP</td>
<td>0,0009</td>
<td>n.ulnaris dex.</td>
<td>Velocity</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>SNAP: sensory nerve action potential.</td>
<td>0,1161</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Our results show that there is no significant difference in the age of onset and diagnose of MS among males and females. According to Zeliunas and Co (2008) study of patients with acute ischemic syndrome, women with MS are significantly older than man (68.1 and 60.2) (3).

Even though in our study males have higher blood sugar levels, there is no difference between sexes after GTT after 120 minutes. The interesting research is that, for example, low level of total testosterone and sexual/hormone bounding globuline (SHBG) independently represent a risk factor for the development MS and diabetes mellitus in middle-aged men. Hypo-androgenism is early marker of disrupted insulin and glucose metabolism, which can progress to MS or diabetes and can contribute to pathogenesis. However, study with late adolescences and early adults has shown that men are more obese, have hypertension and hyper triglyceridemia than women, but all cases of glucose intolerance were in women (15).

Men and women displayed differences in neurophysiological parameters of n.medianus and n.ulnaris. Central values of motoric conduction velocities in our study are lower for the most part, and terminal motoric latences are higher in men. On the other hand, amplitudes of sensory response for the examined nerves on the left side are lower in men. These observations suggest that the researched nerve structures during MS are somewhat more prominently noticed in men.
Conclusion

Motoric velocities of n.medianus sin and n.ulnaris sin and dex are significantly higher, terminal motoric latencies of both n.ulnaris in women are longer, and amplitudes of the highest peak of sensory response are higher in n.medianus sin and n.ulnaris sin in females, which suggests that the examined nerve structures during metabolic syndrome are more prominent in men.

References


7. Rogowski O, Shapira I, Berliner S. Exploring the usefulness of inflammation-sensitive biomarkers to reveal potential sex differences in relation to low-grade inflammation in individuals with the metabolic syndrome. Metabolism 200; 57(9):1221-6.


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e-mail:
Determination of mean glandular dose from routine mammography for two age groups of patients

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¹ University of Tuzla, Faculty of Natural Sciences and Mathematics, Bosnia and Herzegovina
² University of Tuzla, University Center for Distant Education, Bosnia and Herzegovina
³ University of Sarajevo, Faculty of Health Studies, Bosnia and Herzegovina

Abstract

An objective of mammographic screening is an early detection of breast cancer. At this moment there is no any known or published data about doses for women included into mammography screening in Bosnia and Herzegovina. Hence, a potential risk of cancerogenesis caused by radiation in this procedure is increasing. The object of this research was to define a mean glandular dose (MGD) at mediolateral (MLO) and craniocaudal (CC) projection for every individual breast and a total dose for a whole mammographic examination at the Radiology Clinic (of the University of Sarajevo Clinics Centre) for two different age groups (age: 40 – 49 and 50 - 64). Dose estimates were made for 63 patients who were subdued to a routine mammographic examination and they involved corrections in regard to variations of age, breast thickness and applied clinical spectra. A mean MGD for women between 40 and 49 was 1.64 mGy for a MLO screen and 1.36 mGy for a CC screen. For a group between 50 and 64 mean MGD was 1.74 mGy for a MLO screen and 1.45 mGy for a CC screen. Differences of MGD at MLO and CC examination are caused by a huger thickness of a compressed breast at MLO projection, which is 9 - 11 % huger than on CC projection. According to a performed correlation analysis one defined a remarkable significance between MGD and thickness of a compressed breast for MLO and CC screens; the first age group (MLO: r=0.852 , p < 0.01 ; CC : r = 0.817, p < 0.01) and the second age group (MLO : r = 0.721, p < 0.01; CC : r = 0.674 , p < 0.01). MGD for the whole mammographic examination was 3,11 mGy and it was significantly connected to breast thickness (r= 0.77 , p < 0.01).

Key words: mammography, mean glandular dose (MGD), dosimetry on mammography, compressed breast thickness (CBT).

Introduction

There is a risk of cancerogenesis caused by radiation and connected to examination of female breast with X – rays. This risk is small if a modern equipment and technology are used, while a benefit from the examination is significant (1). Numerous authors assessed the risk of radiation and the benefit from mammography in regard to breast screening (2, 3, 4, 5, 6). A working unit of a Board for Protection from Radiation and NHSB (The National Health Service Breast Screening Program in the UK) program of breast screening recently surveyed radiation risks from mammography and concluded that the radiation risk that caused breast cancer was about 1 on 100 000 per mGy with women that were screened in the United Kingdom (7). Although this risk was relatively small, it is important to use appropriate equipment and techniques so that an optimum quality of screens can be achieved with the smallest possible dose that corresponds to quality of the screen. Measuring a dose received by a breast is an important part of the program which ensures quality of mammographic screening. Early detection of breast cancer is a key for a long – term control and a good prognosis of the disease and a high quality mammography is a prerequisite for that (8).
All women who belong to the age group 40 – 64 should be included in a regular screening program every year. This research included women between 40 and 64. On the first mammographic examination one screens mediolateral and cranio-caudal mammograms.

One of responses which need to be found during a mammographic examination of a woman is a risk and a benefit brought with a patient’s dose. A very few data about patient’s dose are available during mammography of younger women. It is expected that patient’s doses for mammography for younger women are somewhat bigger since their breast contain more glandular tissue. Law et al (9) assessed a relative possibility to introduce early detection of the breast cancer in screening of younger women, but without any concrete data about patient’s doses. Young and Burche (10) undertook a similar research and assessed patient’s doses for younger women in the UK from 40 to 48. The mentioned study gave somewhat bigger percentage of doses for women from 40 to 48 than for women from 50 to 64, but deviations are not significant. A set of mammographic studies (10, 11, 12) showed that a basis for an assessment of the radiation risk is defining a mean glandular dose (MGD).

Materials and methods

Data collection

All experimental measuring of the patient’s dose during diagnostic mammographic examinations of patients were done at the Department for Thoracal Diagnostic with Breast of the Radiology Clinic (of the University of Sarajevo Clinics Centre). Siemens Mammomat 1000 (Mo/Mo) was used for diagnostic examinations of patients. Measuring was done in the period between July 2007 and July 2008. Data about patient’s doses were collected for 63 patients (234 screens) from 40 to 64 years during a routine mammographic control.

The following data were recorded during the diagnostic examination:

1. Age of patients
2. Used clinical spectra
3. Compressed breast thickness (CBT) and type of projection
4. Exposition factors and charge (mAs), anode voltage (kVp), clinical spectra (target / filter) for each screen.
5. Size of used film

Patient’s doses were calculated according to the recorded data.

Quality control

During the period of data collection the value of anode voltage, reproducibility of doses and filter half value (HVL) were measured without returnable radiation and compression board was checked for different settings of kVp and a target / filter combination following recommendations of the European Protocol (13), which recommends a frequency and a methodology for measuring. Accuracy of reading of thickness of a compressed breast was checked according to recommendations of the mentioned Protocol. All of quality control tests and dosimetry in diagnostic radiology were done with Barracuda instrument.

Dosimetry

MGD for each mammogram is defined on a basis of conversion factors calculated by Dance et al (14) and a calculated ESAK (entering air kerma measured freely in air without backscatter), using the following relation:

\[ \text{MGD} = g \ c \ s \ \text{ESAK} \]

ESAK for each individual exposition is calculated with exit voltage and charge (mAs) used in an exposition field. Conversion factors were calculated by Dance, for a different clinical spectrum (target/filter combination), HVL, compressed breast thickness and breast glandularity. Factor \( g \) defined by Dance et al (14) corresponds to glandularity of 50 % while factor \( c \) includes every change in breast glandularity of 50 %. Factor \( c \) was defined by Dance et al (14) for a normal composition and for various thickness of a compressed breast (20 – 110 mm) and HVL. C factor was defined by Dance for a normal breast of a woman of age 40...
- 49 and 50 - 64. Estimation of glandular changes of a breast and a composition of both age groups was defined by Beckett and Kotre according to experimental results (15). Finally, factor $s$ includes a correction for used type of the clinical spectrum (12), and all screens were made using the same clinical spectra Mo/Mo.

**Statistical analysis**

The data were statistically processed in SPSS and they were shown as standard deviation and confidence interval. Pearson’s coefficient was used for statistical significance of correlation between MGD and CBT. A value of $p<0.05$ was considered as indicative of significance.

**Results and discussion**

**Age and compressed breast thickness**

Age of examined population varied from 40 to 64 years. Distribution of thickness of a compressed breast was symmetrical, and varied from 23 to 81 mm. Accuracy of defining of thickness of a compressed breast was ± 1 mm. There was a good correlation between the age and the thickness of a compressed breast. Mean value of the thickness of a compressed breast was 52,76 mm (SD : 10,88). It is known that compressed breast thickness shows a tendency of increasing before the age of 60 and then a tendency of decreasing with older women (9), which was the case in our sample of a mammographic analysis.

Mean thickness of a compressed breast with a mediolateral projection was about 9 - 11 % higher than with cronoicaudal. This information is important for understanding an explanation of results achieved for a mean glandular dose of a breast from Table 1.

**Quality control**

Accuracy of measured voltage in a X – ray tube (maximal deviation) was 0.7 kV for a volume of 23 and 31 kVp. Reproducibility was better for 0.14 kV. Exit radiation (mGy/mAs) was measured every 3 months and it was ± 5 % from an initial value. The most frequently used voltage at exposition was 30 kVp.

Voltage of 29 kVp (11 %) was applied in most cases when thickness of compressed breast was from 25 to 43 mm, and voltage of 31 kVp (26,50 %) was mainly applied in situations when thickness of a compressed breast varied from 59 to 71 mm and an appropriate compromise between values should have been made in order to achieve the best possible screening. Voltage of 30 kVp (53,85 %) was most frequently used for a compressed breast thickness of 44 to 58 mm, which indicates that most patients were within those values on the examinations. Rarely used voltage of 32 kVp (8,55 %) was applied with extremely thick compressed breast which varied from 72 to 81 mm.

**X – ray technique**

The hugest number of screens from examinations was two for MLO and two for CC projection. A total number of screens for a complete examination was 4. The same combination of target/filter (same clinical spectra) Mo/Mo was used for all measuring. There were 234 films made for 63 patients, out of which for the whole mammographic examination of 54 (85,71 %) patients there were 212 films (two for each projection). In that way both breast were completely examined. With the rest of 9 (14,29 %) patients we did a regular mammographic control of one breast.

Percentage of 14,29 % patients for whom we examined with two screens shows a need for routine controls of patients and mammography because it represents a percentage of patients to whom a breast cancer was detected in time with a mammography. It is common in all developed countries in the world with developed programs of early detection of breast cancer that most patients are examined with 4 screens in order to get a complete clinical picture. This information is a result of routine examinations that are obligatory every three years in developed countries and as a consequence there is a huge number of patients with early detection of breast cancer.
Patient's doses

The most frequent procedure in the routine mammography imposes 2 screens for every breast, craniocaudal and mediolateral oblique screen. Even though there is anomaly at only one breast, a screen has to be done for both breasts. This procedure enables us to compare breasts and check possible anomalies in details (16). In the last 15 years several studies have been done in Europe and their objective was to define MGD (10, 11, 15, 17, 18). A similar study was done in Thailand (19). There is no any results about defining MGD, exposition factors applied in mammography and sizes of compressed breasts population have been published regarding Bosnian population.

Table 1. shows results achieved for mean glandular doses per every individual projection and all sizes on which it depends for the complete sample during MLO and CC projection.

MGD and CBT values were defined for a sample of 234 screens (117 for MLO and CC projection). A mean dose for CC screen was 1,41 mGy (SD : 0,43) and 1,70 mGy (SD : 0,51) for MLO screen. Defined significant difference between doses (according to achieved values) which is caused by a compressed breast thickness is about 9,05 %. A similar situation was noted in works of other authors (10, 19). A possible cause of the tendency are doses that are somewhat bigger with MLO than with CC projection, which can be explained with the fact that the pectoral muscle overlying in the MLO projection causes greater attenuation and therefore higher exposure. A total dose for the complete mammographic examination was 3,11 mGy (SD : 0,49), which is something lower than 3,2 mGy which on the other hand is prescribed by international authorities. Over 77 % of all mammographic examinations were done with a dose smaller than 3 mGy as recommended by the American College of Radiology (20, 21). According to a correlation analysis (Figure 1.) one defined a remarkable significance between MGD and CBT ($r = 0,77, p < 0,01$).

Table 1. Summary of the statistics for kV, compressed breast thickness, ESAK, and MGD for the total sample and for the two views (CC, MLO)

<table>
<thead>
<tr>
<th>Number of images</th>
<th>CBT (mm)</th>
<th>ESAK(mGy)</th>
<th>MGD per exposure (mGy)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>kVp ± SDc</td>
<td>Mean ± SDc</td>
<td>Mean ± CIc</td>
</tr>
<tr>
<td>Total</td>
<td>234</td>
<td>30,30 ± 0,72</td>
<td>52,76 ± 10,88</td>
</tr>
<tr>
<td>CCb</td>
<td>117</td>
<td>30,29 ± 0,77</td>
<td>50,26 ± 9,91</td>
</tr>
<tr>
<td>MLOa</td>
<td>117</td>
<td>30,31 ± 0,68</td>
<td>55,26 ± 11,27</td>
</tr>
</tbody>
</table>

*MLO : Mediolateral oblique view.
CC : Craniocaudal view.
SD : Standard deviation.
CI : Confidence interval for the mean of 95 %
CBT : Compressed breast thickness.

It was especially important to examine a connection between a position during screening (mediolateral and craniocaudal position), a compressed breast thickness and a mean glandular dose received by a patient during one exposition and the whole examination for two different age
groups. Patients were grouped into a group of younger patients (40–49) and a group of older patients (50–64) according to recommendations of the European Protocol on dosimetry in mammography (22). Table 2. Shows results achieved for MGD per every individual projection (MLO or CC) and for the whole screening for the given projection.

The first group of age 40–49 consisted of 27 patients and 102 screens were made for their routine examination. Average thickness of a compressed breast was 51.70 mm (SD: 12.12). We noted a tendency of increasing of thickness of a compressed breast with age in this group (13.18). A compressed breast thickness on MLO projection was 10.95 % bigger than on CC projection. Obtained patient’s doses on MLO and CC projection of 1.64 mGy (SD: 0.37) and 1.36 mGy (SD: 0.52) are within results promoted by the NHSB (The National Health Service Breast Screening Program in the UK) and K.C. Young (10) for age group 40 – 48. In NHSBA’s recommendations a mean glandular dose for MLO screening is 1.73 mGy and for CC screening 1.40 mGy. In its work from 2002 K.C. Young (10) analyzed the mean glandular doses for the age group 40 – 49 and he found that the MGD for MLO screening is 1.76 mGy and 1.48 mGy for CC projection. Results of correlation analysis for both projections of mammographic screens are presented in Figure 2. with a regression line (MLO: r = 0.852, p< 0.01; CC: r = 0.817, p < 0.01).

**Table 2. Summary of the statistics for kV, compressed breast thickness, ESAK, and MGD for the two age groups and for the two views (CC, MLO).**

<table>
<thead>
<tr>
<th>Age range (years)</th>
<th>Number of images</th>
<th>CBT (mm)</th>
<th>ESAK (mGy)</th>
<th>MGD per exposure (mGy)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>kVp ± SD</td>
<td>Mean ± SD</td>
<td>Mean ± CI</td>
</tr>
<tr>
<td>Total</td>
<td>102</td>
<td>30.25 ± 0.69</td>
<td>51.70 ± 12.12</td>
<td>8.41 ± 0.35</td>
</tr>
<tr>
<td>40 - 49 CC</td>
<td>51</td>
<td>30.22 ± 0.67</td>
<td>49.02 ± 12.09</td>
<td>7.41 ± 0.41</td>
</tr>
<tr>
<td>MLO</td>
<td>51</td>
<td>30.29 ± 0.70</td>
<td>54.39 ± 12.68</td>
<td>9.42 ± 0.53</td>
</tr>
<tr>
<td>Total</td>
<td>132</td>
<td>30.35 ± 0.83</td>
<td>53.57 ± 9.75</td>
<td>8.68 ± 0.31</td>
</tr>
<tr>
<td>50 - 64 CC</td>
<td>66</td>
<td>30.35 ± 0.83</td>
<td>51.21 ± 8.86</td>
<td>7.57 ± 0.36</td>
</tr>
<tr>
<td>MLO</td>
<td>66</td>
<td>30.35 ± 0.83</td>
<td>55.92 ± 10.09</td>
<td>9.78 ± 0.46</td>
</tr>
</tbody>
</table>

aMLO : Mediolateral oblique view.
bCC : Craniocaudal view.
cSD : Standard deviation.
dCI : Confidence interval for the mean of 95 %.
CBT : Compressed breast thickness

![Figure 2. Correlation between MGD and CBT, MLO projection (a) and CC projection (b).](image-url)
The second age group of people from 50 to 64 consisted of 36 patients and 132 screens were made for their routine examination. A mean compressed breast thickness was 53.57 mm. We noted a tendency of growth of a compressed breast thickness up to 60 years of age in this group (15,18), and then a slight tendency of decreasing of the breast thickness. Thickness of a compressed breast with MLO projection was 9.20 % bigger than with CC projection. Patient’s doses obtained during MLO and CC projections of 1.74 mGy (SD: 0.50) and 1.45 mGy (SD: 0.47), respectively, are within a frame of results of a study undertaken by Burch & Goodman (23). The study offered doses of 1.70 mGy for MLO projection (mean thickness 57 mm) and 1.40 mGy for CC projection (mean thickness 52 mm). It is indicative that in the age group of 50 to 64 years MGD value was decreasing with an increase of age, probably due to decreasing of breast glandularity. Correlation analysis for this age group (Figure 3.) showed a remarkable significance for both mammographic projections between MGD and CBT. (MLO: r=0.721, p < 0.01 ; CC : r = 0.674 , p < 0.01 ).

Conclusion

A total dose for the complete mammographic examination was 3.11 mGy, and over 77 % of all mammographic examinations were done with doses less than 3 mGy. We noted a tendency of growth of compressed breast thickness with age for patients from 40 to 49 years of age. This is easily explained since a breast is a very dynamic organ (24) and its evolution does not end so early (sometimes at the age of 40) and it passes through a range of dynamic changes during its growth and development. Patient’s doses obtained for this age group are 1.64 mGy for MLO and 1.36 mGy for CC projection. For patients from 50 to 64 one noted a tendency of growth of a compressed breast up to 60 years of age followed by a slight tendency of decreasing of breast thickness. MGD measured for the mentioned age group was 1.74 mGy for MLO and 1.45 mGy for CC projection. MGD for MLO and CC screens was significantly connected to compressed breast thickness. According to obtained results we can define that mammographic diagnostics at the Radiology Clinic (Clinical Center University of Sarajevo) is done with patient’s doses which are in accordance with European standards.

Acknowledgments

This study was supported by the University Clinical Centre, Clinical for Radiology and Department for Thoracal Diagnostic with Breast in Sarajevo.
List of abbreviations

MGD - mean glandular dose
MLO - mediolateral projection
CC - craniocaudal projection
CBT - compressed breast thickness
ESAK - entering air kerma measured freely in air without backscatter

References


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The serum fructosamine concentration at patients with diabetes mellitus

SERUMSKA KONCENTRACIJA FRUKTOZAMINA KOD PACIJENATA SA DIABETES MELLITUS

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Abstract

Introduction: Hyperglycaemia allows glucose to react with proteins in the plasma and tissues, resulting in the accumulation of glycated products. In clinical practice the term „fructosamine“ is usually reserved for glycated serum proteins. Albumin, the principal protein in plasma, and the other plasma proteins are glycated when exposed to hyperglycaemia, producing fructosamine residues. Since the half-life of albumin is 19 days, measurement of fructosamine gives estimation of average glycaemic control over the previous 2-3 weeks.

The aims of study: The study was to investigate serum lipids and glucose concentration at patients with diabetes mellitus depending on their fructosamine levels were classified as good, satisfactory or poor glycemic controls. The second aim of study was to find correlation between fructosamine, levels of lipids and glucose.

Material and methods: The measurement of fructosamine was done using Hitachi (Boehringer Mannheim) 904 Automatic Analyser at 530 nm wave length. The lipids, lipoproteins and glucose was measurement using Dade Behring Dimension Pand plus. The retrospective studie included one hunderd of patients with diabetes mellitus who were analyses blood on Institute for Clinical Chemistry and Biochemistry, Clinics Center University of Sarajevo, in a period of Juny 2006. to May 2007. The study completed 53 men and 57 women (age 55-70 years). At all subjects we did the following analysis: serum level of fructosamine, glucose, total cholesterol, triglyceride, high density lipoprotein (HDL), low density lipoprotein (LDL) and very low density lipoprotein (VLDL).

Results: The patients classified as good glycemic control has lower concentration of glucose and lipids in comparing with patient classified as satisfactory and poor glyemic controls. Our results have shown statisticaly significant correlation between fructosamine and glucose level. We found significant correlation between fructosamine and level of total cholesterol, triglyceride and HDL. It was not found correlation with LDL and VLDL.

Key words: fructosamine, lipids, glucose, diabetes mellitus.

Sazetak

Uvod: Hiperglikemija omogućuje da glukoza reaguje sa proteinima, prisutnim u plazmi i tkivima što dovodi do nakupljanja glikiranih produkata. U kliničkoj praksi termin „fruktozamin“ obuhvata serumse glikirane proteine. Albumin,
Introduction

Determination of glucose in the blood only is the current image to assess metabolic disorders in diabetic patients which provides information on the status of a few minutes before removing the blood. Glucose is able to bind to a variety of structures, including proteins, in a non-enzymatic irreversible reaction, a process called glycation. Proteins are glycated by a non-enzymic post-translational reaction to form an intermediate Schiff base, which is then transformed by Amadorri rearrangement into stable ketoamine. This ketoamine end-product of protein glycation is fructosamine, the trivial name for 1-amino-1-deoxyfructose. (1,2). Fructosamine is the common name for ketoamine a serum protein, is derived from the name of the product structure ketoamine arising interaction of glucose with N-terminal \(\alpha\)-amino groups or the \(\varepsilon\)-amino group of lysyl residues in proteins. In healthy people non-enzymatic glycation of plasma proteins is less than 2% and in diabetes patients about up to 20%.

Fructosamine testing has been available since the 1980s as a monitoring tool to help diabetics control their blood sugar. The test for serum fructosamine is simpler and less costly than that for hemoglobin A1C, but at present is less frequently used. The level of fructosamine correlates well with fasting glucose and with hemoglobin A1C levels (3, 4). The measurement of fructosamine is useful to monitor the average concentration of blood glucose for an extended period of time (2-3 weeks) in individuals with diabetes mellitus. Therefore, fructosamine is an indicator of the blood glucose concentration over a longer period of time than a single blood glucose measurement (1,2).

The American Diabetes Association (ADA) recognizes the utility of both tests, and says that fructosamine may be a better choice when A1C cannot be reliably measured. These situations include:
1) The evaluation of changes in diabetic treatment, since the effects of adjustment can be evaluated after a couple of weeks rather than months.
2) In pregnancy, since the glucose and insulin needs of the mother and fetus change rapidly during gestation.
3) Any condition that affects the average age of red blood cells, such as hemolytic anemia, sickle cell anemia, or blood loss (5).

Fructosamine test is useful for screening patients with a confirmed diagnosis of diabetes and the test can not be used in controlling glucose levels healthy population. However, it can be used in patients who have acute and systemic diseases that could alter glucose and insulin values and do
not have confirmed diagnosis of diabetes (4,6). The study was to investigate whether the serum lipids in type 2 diabetes mellitus was different between groups of patients classified as good, satisfactory or poor glycemic controls, depending on their serum fructosamine levels. Determination of lipids is of great importance in patients with diabetes mellitus because it increases the risk of disease atherosclerosis and cardiovascular diseases (7,8).

Methods and material

The measurement of fructosamine was done using Hitachi (Boehringer Mannheim) 904 at 530 nm wave length. The fructosamine reagent set is based on the ability of ketoamines to reduce nitroblue tetrazolium (NBT) to formazan dye under alkaline conditions. The rate of formazan formation is directly proportional to fructosamine concentration (9). The lipids, lipoproteins and glucose were measurement using Dimension LxR (Dade Behring). The glucose method is an adaptation of the hexokinase-glucose-6-phosphate dehydrogenase method, presented as a general clinical laboratory method by Kunst (10). The cholesterol method is based on the principle first described by Stadman (11). The triglycerides method is based on enzymatic procedure in which a combination of enzymes are employed for the measurement of serum or plasma triglycerides. The sample is incubated with lipoprotein lipase (LP) enzyme reagent that converts tryglicerides into free glycerol and fatty acids. Glycerol kinase (GK) catalyzes the phosphorylation of glycerol by adenosine-5-triphosphate (ATP) to glycerol-3-phospate. Glycerol-3-phosphate-oxidase oxidizes glycerol-3-phosphate to dihydroxyacetone phosphate and hydrogen peroxide (H$_2$O$_2$). The catalytic action of peroxidase (POD) forms quinoneimine from H$_2$O$_2$, aminoantipyrine and 4-chlorophenol. The change in absorbance due to the formation of quinoneimine is directly proportional to the total amount of glycerol, using measurement is bichromatic (510,700 nm). The high-density lipoprotein (HDL) is measured directly. This method is based on acceleration the reaction of cholesterol oxidase (CO) with HDL unesterified cholesterol and dissolving HDL selectively using a specific detergent. The second reagent consist of a detergent capable to solubili-

Patients

The patient samples of blood were collected in serum separation Vacutainer test tubes (Beckton Dickinson, Rutherford, NJ 07,070 U.S.) in volume of 3.5 mL. The anticoagulant sodium - heparin or EDTA was used. Serum samples were obtained by centrifugation at 3000 rpm using centrifuge (Sigma 4-10). After centrifuging, serum concentration of fructosamine, cholesterol, triglycerides and high-density lipoprotein were determined. The investigation was done respecting ethical standards in the Helsinki Declaration. The retrospective studie included patients (n=100) with type 2 diabetes mellitus and who has analysed blood at Institute for clinical chemistry and biochemistry at Clinical centre University in Sarajevo. Laboratory analyses were performed on blood samples collected after a 12-h after fast.

Statistic

The results were statistically analyzed using NCSS and statistical software SPSS version 12.0 software. Determined by the average value (\( \bar{x} \)), standard deviation (SD), Pearson correlation coefficient (r), equations of linear regression and Student t test with statistical significance level of 0.05 and 0.01 (p <0.05; p<0.01).

Results

The results of serum concentrations fructosamine, glucose, cholesterol, tryglicerides, HDL,VLDL and LDL at patients with diabetes mellitus (53 men
and 57 women) are shown in Table 1. The patients were classified depending on their fructosamine levels as good, satisfactory or poor glycemic controls.

Table 1. Serum concentration of biochemical parameters at patients with diabetes mellitus

<table>
<thead>
<tr>
<th>Fructosamine (mmol/L)</th>
<th>Glucose (mmol/L)</th>
<th>Cholesterol (mmol/L)</th>
<th>Tryglicerides (mmol/L)</th>
<th>HDL (mmol/L)</th>
<th>VLDL (mmol/L)</th>
<th>LDL (mmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean serum concentration of biochemical parameters in group with good glycemic control fructosamine level &lt; 2.8 mmol/ (n=25) (± SD)</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Fructosamine (mmol/L)</td>
<td>2.43 +/- 0.28</td>
<td>Glucose (mmol/L)</td>
<td>5.27 +/- 1.33</td>
<td>Cholesterol (mmol/L)</td>
<td>4.84 +/- 1.35</td>
<td>Tryglicerides (mmol/L)</td>
</tr>
<tr>
<td>HDL (mmol/L)</td>
<td>1.18 +/- 0.50</td>
<td>VLDL (mmol/L)</td>
<td>0.71 +/- 0.36</td>
<td>LDL (mmol/L)</td>
<td>2.99 +/- 1.32</td>
<td></td>
</tr>
<tr>
<td>Mean serum concentration of biochemical parameters in group with satisfactory glycemic control fructosamine level 2.8 – 4.0 mmol/ (n=37) (± SD)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fructosamine (mmol/L)</td>
<td>3.50 +/- 0.35</td>
<td>Glucose (mmol/L)</td>
<td>9.67 +/- 4.08</td>
<td>Cholesterol (mmol/L)</td>
<td>6.58 +/- 0.75</td>
<td>Tryglicerides (mmol/L)</td>
</tr>
<tr>
<td>HDL (mmol/L)</td>
<td>1.11 +/- 0.34</td>
<td>VLDL (mmol/L)</td>
<td>0.90 +/- 0.42</td>
<td>LDL (mmol/L)</td>
<td>3.42 +/- 0.94</td>
<td></td>
</tr>
<tr>
<td>Mean serum concentration of biochemical parameters in group with poor glycemic control fructosamine level &gt; 4.0 mmol/ (n=38) (± SD)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fructosamine (mmol/L)</td>
<td>4.86 +/- 0.71</td>
<td>Glucose (mmol/L)</td>
<td>10.6 +/- 1.98</td>
<td>Cholesterol (mmol/L)</td>
<td>6.93 +/- 0.75</td>
<td>Tryglicerides (mmol/L)</td>
</tr>
<tr>
<td>HDL (mmol/L)</td>
<td>0.84 +/- 0.40</td>
<td>VLDL (mmol/L)</td>
<td>1.01 +/- 0.32</td>
<td>LDL (mmol/L)</td>
<td>3.48 +/- 0.34</td>
<td></td>
</tr>
</tbody>
</table>

Increasing concentrations fructosamine followed an increase concentration of glucose, cholesterol, triglycerides and VLDL. The concentration of HDL cholesterol was lower in all three groups. The results of correlation between fructosamine and glucose, lipids using Pearson coefficient of correlation are shown at Table 2.

Table 2. Correlation between fructosamine glucose and lipids

<table>
<thead>
<tr>
<th>r</th>
<th>Glucose</th>
<th>Cholesterol</th>
<th>Tryglicerides</th>
<th>HDL</th>
<th>LDL</th>
<th>VLDL</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.740</td>
<td>0.605</td>
<td>0.409</td>
<td>-0.242</td>
<td>0.012</td>
<td>0.470</td>
<td></td>
</tr>
<tr>
<td>0.000**</td>
<td>0.000**</td>
<td>0.000**</td>
<td>0.015*</td>
<td>0.906</td>
<td>0.640</td>
<td></td>
</tr>
</tbody>
</table>

It is determined a significant difference between the average concentration fructosamine and glucose (p < 0.01) with Pearson correlation coefficient (r = 0.740). Using the same test identified significant differences between the average concentration fructosamine the average concentration of cholesterol and triglycerides (p < 0.01). According to our results identified a significant difference between the average concentration fructosamine and HDL cholesterol (p < 0.05) with negative Pearson correlation coefficient (r = -0.242). The current study has not been established fructosamine statistically significant correlation with LDL and VLDL cholesterol. A comparison of fructosamine and glucose at patients with diabetes are shown at Figure 1.

Figure 1. Correlation between fructosamine and glucose at patients with diabetes mellitus

The correlation coefficient was 0.740 and regression line had slope of 1.3662 and y axis intercept of 1.9874. The mean difference between fructosamine and glucose was statistically significant p < 0.01 using Student t-test. Increasing concentrations fructosamine follows an increase of glucose in the blood so that allows us to track changes over a longer period of time. Therefore, with a linear regression equation can be predict the concentration of glucose in the blood based on the value fructosamine.
Discussion

Increasing concentrations of glucose increases the rate glycation of serum proteins. Fructosamine considered medium parameter control of diabetes, although the method of determining a cheaper and more accessible than those used for the determination of HbA1c. On the basis of a recent European Diabetes Study Group recommendation on targets for a diabetic control, we defined good metabolic control as serum fructosamine less than or equal to 2.8 mmol/L, satisfactory 2.8-4.0 mmol/L and poor fructosamine level more or equal to 4.0 mmol/L (15). Results of our study have shown that increasing fructosamine and glucose concentrations rise cholesterol, triglycerides and VLDL. The concentration of VLDL with regard to the groups with good, satisfactory and poor control was not changed. The results of our study showed a lower concentration of HDL in all these groups. With good glycemic control and fructosamine values 2.0-2.8 mmol/L, it is achieved that the lipids are in the reference area. The high levels of fructosamine is associated with an increased risk of death from cardiovascular causes. The association between fructosamine and cardiovascular mortality was confirmed at women patients with elevated fructosamine levels > 2.8 mmol/L. The diabetes is a risk factor for cardiovascular disease and other measurements of glucose control, such as hyperglycemia or glycosylated hemoglobin levels, correlate with the risk of cardiovascular disease with known diabetes (16).

The results of our study showed a significant correlation between glucose and fructosamine the coefficient of correlation $r = 0.740$ (p <0.01). The results of other groups show that blood glucose concentration were positively correlated with serum fructosamine ($r = 0.42$) (15). Baker and investigators have found that correlation of fructosamine and mean plasma glucose was significant with Pearson's correlation coefficient 0.75 (p<0.01) (15). Our results have showed that increasing concentrations of cholesterol and triglyceride levels paralleled the increase in the concentration and fructosamine statistically significant difference (p <0.01). These changes, which manifest as an increase in plasma triglyceride and cholesterol are exacerbated by poor metabolic control (16). It is positive correlation between triglycerides and fructosamine at patients with diabetes (17).

The high density cholesterol was low in all groups. According to our results identified a significant negative correlation between the concentration fructosamine and HDL cholesterol (p <0.05). Fructosamine and increase of glucose concentration is accompanied by declining concentrations of HDL. The primary biochemical abnormality is an decrease in high-density lipoprotein cholesterol. Values of LDL are usually within normal limits (18,19). The products from of lipid peroxidation and from fructosamine oxidation are associated with pronounced dislipidemic disorders and reduction of HDLolesterol (20,21). The other investigators have found similar results of lipids and lipoproteins in comparison with fructosamines level (22).

Today, more fructosamine associated with various cardiovascular diseases and even. Therefore it is consider possible future parameter for patients with cardiovascular diseases such as stroke and cardiac shock. Good control at diabetes has a direct impact on the reduction of lipids and it is one of the major risk for coronary artery disease in patients with type 2 diabetes.

Conclusion

The fructosamine, glycated serum protein in control of type 2 diabetes mellitus show significantly significant correlation with diabetic related dyslipidemia and possible reduced risk of atherosclerosis. Over periods of months and years, these form of glycation products are resulting in dysfunction and the pathogenesis of diabetic complications such as vascular stiffening, hypertension, nephropathy and retinopathy. It is high specific test in monitoring of diabetic patients in regard of antidiabetes therapy and lipids control. The serum fructosamine measure gives a good index for the glycemic control, and its value can reflect the profile of serum lipids. The patients with diabetes mellitus have an increased risk of developing cardiovascular disease and atherosclerosis, so maintenance fructosamine at referent scope is important.
References


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Dosage of Erythropoietin and iron-replacement therapy in patients on chronic hemodialysis

DOZIRANJE ERITROPOETINA I NADOMJESNA TERAPIJA ŽELJEZOM U BOLESNIKA NA HRONIČNOJ HEMODIJALIZI

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Abstract

Anemias are diseases of decreased number of erythrocytes or hemoglobin in a volume blood unit with hypoxia of muscles as a result. The objective of the study was to establish iron-replacement therapies to achieve target values of hemoglobin and hematocrit in renal anemia treatment by erythropoietin in chronic hemodialyzed patients. The study involved 60 patients, both sexes, randomly chosen and divided into two groups. The first (experimental) group numbered 20 examinees administrated epoietin alpha intravenously, while the other group numbered 40 patients administrated epoietin beta (control group). In this group 20 patients were administered epoietin beta intravenously, 20 of them subcutaneously. All the patients were administered epoietin alpha or beta weekly after hemodialysis. Erythropoietin dose was determined and adjusted according to the blood picture findings. Comparison of the mean doses of erythropoietin between experimental and control groups showed no statistically significant difference (p>0.05). The highest dose of iron-replacement was administered to the patients on subcutaneous therapy by epoietin beta, but no significant difference in intravenous iron-doses was found (p>0.05). We found that increased levels of hemoglobin result in increased need for iron, while decreased dose of intravenous iron results in fall of hemoglobin level. Insufficient replacement therapy of iron resulted in weaker respond to the erythropoietin therapy in the patients with renal anemia who were administered erythropoietin alpha and beta intravenously.

Key words: renal anemia, erythropoietin, hemodialysis

Sažetak

Anemije su bolesti sa smanjenom količinom eritrocita ili hemoglobina u volumnoj jedinici krvi s posljedičnom hipoksiom tkiva. Cilj studije je bio utvrditi uticaj nadomjesne terapije željezom na postizanje ciljnih vrijednosti hemoglobina i hemotokrita u liječenju renalne anemije eritropoetinom kod hroničnih hemodializnih bolesnika. Istraživanjem je obuhvaćeno 60 ispitanika, oba pola, odbranih metodom slučajnog odabira i podijeljenih u dvije grupe. Prva (eksperimentalna) grupa se sastojala od 20 ispitanika koji su primali epoetin alfa intravenski, dok je u drugoj grupi bilo 40 ispitanika koji su primali epoetin beta (kontrolna grupa). U ovoj grupi 20 ispitanika je primalo epoetin beta intravenski, a 20 bolesnika epoetin beta subkutano. Svi ispitanici su primali epoetin alfa ili beta tri puta sedmično nakon hemodijalize. Doza eri-
tropoetina određivala se i prilagođavala prema nalazu krvne slike. Upoređivanjem vrijednosti srednjih doza eritropoetina između eksperimentalne i kontrolnih grupa nije nađena statistički značajna razlika (p>0,05). Najveću dozu nadomjesnog željeza dobili su bolesnici na subkutanoj terapiji epoetinom beta, ali u dozama intravenskog željeza nije uočena značajna razlika (p>0,05). Našli smo da viši nivoi hemoglobina vode povećanoj potrebi za željezom, te da smanjenjem doze intravenskog željeza dolazi do pada nivoa hemoglobinina. Nedovoljna supstituciona terapija željezom bila je razlog slabijeg odgovora na terapiju eritropoetinom u bolesnika sa renalnom anemijom koji su liječeni intravenskim eritropoetinom alfa i beta.

Ključne riječi: renalna anemija, eritropoetin, hemodijaliza

Introduction

Anemias are diseases of decreased number of erythrocytes or hemoglobin in a volume blood unit with hypoxia of muscles as a result. After long-years unsuccessful treatment of renal anemia, introduction of recombinant human erythropoietin (rHuEPO) brought revolutionary progress in therapeutical approach. Two forms of erythropoietin should be distinguished, erythropoietin alpha and erythropoietin beta. Safely and successfully rHuEPO has been used nearly 20 years in the treatment of renal disease, chronic renal damage and renal anemia induced by hemotherapy in the case of malignants (1). It is particularly effective in the anemia treatment of the patients in the course of renal disease terminal phase (2). Presently, a majority of patients are not anemic and have greater quality of life than before (3). European Best Practice Guidelines (EBPG) recommends maintaining hemoglobin values over 11g/dL and hematocrit over 33% in all chronic renal patients. In fact, erythropoietin dose should be harmonized with hemoglobin level. Increased needs for iron in hemodialyzed patients are the result of great loss of iron through gastrointestinal tract, decreased absorption of iron, frequent laboratory check-ups, and loss of blood in the course of hemodialysis. Adequate amount of the iron available increases erythropoiesis and decreases needs for therapy by the erythropoiesis stimulating agents (ESA) (4). To achieve target hemoglobin levels it is necessary to maintain serum ferritin between 200 and 500 µg/L, and the percentage of hypochromic erythrocytes below 2,5%. Suggested upper limit of the serum ferritin for all the patients is 800 µg/L. At the time before ESA, dialysed patients often had access of iron (with ferritin over 1000 mg/L) as a result of polytransfusions (5). In the case of absolute or functional iron deficit identified or suspected, it is necessary to introduce iron-replacement, in order to achieve maximal effects of rHuEPO-therapy (6). General recommendation of rHuEPO is to administer 25-150 mg of iron intravenously in the course of the first 6 months of the ESA-therapy. Extra good results were achieved when that dose was administered after „filling dose“ of 400-600 mg of iron through two weeks (4).

Objectives

The objective of the research was to establish the effects of the iron-replacement therapy in order to achieve target values of hemoglobin and hematocrit in the treatment of renal anemia by erythropoietin in the chronic hemodialyzed patients.

Patients and methods

The study involved 60 patients, both sexes, randomly chosen, divided into two groups. The first one (experimental) consisted of 20 patients being administered epoietin alpha intravenously, while the other one consisted of 40 patients being administered epoietin beta (control group). The control group was divided into two subgroups: one consisting of 20 patients treated by epoietin beta intravenously, the other one consisting of 20 patients treated by epoietin beta subcutaneously. The control group was divided into two subgroups: one consisting of 20 patients treated by epoietin beta intravenously, the other one consisting of 20 patients treated by epoietin beta subcutaneously. Before the research all the examinees, who were longer than three months on hemodialysis treatment, were treated by epoietin beta subcutaneously. When introduced into research, the examinees had a stable hemoglobin level between 9 and 11 g/dL at least during two successive measurements. Patients with malignant disease were not included into research. The study was prospective and performed in the
Clinic for Internal Diseases, University Clinical Center of Tuzla, lasting six months. Before the research, complete blood picture (check-up), iron and ferritin, were done before being dialyzed, for each examinee. All the said parameters were measured for all the patients in the course of the first month every week, then after the third and sixth month. Erythropoietin dose has been determined and adjusted according to the blood picture findings according to the following principles:

- in the case of hemoglobin level fall for 1-1,9 mmol/L, erythropoietin dose increased for 25%
- in the case of hemoglobin level fall for 2 mmol/L, erythropoietin dose increased for 50%
- in the case of hemoglobin level rise for 1-1,9 mmol/L, erythropoietin dose decreased for 25%
- in the case of hemoglobin level rise for 2 mmol/L, erythropoietin dose decreased for 50%.

All the examinees were administered epoietin alpha or beta three times a week after hemodialysis, intravenously, or subcutaneously. The majority of the patients were treated by iron replacement therapy intravenously (generic name Venofer) in order to maintain ferritin level between 300 and 500 ug/L.

Statistical significance of the mean values of the parameters measured were tested by the Student’s t-test. For all the calculations we used significance level of p≤0,05.

**Results**

Out of 60 patients analyzed, 29 (48,3%) were males, 31 (51,7%) females. Average age was 57, 6 ±13,18 (27-80) years in experimental, and 54,2 ±13,5 (27-79) years in control group (p=0,66). Comparison of the mean values of erythropoietin doses through six-month period of therapy, no statistically significant difference was found (p=0,64).

Average dose of epoietin alpha in experimental group of patients was 3314,6 ±619,79 i.u. Patients on intravenous epoietin beta therapy received approximately 3242,6 ±792,61 i.u. of epoietin, and patients on subcutaneous epoietin beta received approximately 3341,9 ±829,13 i.u. of epoietin. Mean dose for all the examinees in the experimental period was 3291,9 ±962,92 i.u. of epoietin (Figure 1).

Examinees on intravenous epoietin beta therapy received approximately some smaller dose or erythropoietin in relation to the other two groups of examinees. Average doses of epoietin between the examined groups are minimally different. Comparison of the values of weekly doses of epoietin/kg of body weight no significant difference was found (p>0,05). No difference was found in the weekly doses among examinees on intravenous epoietin alpha or subcutaneous epoietin beta. Namely, average weekly dose for these two groups of patients amounted 40 i.u./kg of body weight, while intravenous weekly epoietin beta dose was some higher, 45 i.u./kg of body weight.

Out of total 60 patients 46 (76, 7%) of them received iron-replacement therapy during the experiment. In experimental group 12 (60%) patients received iron-replacement in average dose of 578,6 ±392,58 mg (100-1600 mg). Out of total of 20 patients 17 (85%) of them were administered iron-replacement in average dose of 473,3 ±334,80 mg (100-1500 mg). In the group of patients on the subcutaneous epoietin therapy, iron-replacement therapy was applied for 16 patients (80%), and the mean dose amounted of 700 ±413,11 mg (100-1500 mg) of intravenous iron. Average dose of intravenous iron, during six-months therapy by epoietin, amounted 586,7 ±385,29 mg (Figure 2) for all the patients in total.

So, the patients on subcutaneous epoietin beta therapy received the highest dose of iron-replacement, then come the patients on intravenous epoietin alpha and beta therapy. Testing the statistical significance of difference among the mean values of iron doses in the tested groups showed no statistical difference (p=0,27). Comparison of the mean values of ferritin, a month before including
the patients into research with ferritin measured after three and sixth months of research, no significant difference was found in the testing groups (p>0.05). Relation of average values of ferritin is shown in the Figure 3.

![Figure 2. Relation of the mean values of iron doses in the tested patients](image)

**Figure 2. Relation of the mean values of iron doses in the tested patients**

Values of ferritin in the experimental group of patients in the course of six month-therapy by epoietin alpha increased from 796.3 to 820.3 µg/L. After three months of intravenous epoietin beta and iron-replacement therapy, average value of ferritin increased from 806.7 to 1037.5 µg/L. Decreased dose of iron-replacement, ferritin fell to 1003.7 µg/L. Average values of ferritin in the patients on subcutaneous epoietin beta therapy were increasing from the initial 675.3 µg/L (start of the experiment) to 743.4 µg/L after six months (Figure 3).

![Figure 3. Average values of ferritin in the tested patients](image)

**Figure 3. Average values of ferritin in the tested patients**

Discussion

Results of different studies (7, 8) show that subcutaneous epoietin is equally effective as well as the intravenous one in chronic renal patients who are on hemodialysis, but to achieve target values of hemoglobin and hematocrit, smaller doses of subcutaneous epoietin could be used, and that way to low the treatment cost. Vanrenterhem et al., found that needed dose of subcutaneous epoietin (alpha and beta) is 22% lower in comparison to intravenous epoietin (9).

The highest dose of epoietin (though it is slightly increased) in correction of renal anemia, received the patients on subcutaneous epoietin beta therapy (p>0.05). Average dose of subcutaneous epoietin beta was higher for 0.8% than the average dose of intravenous epoietin alpha and for 2.9% in comparison to intravenous epoietin beta. Dose of epoietin alpha was approximately higher for 2.2% in comparison to average dose of intravenous epoietin beta.

However, there was no difference (40 i.u./kg of body weight), in weekly dose of erythropoietin among the patients on intravenous therapy by epoietin alpha and subcutaneous epoietin, while weekly dose of intravenous epoietin beta was approximately higher for 5 i.u./kg of body weight.

Beside that, no statistically significant difference was found in hemoglobin, hematocrit, and biochemical parameters levels depending on a remedy dose, in the tested groups, what shows that in our study epoietin alpha and beta were equally effective.

As there was no difference in weekly doses of erythropoietin, we could speculate with the reasons of better therapeutical respond in the patients treated by subcutaneous epoietin beta, concerning to the prevalence of males in comparison to females in this group, or differences in isomorphous composition of epoietin alpha and beta (caused by glycolisation form), that is most possible reason of variations in the potential of remedy (10).

Our study results also show that doses of epoietin were slightly smaller than in recommendations of EBPG on the treatment of renal anemia. Concerning the results cited, except in erythropoietin dose, explanations could be found in differences in iron-replacement doses in the tested groups.

Titration of iron administration was followed by measuring serum ferritin level. In our research 76.7% (60% of patients in experimental, and 85% and 80% in control groups) were administered replacing iron. The patients on subcutaneous epoietin beta therapy received approximately the highest dose of intravenous iron, what is in accordance with the study showing that higher levels of hemoglobin cause higher need for iron (11). Slightly smaller dose
of replacing iron was administered the patients on epoietin alpha therapy. It should be mentioned that these patients had lower level of hemoglobin, either. On the contrary, the patients on intravenous epoietin beta therapy after three months had increased level of ferritin over suggested upper limit of 800 µg/L (1037.55 ±473.32 µg/L), that remained of the same values till the end of the study (1003.7 ±424.66 µg/L). Considering the safety measures pointing to the fact that high doses of iron can cause organ’s damage because of iron deposit in such patients (12) iron dose was decreased in the course of the last three months of therapy. The lowest dose of replacing iron in these patients is probably one of the reasons of hemoglobin levels fall in the course of the last three months of therapy.

As none of the patients in this group was transfunded in this period, our results are not in accordance to the findings in Locatelli’s et al. study (5) that shows that such high values of iron deposit (>1000 µg/L) should be caused by frequent blood transusions. All the cited above bring a number of dilemmas. Firstly, it is possible that combination of erythropoietin beta and intravenous iron in higher doses had better effect, and that replacing epoietin beta with epoietin alpha in experimental group resulted in a weak hematopoietic respond, while continued therapy by beta epoietin resulted in achieving target values of hemoglobin and hematocrit (hemoglobin >11 g/dL and hematocrit >33%).

Conclusion

Insufficient supstitutional iron therapy was the reason of a weaker respond to the erythropoietin therapy in the patients with renal anemia who were treated by intravenous epoietin alpha and beta.

References


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Abstract

The primary value of DNA typing has been significantly increased over the last fifteen years due to introduction of short tandem repeat (STR) loci in paternity testing, as well as in forensic cases and mass disaster human identification. Nowadays, several commercial multiplex kits are available, allowing routine use of this powerful forensic-genetic tool. In addition, it is well known that even extremely highly degraded nuclear DNA may be successfully analyzed using PCR primers that are close to the STR repeat. This modification of STR molecular markers is described as miniSTR approach. In this study we have examined possible application of nuclear miniSTR loci in forensic DNA analysis of 65 telogenic hair that collected from various locations within the facility of Institute for Genetic Engineering and Biotechnology. All samples were briefly washed in absolute ethanol and extracted using Qiagen DNA Dnaeasy™ Tissue Kit. DNA concentration was determined using Quantifiler Human DNA Quantification Kit as described previously. The reaction was carried out in AB 7300 Real-Time PCR System according to the manufacturer’s recommendations. The PowerPlex S5® system has been used to amplify 4 miniSTR loci in 10µl total reaction volume. PCR amplification was carried out in AB GeneAmp PCR System Thermal Cycler. Electrophoresis of the amplification products was performed on an ABI PRISM 310 Genetic Analyzer. Raw data have been compiled, analyzed and numerical allele designations of the profiles were obtained using the accessory software: ABI PRISM® Data Collection Software v3.0 and GeneMapper™ ID Software v3.1. As the result of these analyses, 19 telogenic hair were completely or partially profiled and for 46 of them no profiles were detected. The most stable results were detected at TH01 locus. These facts, together with the other results of this study, imply that PowerPlex® S5 System may be useful in forensic analysis of the samples with very low amount of nuclear DNA such as telogenic hair. However, its application has certain limitations in the field that should also be considered and overcome in the future application of miniSTR approach in the field of forensic genetic.

Key words: telogen hair, miniSTR, forensic DNA analysis

Sažetak

Primarna vrijednost DNK analize je signifikantno porasla u posljednjih petnaest godina primjenom STR (Short Tandem Repeats) markera u DNK analizama kako u sklopu testiranja spornog
Hair is one of the most common types of physical evidence that could be found at the crime scene. Hairs can provide investigators with valuable information for potential leads. Also, hair shaft is desirable forensic evidence, because it is sturdy and can maintain its essential distinctiveness for years. They carry plenty of biological information and they are easy to examine (1). Until recently, the comparison by microscope was considered the only reliable tool for hair identification. Today, DNA testing, both nuclear (nuDNA) and mitochondrial (mtDNA), frequently provides valuable information about biological source of the examined evidence (1).

The primary component of hair is protein keratin. It is defined as slender outgrowth in the skin of mammals (3). Its growth is characterized by three phases: anagen, telogen and catagen. Anagen is the phase of active growth when follicle produces new cells and pushes them up the hair shaft (4). Because of massive presence of surrounding bulb cells, this phase of hair growth is preferable for forensic nuclear DNA analysis. Catagen is transitional phase. During this phase of growth, the follicle begins to shut down production of cells (1). Almost 80% of human hairs found at the crime scene are in telogen phase, the terminal, degenerative phase of the hair’s development cycle (5). Telogenic hairs are characterized by the presence of club roots. They contain few bulb cells, which produce extremely low amount of highly degraded nuDNA, hardly suitable for this kind of DNA typing. Until recently, catagen hair shafts were used only for mtDNA analysis.

Considerable distinction exists among the types of hairs originating from different regions of the human body, such as head, pubic region, arms, legs etc. The region of the body where a hair originated can be determined with considerable accuracy by its gross appearance and microscopic characteristics. Length, shape, size, color, hardness, curliness, and microscopic appearance all contribute to the body area determination (2). The first step in examination of hair routinely involves the identification of hairs and their visual (microscopic) comparison with the reference. Primarily, the origin of the hair is confirmed (human or animal). Afterwards, comparison of specific features
may reveal whether particular individual should be considered as a possible biological source of the physical evidence.

However, hairs that have been matched or associated by microscopic examination should also be examined by DNA analysis. In fact, nuclear DNA testing provides the most relevant information in the sense of individualization of the possible origin of the hair (5). However, the amount and condition of recovered nuDNA vary depending on the phase of hair growth.

The primary value of DNA typing has been significantly increased in the last fifteen years due to introduction of short tandem repeat (STR) loci in routine paternity testing, as well as in forensic cases and mass disaster human identification (6). Nevertheless, the ability to obtain DNA profiles from very small amounts of sample still presents certain type of challenge in forensic casework (7). As it is already known, low-copy number (LCN) DNA testing typically refers to examination of less than 100 pg of input DNA (5, 8). In such cases, improvement of the result is frequently attempted by increasing the number of PCR cycles. Nevertheless, application of LCN results should be approached with caution due to the possibilities of allele dropout, allele drop-in, and increased risks of collection-based and laboratory based contamination. Therefore, additional DNA analysis of these samples with an available miniSTR system is sometimes required (7, 9).

At the beginning of the 21st century, it was demonstrated that highly degraded DNA as well as very low amounts of DNA could be more successfully typed using new redesigned PCR primers positioned closer to the STR repeat (10). Many authors consider that it is likely that miniSTRs will play major role in the future of degraded DNA analysis found in physical evidence such as human telogen hair. Several commercial miniSTR multiplex were released over the last few years. PowerPlex S5 (Promega corporation, Madison, USA) is one of them and its potential was already described in our previous work (7,9,11).

**Aim/objectives**

The aim of this study was to examine and optimize the application of miniSTR multiplex system, and consequently, to analyze the capacity of this forensic genetic tool within forensic DNA analysis of human biological traces that yield small amounts of highly degraded DNA.

Also, the goal was to estimate the level of success of miniSTR multiplex system, particularly PowerPlex S5 (Promega corporation, Madison, USA) applied to human telogenic hairs, and potentially optimize nuDNA analysis process of human telogenic hairs.

**Material and methods**

Hair samples were collected using sterile tweezers from various locations within the facility of Institute for Genetic Engineering and Biotechnology (INGEB). In total, 100 of hair samples were collected and stored separately in paper envelopes labeled with unique lab code. The collected samples were processed in the Laboratory of Forensic Genetics at INGEB, University of Sarajevo. The hairs were visually analyzed using light microscope. Accurate detection of the hair growth phase was performed using binocular light microscope, type Novex B-range, Euromex Holland. Telogenic hairs, which were the study target, were separated from anagenic and catagenic hair specimens.

Hair specimens were transferred to Petri-dish and washed first with absolute ethanol and, after that with DNA-free ddH2O. The cut was made approximately one centimeter from root-region, to avoid melanin containing keratinized fragment. With the aid of one glycerol drop, hairs were easily placed on glass slide and then covered with slips. Microscopic examination was performed using 10 x magnification. All hair specimens were photographed using Olympus BX51 camera and viewed using Studio Lite and Viewfinder Lite software. Hairs identified as telogenic were selected for further DNA analysis.

Each selected telogenic hair was washed successively in absolute ethanol, and DNA free ultrapure water, and dried in 1,5ml sterile tubes. DNA extraction was performed using QIAGEN DNeasy™ tissue kit (12). Extraction procedure was additionally optimized for telogenic hair specimens by adding 1M DTT solution. Some samples required additional purification and concen-
tration step applying Centricon-100 centrifugal filter units (Millipore, Billerica, MA, USA). The concentrates were transferred to 1.5ml centrifuge tubes and diluted with DNA free ultra-pure water to a final volume of 50μl. DNA concentration was determined using Quantifiler Human DNA Quantification kit (Applied Biosystems) (13). The reaction was carried out in AB 7300 Real-Time PCR System (ABI, Foster City, CA, USA) according to manufacture’s recommendations. Amplification of STR loci was performed using PowerPlex S5 miniSTR amplification system (Promega corporation), that contain 4 STR loci: D18S51, D8S1179, TH01 and FGA, and sex determining marker, amelogenin. The total reaction volume was 10 μl. PCR amplification was carried out in an AB Gene Amp PCR System 9700. Electrophoresis of the PCR products was performed on an ABI PRISM 310 Genetic Analyzer. Raw data were compiled and analyzed, and numerical allele designations of the profiles were obtained using the accessory software: ABI PRISM Ò Data Collection Software v3.0 and GeneMapper™ ID Software v3.1.

Results

Microscopic analysis of the collected hair specimens

Microscopic analysis identified all the collected hair specimens as human, originating from head (Table 1). In addition, the same analysis focused on root appearance implied that most of hairs, 65 of them exactly, were in telogen phase of growth, (Figure 1, Table 2).

Quantitative analysis of nuDNA extracted from telogenic hair samples

Real-time based quantification using Quantifier® DNA Identification kit (Applied Biosystems) detected nuDNA in 14 (22%) DNA extracts from telogenic hairs. For the remaining 51 telogen hairs extract, either no nuDNA was detectible or PCR inhibitors were present (6 samples; Table 3). In

| Table 1. The origin of hair specimens as determined by microscopic analysis |
|------------------|------------------|------------------|------------------|
| Collected hairs - total | Hairs of human origin | Hairs of animal origin |
|                  | Head | Other body areas |                  |
| 100              | 100  | 0                | 0                |

| Table 2. Microscopic identification of hair growth phase |
|------------------|------------------|------------------|------------------|
| Collected hairs - total | Anagen phase of growth | Catagen phase of growth | Telogen phase of growth |
| 100              | 23              | 12               | 65               |
samples with detectable DNA, nuDNA concentration ranged from $8.69 \times 10^{-4}$ ng/µl to $9.50 \times 10^{-2}$ ng/µl. (Table 4).

The analysis of the obtained miniSTR profiles

The profiles obtained using miniSTR markers are presented in Table 5. DNA profiles were obtained for 19 (29%) telogenic hair specimens. Number of the detected loci varies from one to five per

Table 3. Overall results of DNA quantification

<table>
<thead>
<tr>
<th>Total number of processed hairs</th>
<th>Samples with determined nuDNA concentration</th>
<th>Samples with non-detectable nuDNA</th>
<th>Samples with PCR inhibitors</th>
</tr>
</thead>
<tbody>
<tr>
<td>65</td>
<td>14</td>
<td>45</td>
<td>6</td>
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</table>

Table 4. The results of DNA quantification presented per processed sample

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<tr>
<th>Hair Sample</th>
<th>Concentration (ng/µl)</th>
<th>Hair Sample</th>
<th>Concentration (ng/µl)</th>
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<td>HS 34</td>
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<tr>
<td>HS 2</td>
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<td>HS 35</td>
<td>$1.39 \times 10^{-2}$</td>
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<td>HS 36</td>
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<td>-</td>
<td>HS 37</td>
<td>$3.07 \times 10^{-3}$</td>
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<td>HS 5</td>
<td>-</td>
<td>HS 38</td>
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<td>HS 7</td>
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<td>HS 40</td>
<td>$7.53 \times 10^{-3}$</td>
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<td>HS 41</td>
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<tr>
<td>HS 10</td>
<td>$8.59 \times 10^{-4}$</td>
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<td>$1.49 \times 10^{-2}$</td>
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<td>HS 33</td>
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### Table 5. The profiles obtained by miniSTR typing of the analyzed telogenic hairs

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<th>AMEL</th>
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<th>FGA</th>
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<td>8</td>
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<td>10</td>
<td>Y</td>
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profile. Complete miniSTR profiles were obtained for four hair specimens only. Figure 2 presents one of the full DNA profiles. Other fifteen miniSTR profiles were partial (Figure 3). MiniSTR profiling did not provide any results for 46 processed hair samples. Finally, THO1 locus was the most frequently detected locus in this study. On the other hand, FGA locus provided the weakest results in the typing of the telogen hair samples.

**Discussion**

As reported previously, microscopic analysis identified all the collected samples as human, originating from the head area. Absence of animal specimens was expected since the hair samples were collected from the various locations within the INGEB facility, where animals are not allowed. In addition, the same analysis focused on root appea-
rance implied that 65% of the collected hairs were in telogen phase of growth. This result mainly concurs with previously published information, which reports 80% of human hairs found on crime scenes to be in telogen phase of growth (5). Slightly increased number of the recovered anagen hair samples may be explained by the fact that some of the specimens were collected from the personal INGEB employees’ clothing, where this type of specimens could be expected with higher frequency.

The quantification categorized all telogenic hair samples processed in this study as, so called, LCN (low copy number) DNA evidence, since the detected amounts of extracted nuDNA were well below 100pg/µl (8). Similar study was conducted before (14). Previous study has shown that the concentration of DNA extracted from hair samples collected from various combs was below 100 pg/µl in more than 30% of the specimens. Of course, there is a marked difference in the modality of specimens’ collection between these two studies. Therefore, the detection of higher amounts of DNA in almost 70% specimens from the combs was expected.

Interestingly, higher mean DNA concentrations were obtained from 60 years old skeletal remains’ samples (15) than from telogen hair samples processed in this study. That also serves to prove how challenging the DNA analysis of telogen hair evidence may be. Therefore, the selection of the most suitable DNA extraction protocol is a crucial step in successful profiling of telogenic hair samples. Guided by the available data from literature, (16, 17) and earlier gathered experience from our laboratory, we have chosen alcohol pretreatment, which significantly increases the possibility of successful isolation of DNA from telogen hair specimens. Also, based on the same premises, we selected DNA extraction procedure based on the use of silica membrane (12), with the addition of dithiothreitol (DTT), which prevents renaturation of disulphide bonds in keratin that prevents successful isolation of DNA from the hair specimens (18). Although, several studies indicate that DTT reduces the concentration of extracted DNA (19), our previous experience shows significantly better results in its presence.

Finally, considering four full and fifteen partial miniSTR profiles obtained from hair specimens in this initial study, we tend to maintain positive attitude towards usefulness of this genetic tool in forensic DNA analysis of these challenging physical evidences. Of course, it is already well known that miniSTR assays can help recover information from degraded DNA samples that typically result in partial profiles and total loss of information using regular STR amplicons (7). This approach has already been used in the analysis of highly degraded samples like those processed within the identification of victims from the World Trade Center terrorist attacks (7), in identification of World War II victims (7), but it could also be used within case studies in the analysis of telogenic hair samples (11). It is noteworthy that in even though RealTime-PCR quantification assay was unable to detect DNA, in some cases, miniSTR provided useful profile. The same observation was also recorded in previous study (7). Considering all the relevant information, it is expected that the most recent concept of miniSTR kits should certainly upgrade the analysis of LCN DNA biological evidence, including human telogenic hair samples.

**Conclusion**

In latest years, DNA forensic analysis of hair shafts has significantly improved both in terms of selecting the most useful genetic markers, as well as, in terms of the optimization of the analysis procedures. It is likely that miniSTR assay will certainly play a role in the future of degraded DNA analysis. The results of this initial study indicate that miniSTR PowerPlex S5 System, as well as miniSTR concept in general, has the potential in DNA analysis of telogenic hair specimens.

Until recently, usage of miniSTRs had several disadvantages, such as differences in heterozygous allele call detected in comparison with standard STR markers, or low discriminatory power within individualization of miniSTR profiles due to low number of miniSTR loci within existing multiplex kits, which have restricted the power of its usage in the field of forensic genetics.

Well planned concordance studies as well new concept of the joint STR and miniSTR multiplex kit promoted by Promega Corporation successfully work towards solving these items. All these joint efforts, together with the new solution in specimen
pretreatment procedures and optimized DNA extraction protocol will certainly significantly improve usage of miniSTR concept in DNA profiling of telogenic hair shafts.

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Evaluation of Serologic tests for diagnosis of Brucellosis

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Abstract

In the past fifteen years, Bosnia and Herzegovina has been among the countries with endemic form of brucellosis, i.e. with high incidence of the disease in animals and humans. Brucellosis has become a significant public-health problem in a major part of the area of Bosnia and Herzegovina, due to this fact. Since both the causal agent of the disease and the disease belong to the group of zoonoses, the infection in humans is narrowly related to the infection in animals. Diagnosis of the disease implies isolation of microorganisms from biological material samples or detection of specific antibodies in serum. Results of the laboratory confirmation of brucellosis suspicion, based on determining of the presence of specific antibodies in the sera of 43 hospitalized individuals, are presented in this paper. The presence of specific antibodies was confirmed in 16 (37.2%) individuals using the method of Rose Bengal agglutination, while positive finding was obtained for 10 (23.2%) individuals using the CBR method. Result of the Rose Bengal test was indicated as positive or negative. There were 12 male and 4 female individuals, out of a total of 16 seropositive patients. Concerning the age of individuals, it was determined that there had been 3 (18.75%) positive individuals in the group aged up to 30, and 13 (81.25%) in the group aged older than 30. Concerning the obtained results of antibody titer levels determined by CBR, it is evident that they varied between 1:8 and ≥ 1:312.

Key words: brucellosis, Bosnia and Herzegovina, Rose Bengal, CFT.

Bosna i Hercegovina se u zadnjih petnaest godine ubraja u jednu od država sa endemskim oblikom bruceloze, odnosno sa visokom incidencom oboljevanja životinja i ljudi. Zbog ove činjenice, brucelzoa je postala značajan javnozdravstveni problem na velikom dijelu teritorije Bosne i Hercegovine. Pošto uzročnik oboljenja, kao i oboljevanje spada u skupinu zoonoza, to je i oboljevanje ljudi usko povezano sa oboljevanjem životinja. Dijagnoza oboljenja podrazumijeva izolaciju mikroorganizama iz uzoraka bioloških materijala ili nalaz specifičnih antitijela u serumu. U ovom radu, prikazani su rezultati laboratorijske potvrde sumnje na brucelozu ispitivanjem prisustva specifičnih antitijela u serumu 43 hospitalizirana ispitanika. Metodom aglutinacije Rose Bengal je kod 16 (37,2%) ispitanika dokazano prisustvo specifičnih antitijela, dok je metodom RVK, pozitivan nalaz dobiven kod 10 (23,2%) ispitanika. Rezultat Rose Bengal testa se iskazivao kao pozitivan ili negativan. Od ukupno 16 seropozitivnih pacijenata, na muški spol otpada 12, a na ženski 4 ispitanića. U odnosu na dob ispitanića, ustanovljeno je da je u dobroj skupini do 30 godina bilo 3 (18,75 %) pozitivna ispitnika, a u dobroj skupini preko 30 godina 13 (81,25 %). U odnosu na dobivene rezultate visine titra antitijela dobivenih RVK, vidljivo je da su se kretali od 1: 8 do ≥ 1:312.

Ključne riječi: brucle, Bosna i Hercegovina, Rose Bengal, CFT.
1. Introduction

In the past fifteen years, Bosnia and Herzegovina (BiH) has been among underdeveloped countries with endemic form of brucellosis and Q fever, i.e. with high incidence of the disease in animals and humans, caused by related infectious agents (1, 2, 3, 4, 5). In the analyzed areas in BiH, infections are registered in cattle, sheep, goats, and other animals, as well as in humans. Human infections are diagnosed clinically, epidemiologically, and serologically, using adequate methods. In some cases, the attempt of isolation of brucellas results in isolation from blood samples or other biological materials, when suspicion of the disease is confirmed by isolation of the causal agent as well.

Small, non-motile, Gram-negative aerobic cocccobacilli are causal agents of brucellosis. They belong to the group of aerobic bacteria that are oxidase- and catalase-positive, do not reduce nitrites, do not produce indole, and do not degrade gelatin. They are intracellular parasites, which are difficult to cultivate in standard nutritional media. The most reliable method of isolation of these bacteria is their isolation from blood, by cultivation of hemoculture that lasts up to one month. Reliable method of confirmation of brucellosis includes observing the titer of specific antibodies, or detection of occurrence of specific IgM antibodies, and then IgG as well, in the sera of infected patients. Specific anti-Brucella antibodies or increase in the overall antibody titers is searched for in serum samples in acute phase of the disease, which are collected after the infection. Quality of detected antibodies is determined in even-numbered and each subsequent serum sample, collected in the interval of 14 to 21 days, i.e. increase or decrease in the titer of specific antibodies is observed.

Brucellosis, as well as Q fever, represents an infectious disease in the group of zoonoses. Brucellas (B. abortus, B. melitensis, B. suis, B. canis, etc) primarily infect domestic animals (goats, sheep, cattle, pigs), causing unapparent or manifest diseases, or abortion in gravid animals. Cattles represent a natural reservoir and they are carriers of B. abortus, goats and sheep of B. melitensis, and pigs and dogs of B. suis and B. canis, respectively. Brucellas are transmitted from animals to humans by direct contact, via damaged skin or mucous, by consuming contaminated milk and dairy products, or via the aerogenic route. Frequency of the infection in humans is narrowly related to their occupation, as well as to the presence of animal infections. The infection and disease are more frequent in cattle-breeders, veterinarians, technicians, as well as those who handle the dairy and meat products and animal products. Interhuman infections are rare. Brucellosis is also one of the possible laboratory infections. The infection is likely to occur in working conditions that include unprotected environment or working without protective wear (gloves, masks, protective glasses), mouth pipetting, i.e. exposing the skin and mucous of eyes, nose or mouth to contaminated aerosol. Brucellas cause chronic infections in animals, since they are located within the cells of various organs and systems, cells of mammary glands or reproductive organs. Depending on infection of organs or organ systems, various forms of clinical features develop.

Brucellosis in humans is a multisystemic disease, which is clinically manifested depending on organs and systems that are infected. Clinical symptoms of brucellosis can be flu-alike, with the occurrence of high temperature, headache, pain in muscles and joints, hepatosplenomegaly, feel of cold, anorexia, and general weakness. Brucellosis is characterized by the occurrence of undulant, low temperature in the morning and high temperature in the evening. Immunity remains solid after the recovery. Complications occur in certain number of infected individuals. These bacteria have been found to inhabit the cells of reticuloendothelial system, liver, spleen, bones, joints, urogenital tract, central nervous system, skin, lungs, and heart. As a consequence of the infection and complications, organ damages, such as endocarditis, or damages of various localizations are likely to occur in a long period of time (6, 7, 8). Human brucellosis is difficult to treat; the treatment requires long-term application of certain antibiotics, with the possibility of their penetration into an infected cell (for adults - doxycycline combined with streptomycin, for children – gentamicin and sulfametoxazol+trimethoprim, throughout six
weeks). The therapy is strictly prescribed (doses and duration), aimed at eradication of the causal agents from organism, by avoiding the occurrence of complications or relapse of the disease. Modified therapeutic regimen is recommended for children younger than 8, pregnant women, and other groups at risk (9, 10).

Specific and unspecific protection measures are available, aimed at prevention of the occurrence and spreading of this disease. Live attenuated vaccine has been produced for certain animal species (Rev 1), while an adequate vaccine is intended for persons exposed to the risk of infection. The most important unspecific protection measures include the available veterinary-sanitary measures, since veterinarian, as well as human medicine, is responsible for spreading of the causal agent and disease in humans. Constant veterinary control of the animals is necessary, as well as to vaccinate healthy animals, to sacrifice infected animals, and to initiate eradication of focal points of the infection. It is also necessary to pasteurize milk and dairy products. Veterinarians and other medical staff in the field must regularly apply personal protective wear. In the area of occurrence of the infection, it is necessary to educate the population, to apply certain procedures of disinfection, to recommend boiling or pasteurization of milk, to test animals, and to initiate their immunization (9, 10).

2. Material and methods

A total of 53 sera of 43 patients with clinical suspicion of brucellosis were tested in the period from October 1st to 31st 2009. Blood samples were collected by venepuncture; a part of the blood was used for isolation of bacteria and the other was centrifuged, i.e. serum was separated from the blood, in order for certain serological reactions to be carried out. The sera collected were kept at +4°C or −20°C until initiation of certain tests. Clinically suspicious cases of brucellosis were confirmed by examination of sera to the presence of specific antibodies, using the qualitative Rose Bengal agglutination test (screening method) and the complement-binding reaction (CBR) (7, 9). Rose Bengal agglutination test (Pourquier) and CBR (Pourquier) were carried out in accordance with the original, i.e. standard procedures and recommendations of the test producers. The antigen in both tests was represented by the bacteria *Brucella abortus*. CBR test result was indicated as antibody titer, i.e. increase or decrease in the titer of specific antibodies was observed in even-numbered serum samples. Rose Bengal test result was indicated as positive or negative.

*Picture 2. Results of the sera examined by the Rose Bengal agglutination test*

*Picture 1. Euthanasia and safe removal of animals, in accordance with the legislation in force*
3. Results

The presence of anti-Brucella antibodies was confirmed in 16 (37.2%) individuals, out of a total of 53 tested sera of 43 patients with clinically manifested suspicion of brucellosis, using the screening method, i.e. the Rose Bengal agglutination test, in the period from October 1st to 31st 2009. Significant increase in the titer of anti-Brucella antibodies in even-numbered serum samples was confirmed in 10 (23.2%) individuals, out of 43 tested patients, using the CBR method. If the significant finding of antibodies obtained by the CBR method is compared to the overall number of positive anti-Brucella antibodies in the patients examined, it is evident that the result did not match in 6 (37.5%) individuals, i.e. significant difference (p=0.001) is evident (Chart 1).

There were 12 (75.0%) male and 4 (25.0%) positive female patients, out of 16 seropositive patients, using one of the two applied methods, in the period from October 1st to 31st 2009. There were 7 (70.0%) male and 3 (30%) female individuals, out of 10 individuals with significant finding of anti-Brucella antibodies, obtained using the CBR method (Table 1).

Concerning the age of individuals, it was determined that there had been 3 (18.75%) positive individuals in the group aged up to 30, and 13 (81.25%) individuals in the group aged older than 30, out of 16 individuals with positive finding of anti-Brucella antibodies, obtained by both methods. There were 4 (40.0%) individuals in the group aged up to 30, and 6 (60.0%) in the group older than 30, out of 10 (100.0%) patients with significant finding of anti-Brucella antibodies, obtained by the CBR method. Level of the antibody titer obtained by CBR varied from 1:8 to 1:312 and more.

4. Discussion

It is well-known that the occurrence of human brucellosis is related to the presence of its causal agent in certain natural hosts, from which it is

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<th>Method</th>
<th>Examined individuals</th>
<th>Positive, with % of the presence</th>
<th>Positive males, with % of the presence</th>
<th>Positive females, with % of the presence</th>
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<td>Rose Bengal</td>
<td>43</td>
<td>16 (37.2)</td>
<td>12 (75.0%)</td>
<td>4 (25.0)</td>
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<td>CBR</td>
<td>43</td>
<td>10 (23.2)</td>
<td>7 (70.0%)</td>
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transmitted to humans as well, via certain routes. Since brucellosis is a zoonosis that is significantly present in the Mediterranean Basin, in the surrounding and developing countries, it is important, from epidemiological aspect, to reveal its reservoirs on time, to eradicate focal points, to confirm suspicion of the disease in laboratory, and to initiate the accurate treatment of infected individuals (11, 12). Brucellosis occurred sporadically in the area of BiH in the pre-war period (until 1992). It was registered for the first time in 1952. It occurred in individual cases in the following period. The number of infected animals, as well as humans, has progressively increased in the post-war period (since 1995). In the post-war period, the disease has been registered in certain regions of BiH; in 2009, its distribution was registered in the entire area of BiH (1, 3, 5, 13, 14). According to reports of the cantonal public-health institutes in the Federation of BiH, only four cases of brucellosis were registered during the year of 2001. The number of infected individuals was constantly increasing during the subsequent years. In the period from 2006 to September 2009, the number of infected individuals in the area of the Federation of BiH was 1741. The same trend of increase in the number of infected animals was registered in the Federation of BiH (1, 3, 5, 14). The studies in the surrounding of BiH suggest that 1543 human blood samples were serologically examined in the period 1990 – 2007 at the Croatian Veterinary Institute in Zagreb, Croatia, as well as 452212 blood samples of cattle, 91948 blood samples of goats, 218949 blood samples of sheep, and 483036 blood samples of pigs from the area of the Republic of Croatia. In the sera of examined persons, specific antibodies were confirmed in 73 individuals, in cattle in seven cases, in goats in 478 cases, in sheep in 687 cases, and in pigs in 2040 cases (12).

In the period 2000 – 2005, 245 persons infected with brucellosis were registered in Bosnia and Herzegovina. In the period from 2000 to mid-2006, 152 infected persons were registered in the area of Zenica-Doboj Canton, with the morbidity rate of 37.2‰. Brucellosis was also registered in 1.57% of examined animals in the cantons of the Federation of Bosnia and Herzegovina (1, 14). These indications suggest that animals with the infection and disease are present in all areas of Bosnia and Herzegovina, disseminating the causal agent of the disease in their nearby environment, which is transmitted to humans via the contact route, aerosol, i.e. via animal excretions, meat, milk, and dairy products. By presenting the results of examination of serum samples of 43 individuals, we wanted to highlight the significance of this disease in wider context. We also wanted to highlight the importance of serological methods applied in laboratory confirmation of the suspicion of this disease, i.e. significance of findings of specific antibodies in serum samples, or observation of dynamics of specific antibody titer in even-numbered serum samples, as a relevant laboratory finding.

In our examination of the age and gender structure of individuals, it is evident that the infections were more frequently registered in males, which matches the finding obtained in the study during the period 2000 – 2006, from a close or the same geographic area, where there were 62.50% of infected males. Although brucellosis is present in all age groups, due to general susceptibility of the population to this infectious agent, our study confirmed that it was present in persons older than 30, which matches the finding of other researches in the mentioned period and in the same geographic area (4, 14).

5. Conclusions

Brucellosis occurs in Bosnia and Herzegovina in sporadic and epidemic forms; during the past several years, it has acquired endemic nature of occurrence in certain regions of BiH and become a significant public-health problem. Occurrence of the infection in humans is narrowly related to the occurrence of infection in domestic animals, cows, goats and sheep.

Positive result was obtained in 16 or 37.2% of a total of 43 tested individuals, using the adequate serological methods, and significant finding of specific antibody titer was obtained in 10 or 23.2% of individuals, using the CBR method.

Concerning the age and gender of infected individuals, our study confirmed that this disease was present both in males and persons older than 30.

In order to prevent the occurrence of brucellosis or to put it under medical control, close coope-
ration between veterinarian and human medicine is necessary, i.e. it is responsibility of veterinary institutions to introduce comprehensive measures, which will be implemented in certain areas, in cooperation with human medical institutions.

6. References


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Abstract

The introduction of ICT in medical education as well as additional qualification and training in medicine, contributing directly to improvement in the efficiency of this segment of the educational system, especially through reducing the cost, especially of visiting professors travel costs (video-conferencing).

This article describes the application of modern information and communication technologies and the introduction of combined methods of teaching at the Medical Faculty in Sarajevo.

This research aims to identify the information infrastructure and the possibility of introduction and application of modern ICT and education combined approach of medical education at the Medical Faculty in Sarajevo.

This research aims to identify the information infrastructure and the possibility of introduction and application of modern ICT and education combined approach of medical education at the Medical Faculty in Sarajevo.

For the purposes of the application of blended methods of education is planned to develop electronic educational content, based on multimedia. This content can be developed and delivered through the platform for the development and content delivery, and monitoring activities of students, e-learning, e-net. For the purpose of electronic communication with students used will be forums, chat and e-mail on the same system.

Previous activities in this field are quite modest and done partially within the eContent program of WUS Austria program.

Focus of this research and the methods used in research at the Medical Faculty of the University in Sarajevo, as the central institution for medical education. Identification and testing of educational content is determined in advance, which requires this type of research.

Applied is the methodology of system approach and system analysis and the analysis as a method for identifying opportunities and threats from the environment, or to analyze strengths and weaknesses.

In cooperation with Indiana University - USA and professor Dey Sukhen MD. PhD prepared is the frame (application) for online learning in the Moodle (LMS), aimed primarily to post graduate students and other target groups of students and health professionals

Key words: education, combined education, medicine, information technology
Sažetak

Uvođenje ICT u medicinsku edukaciju i dodatnu kvalifikaciju i trening u medicini, doprinosi direktno poboljšanju efikasnosti ovog segmenta obrazovnog sistema kroz smanjenje troškova načitito gostujućih profesora troškova putovanja (vidokonferencija).

U radu je prikazana primjena modernih informacijsko-komunikacijskih tehnologija i uvođenje kombinovane metode učenja na Medicinskom fakultetu u Sarajevu.

Ovo istraživanje ima za cilj identifikaciju informacione infrastrukture i mogućnosti uvođenja i primjena modernih ICT i kombinovanih obrazovnih pristupa medicinske edukacije na Medicinskom fakultetu u Sarajevu.

Za potrebe primjene blended metode obrazovanja na planirano je razviti elektronske obrazovne sadržaje, bazirane na multimedijski. Navedeni sadržaji se mogu razviti i isporučivati na platformi za razvoj i isporuku sadržaja, te praćenje aktivnosti studenata, e-Learning.unsa, ili e-learning e-net.

U cilju elektronskog komuniciranja sa studentima koriste se mogućnosti foruma, chat-a i e-maila na istom sistemu.

Dosadašnje aktivnosti na ovom području su dosta skromne i odvijane su samo u okviru eContent WUS Austria programa.

Fokus ovih istraživanja kao i metode korištene u istraživanju je na Medicinskom fakultetu Univerziteta u Sarajevu, kao centralnoj instituciji medicinskog obrazovanja.

Identifikacija ispitivanih i obrazovnih sadržaja unaprijed je određena, što i zahtjeva ovaj tip istraživanja.

Primijenjena je metodologija sistemskog pristupa i sistemske analize i analiza kao metoda za identifikaciju šansi i prijetnji iz okruženja, odnosno za analizu snage i slabosti.

U suradnji sa Indiana univerzitetom – USA i prof. Dr Sukhen Dey –om pripremljen je i okvir (aplikacija) za online learning u Moodle-u (LMS), naimjenjen prije svega, postdiplomcima i drugim ciljnim grupama studenata i zdravstvenih profesionalaca.

Ključne riječi: obrazovanje, kombinovano obrazovanje, medicina, informaciona, tehnologije

Introduction

The introduction of ICT in medical education and additional qualifications and training in medicine, contributing directly to improving the efficiency of this segment of the educational system, especially through reducing the cost especially of visiting professors travel costs (videoconferencing).

Educational institutions that respond to these opportunities will stand out from other in the coming years by improving the quality of their educational program, which are enabled by the innovative integration of various information and communication technologies.

Time of development of global information and telecommunications technologies, with simultaneous development of web based educational material imposes a change in the philosophy of educational content delivery.

Not long ago, the teachers use only chalk and the board as a tool for delivering educational content. Implementation of projector and content in the form of prepared slides introduced novelty in this kind of education process. Today, more and more teachers use a computer and projector for the presentation of educational materials.

The first modern alternative to the delivery of educational material was computer-based system of learning (CBT - Computer Based Training) which used author systems, multimedia and CD. Web brings radical change and rapid transition from development technology like HTML (Hyper-text Markup Language) and scripting languages (Java, ActiveX, XML) on server systems that use databases (1). Due to the rapid development of electronic remote-supported education in the USA and Europe there was a need to develop web based tools for education in order to generate interactive educational content on the web.

At the same time, increased is the frequency of personal communication based on the use of computer technology, such as email, chat, forums and videoconferencing (2) The use of real time video content (streaming video) gets more and more importance in the delivery of courses on demand (3). Previous activities in this field are quite modest and done partially within the eContent program of WUS Austria program.
The article describes the application of modern information and communication technologies and the introduction of combined methods of teaching at the Medical Faculty in Sarajevo.

The modern form of education offers a user-appropriate and adaptable education system. Unlike traditional education, here the student and teacher are generally physically separated. Educational materials are distributed through various media, in the classical and/or electronic form.

**Goals and research methods**

This research aims to identify the information infrastructure and the possibility of introducing and application of modern ICT with combined education approach to medical education at the Medical Faculty in Sarajevo.

For the purposes of the application of blended methods of education is planned to develop electronic educational content, based on multimedia. The above mentioned content can be developed and delivered through platform for the development and content delivery, and monitoring activities of students, e-Learning.unsa, or e-learning e-net.

For purpose of electronic communication with students should be used forums, chat and e-mail on the same system.

Focus of this research and the methods used in research are at the Medical Faculty in Sarajevo, as the central institution of medical education.

Identification of tested educational content is determined in advance, which require this type of research.

Applied is the methodology of system access, system analysis and analysis as a method for identifying opportunities and threats from the environment, or to analyze strengths and weaknesses.

**Previous activities**

Previous activities in this field are quite modest and done partially within the eContent program of WUS Austria program and University Tele-information Centre.

In October 2003, University of Sarajevo began with e-learning education, the project conducted by the University Tele-information Centre (UTIC) and four faculties from University of Sarajevo were involved: Electro-technical, Machine-engineering, Business and economy, and Medical faculty. On UTIC web site, seven students enrolled from Medical faculty.

Platform for the course of e-learning is achieved in collaboration with UTIC. University Tele-information Centre, established as part of University of Sarajevo and first ISP in Bosnia and Herzegovina in 1996 (www.utic.net.ba). It is scientific-organizational unit of the University of Sarajevo for improvement of scientific research work and through UTIC members of the University can be gathered in the unique computer-communication structure.

Objectives of UTIC are: to connect members of the University with similar institution in the country and abroad due to more efficient use of scientific, research and educational resources, use of educational databases and other information for the needs of the University and its members. Also, development of an integration of informatics computer technologies in education, creation of flexible infrastructure which will enable e-Learning to be accessible to all students and University staff, improvement of general digital literacy of academic population, development of top quality educational content which could be integrated in the actual European processes of e-Learning revolution. With their help center for e-learning, “LUCUS CENTRUM”, is created (Picture 1.).

We hope that this is just a beginning step towards improvements of the

**Application of ICT in medical education**

Project “Application of modern ICT and educational technology in medical education” which is endorsed by the Ministry of Education and Science of Sarajevo Canton provided the research activities for a period of 2 years on its implementation, so that during the 2008-2009 the following activities are performed:

- Made is the identification and assessment of ICT infrastructure;
- Made are the necessary preparations of framework for educational content;
- Identification of ICT infrastructure is made at the macro and micro level and was evaluated as satisfactory for this project needs.

Also conducted is the selection of web platform for presentation of educational content, which should satisfy all the criteria and standards of e-learning, as well as the planned project activities.

Framework for educational content is the basis for presentation and publication of the educational content by selected topics/subject.

In cooperation with Indiana University - USA and professor Dey Sukhen MD. PhD prepared is the frame (application) for online learning in the Moodle (LMS), aimed primarily to post graduate students and other target groups of students and health professionals.

The appearance of web applications is given in the following figure:

![Figure 1. Web applications for online medical courses](image)

Participants in the project besides the teachers and associates are the students of postgraduate courses at the Faculty of Medicine in Sarajevo, a total of 12 of them, who directly participate in education, and development of the course “Information Technology in Healthcare.”

Partner institutions in this project are the Maharaja Institute of Technology and Certification Institute PKCOE.

The Web application has the interface, or enables the communication from the student and the professor’s environment.

![Figure 2. Login to online medical courses](image)

After login, student or teacher enters the desired course area.

![Figure 3. The appearance of the home page from one medical course](image)

Each course is developed according to the needs and demands of students.

**Information Technology in Healthcare**

Healthcare is “Mission Critical”. Caregivers, managers, physicians and any healthcare personnel are responsible for day-in-day-out welfare of patients. The ultimate goals of healthcare professionals including nurses are to preserve patient’s welfare and “save lives”. Every aspect of healthcare from patient admission, treatment, billing to post discharge care depend on Information Technology and that qualifies informatics as one of the most important knowledge base in making ‘critical thinking’ oriented decisions. This five week course discusses the various aspects of IT including foundation, application, infrastructure and future trends of Information Technology within healthcare settings.
Conclusions

The rise of IT as an artefact of everyday life in the modern world has brought with it the dawn of a new era, often dubbed the “Age of Information”. These technologies are changing the way we perceive the world, how we think and communicate with another but especially in education human influence is irreplaceable.

References


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Alopecia areata: New treatment modalities

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Abstract

Alopecia areata (AA) is a relatively common reversible hair loss disorder usually manifesting as patchy areas of complete hair loss on the scalp and other body parts that can progress to complete loss of all body hair. This disorder affects all age groups, with a higher prevalence in children and adolescents. The etiology of AA is unknown but is characterized by hair cycle disfunction and the presence of peribulbar and perifollicular mononuclear cell infiltrates. Much evidence suggests that AA is tissue restricted autoimmune disease. Current traditional therapies are predominantly immunomodulating modalities, including corticosteroids, topical immunotherapy, anthralin, and photochemotherapy (PUVA). A nonspecific modality is topical minoxidil, which prolongs anagen and promotes growth of longer and wider hair. Improved future treatments may be immunosuppressive or immunomodulatory or they may otherwise protect hair follicles from the injurious effects of inflammation.

Key words: alopecia areata, immunosuppressive therapies

Introduction

Alopecia areata (AA) is a relatively common reversible hair loss disorder usually manifesting as patchy areas of complete hair loss on the scalp and other body parts that can progress to complete loss of all body hair (alopecia totalis, alopecia universalis). This disorder affects all age groups, with a higher prevalence in children and adolescents. The patients are usually otherwise healthy, but atopy, thyroid disease and vitiligo are more common than among the general population (1). The etiology and pathogenesis of AA is still uncertain, but many factors have been assumed concerning its pathogenesis, e.g. the patients genetic constitution, family history, the atopic state, non specific immune and organ-specific autoimmune reactions, possible emotional stress, infectious agents, and neurological factors (2, 3, 4). However, it is hypothesized that AA is an organ-specific autoimmune disease mediated by T lymphocytes directed to hair follicles. AA may be passively transferred by T cells and there is some evidence that serum IgG may also disturb hair cycling (5). Immunohistochemical studies have shown peri- and intrafollicular inflammatory infiltrate which damages hair follicles (6). Hair follicles are not destroyed in patients with AA, and the potential for regrowth always remains (1). The course of disease is not predictable and it is often associated with periods of hair loss and regrowth. The prognosis of AA is influenced by several factors, in particular by the type and extent of AA (7) with a worse prognosis for patients with AA totalis or universalis or with extensive patchy AA as compared to limited patchy AA.

Current treatments for alopecia areata

Because of their psychosocial stigmatization, the medical attendance and therapy of patients who suffer from distinct form of AA is difficult to challenge. Although spontaneous remission is possible, it occurs rarely. At present, all treatments are palliative, only controlling the problem, they certainly do not cure the condition.

Treatment of AA may be divided into four different categories of widely accepted therapeutic...
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modalities: immune inhibitors (steroids or psoralen and UVA light- PUVA therapy); topical sensitizers (squaric acid dibutylester and diphenylcyclopropenone); non specific irritans (anthralin) and the vasodilatator minoxidil. These treatments stimulate hair growth but do not prevent hair loss and probably do not influence the course of the disease (1). Mild forms of AA are mostly treated by intralicesional injection of a glucocorticoid, usually triamcinolone, every four to six weeks. Topical steroid application to areas of hair loss, usually applied twice daily, has also been found to be efficacious clinically, although combination treatment with minoxidil, anthralin or injected steroids is probably more therapeutic (1, 9). Systemic steroids are reserved for use in rapidly progressive or extensive AA. Topical sensitizers have proven efficacy in patients with long-standing AA involving more then 50 percent of the scalp (8). They have shown good tolerability and mild side effects. Photochemotherapy with psoralen and ultraviolet A light (PUVA) has also resulted in hair regrowth in some patients.

Current traditional therapies are predominantly immunomodulating modalities, these treatments have been used for many years, and new targeted therapies are particularly needed for children, for those with chronic, persistent patchy disease and for those with alopecia totalis and alopecia universalis.

New immunomodulatory therapies

Topical immunomodulators are a new class of agent that acts locally on T cells by suppressing cytokine transcription (10).They are now emerging as the therapy of choice for several immune-mediated dermatoses, because of their comparable efficacy, ease of application and greater safety than their systemic counterparts (11). The two most studied topical immunomodulators are tacrolimus and pimecrolimus. A third new member of this group is topical cyclosporine A (CsA). All three drugs inhibit calcineurin, thereby inhibiting interleukin-2 production (12).

Topical tacrolimus

It is macrolide, produced by Streptomyces tsukabaensis, a fungus found in the soil of Mount Tsukuba, the science city of Japan, where initial isolation and characterization of this drug was performed. The name of the drug is a neologism, composed of tsukuba, macrolide and immunosuppression.

Tacrolimus is an immunosuppressive agent that can be applied topically to the skin. It acts directly on T cells to inhibit interleukin-2 transcription, which results in decreased growth and proliferation of T lymphocytes in response to foreign antigens (13). It also inhibits other cytokines, including TNF-α and IFN-γ, both important in T cell activation. Moreover, topical application of tacrolimus also has a hair growth stimulatory effect, independent of its T cell suppressive effect (14). Tacrolimus ointment does not cause skin atrophy, pigment changes, or telangiectasia. It is only minimally absorbed, with 0,5 % of the locally applied drug detected in blood (11). Therefore, tacrolimus is promising candidate for the treatment of alopecia areata.

Topical pimecrolimus

Pimecrolimus is a semi-synthetic product of ascomycin, which is a fermentation product of Streptomyces hygroscopicus var. ascomycetces. Similar to tacrolimus, it is a cell-selective cytokine inhibitor developed for the treatment of inflammatory skin diseases. It binds to macrophilin-12, inhibits calcineurin, inhibits synthesis of inflammatory cytokines, such as IL-2 and IFN-γ, and inhibits T cell and mast cell activation (12). Pimecrolimus has high skin-specific-inflammatory activity with low potential for affecting the systemic immune response. The cream 1% formulation is safe and effective and does not cause skin atrophy or telangiectasia. Adverse effect includes mild burning sensation. Unfortunately, the cream is not expected to be effective for hair regrowth because it permeates no lower than the superficial dermis, which is an insufficient depth for targeting T cells involved in AA (12).
Topical cyclosporine A

Cyclosporine A (CsA), isolated from the fungus *Tolypocladium inflatum* gams, is a lipophilic cyclic polypeptide and calcineurin inhibitor. CsA is a potent immunomodulatory agent whose mechanism involves inhibition of T-4 lymphocyte activation (15). Although systemic CsA appears to be effective in AA, the adverse effect profile, recurrence rate after treatment discontinuation and inability to produce long-term remission make CsA unattractive for the treatment of AA.

In the past, topical formulations of CsA were ineffective because of poor skin penetration. To surmount this problem, a heptamer of arginine was conjugated to CsA through a pH-sensitive linker designed to release CsA at physiologic pH within the skin (16). The oligoarginine transporters enable full-skin-thickness penetration of CsA into cells throughout the epidermis and dermis of human skin, with functional inhibition of cutaneous inflammation (17).

New biologic therapies

Biologic agents are proteins that possess pharmacologic activity and can be extracted from tissue. With the development of recombinant DNA technology, biologic agents can be synthesized in large quantities and designed to alter specific physiologic responses (18). Biologic therapies target cell surface receptors, and their theoretical advantage is that their greater specificity will provide better safety profiles (12). Biologics are larger than ‘small-molecule’ drugs and are most often administered by injection. They include etanercept, infliximab, efalizumab and alefacept.

Liposomes

Another novel approach in treating AA is to create a vehicle that allows penetration to the subcutaneous fat where the bulbs of anagen hair follicles are located and where the pathomechanism takes place (19). Liposomal drug delivery may increase penetration of skin and allow slow release of active compound locally with diminished toxicity. At present, liposomes seem to be the best candidate as a vehicle topical treatment. Topically applied liposomes have been shown to deliver melanin, proteins, genes and various small molecules selectively to hair follicles and hair shafts of mice in vivo (20). Liposome-targeting of molecules to human hair follicles has been demonstrated in human scalp in histoculture (21). However, future experiments have to show whether liposomes are able to deliver molecules to the hair bulb in human scalp in vivo.

Miscellaneous agents

Inhibition of the Fas-FasL system

Induction of hair follicle apoptosis by the Fas-FasL system seems to be involved in the pathogenesis of AA (6). Therefore, inhibition of the Fas-FasL system might protect hair follicles from injury caused by the inflammatory infiltrate. However, such treatment could only be applied topically and specifically limited to hair follicles, because systemic inhibition would disturb essential control mechanisms of lymphocyte homeostasis (19).

Imiquimod

Imiquimod is the first member of a new class of immune response modifiers, it was first improved 1997 for the topical treatment of genital warts. It is a synthetic molecule, which enhances both innate and acquired immune response, in particular, cell mediated pathways, by stimulating monocytes and macrophages via binding to cell surface receptors to produce several specific cytokines including IFN-α, IL-1, 6, 8, 10, 12 and tumor necrosis factor (11, 22), resulting in local immunoregulatory activity. Imiquimod also stimulates natural killer and B cells and enhances migration of Langerhans cells. In the future, imiquimod and newer generation of imidazoquinolines (resiquimod) require further investigation for potential clinical utility in treating AA.
Conclusion

AA has an unpredictable course that is not easily altered by treatment. Different treatments will provoke regrowth of terminal hair to a variable extent but may not prevent further hair loss. At present, corticosteroids are the most popular form of treatment and can be given topically, intralesionally, or, in rare cases systemically. Minoxidil has had limited success in stimulating hair regrowth without altering the course of AA. Topical immunotherapy with diphenylcicropenone or PUVA therapy may be effective in long-standing and widespread disease. These treatments stimulate hair growth but do not prevent hair loss and probably do not influence the course of the disease (1).

As long as no causal treatment is available, future approaches should focus on a more specific targeting of the underlying pathomechanism with a topical action around the hair bulbs and without serious side-effects (19). New immunomodulators and biologic therapies target specific immunologic responses and offer new strategies for treating pathogenic T cells and the cytokines they produce (12). In the future, AA should receive first-line consideration for clinical studies with new specific therapies for T-cell-mediated inflammatory diseases.

References


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Abstract

The aim of our study was to examine sustained attention in Bosnian War Veterans diagnosed with PTSD.

The study was based on the testing of 79 Bosnian Army war veterans, who participated in the B&H war from 1992 to 1995. Of 79 subjects, 45 developed PTSD, while 34 remained PTSD free. The latter group constitutes the control. The subjects' age ranged from 30 to 50. Also, the groups were harmonized with respect to the education level (elementary and secondary education). The subjects were tested with Sustained Attention to Response Task – SART. The task includes frequent button pushing for untargeted stimuli or withholding from pushing as a response to the targeted stimulus. The duration of this computer based test is 4.3 minutes. During that time, 225 figures (1-9) randomly appear in the center of the screen. The results include three measures: the number of false positive responses, the number of false negative responses and average response time for all responses.

In the Sustained Attention to Response Task (SART) test, subjects with PTSD made more errors of both types (both false positive and negative responses). Statistically significant difference between PTSD and the control group was not found only in the case of average response time to task.

PTSD patients made more errors that were related to the difficulties with the maintenance of vigilance over time. PTSD patients reacted faster which may be related to the anxiety symptoms that accompany PTSD. Excessive anxiety may be responsible for faster reaction as a response to these tasks, but for an increased error rate as well.

Key words: posttraumatic stress disorder, trauma, war veterans, sustained attention, SART

Sažetak

Cilj: ovoga istraživanja je ispitati odgođenu pažnju kod boraca Armije BIH sa diagnozom PTSP-a.

Rezultati: Na testu održavane pažnje pri odgovoru na zadatak (SART), ispitanici sa PTSP–om pravili su više pogreški i jedneg i drugog tipa (pozitivne i negativne greške). Statistički signifikantna razlika između PTSP grupe i kontrolne grupe jedino ne postoji kod mjerenja vremena reakcije na SART testu.


Ključne riječi: posttraumatski stresni sindrom, trauma, ratni veterani, odgođena pažnja, SART

Introduction

The last two decades have witnessed worldwide growth of interest in the study of stress as a result of stressful events of the past century. The abundance of stress dedicated publications has increased, while stress became ever-present subject in everyday life, press and television. Thus the general opinion that we share particularly stressful era and that the consequences of stress for mental and somatic plane may be numerous and difficult to anticipate. War in a certain area fundamentally affects the course of life for large part of population and causes series of stressful events. We can establish with certainty that no person escapes the stress caused by war induced pressure, which requires new models of adjustment. The past war in our country provided us with an unfortunate opportunity to acquire better understanding of stress-related events and stress-induced psychotic disorders. Posttraumatic stress disorder (PTSD) certainly belongs into this group of disorders.

In consideration of the above, our study was constructed around patients – soldiers who were exposed to the atrocities of war and who sustained changes in the behaviour modalities along with psychotic disorders. Therefore, this study should represent a contribution to the research into association between PTSD and cognitive dysfunction.

The aim of our study was to examine damaged attention processes in patients with PTSD, which may underlie memory disorder as a cognitive dysfunction in these patients.

Material and Methods

We have tested 79 B&H Army soldiers, who participated in the past B&H war between 1992 and 1995. Of the 79, 45 developed posttraumatic stress disorder (PTSD), while 34 remained PTSD-free and those constitute the control group. From the range of neuropsychological tests, we selected Sustained Attention to Response Task (SART) (1). It is a task of continuous performance. The attention sustenance deficit was assessed by SART (1). The task includes frequent button pushing for untargeted stimuli or withholding from pushing as a response to the targeted stimulus (1). The duration of this computer based test is 4.3 minutes. During that time, 225 figures (number from 1 to 9) randomly appear in the center of the screen (each figure appears 25 times). The appearing figures differ in size (12 to 29 mm in height, font sizes: 48, 72, 91, 100 and 120). Each figure remains on screen for 250 ms. It is followed by a 900 ms mask in the form of an “X” positioned in the center of the screen. The subjects’ task consists of pushing the response-box button each time a figure appears except in 25 cases when the screen displays figure 3 and the pushing response needs to be withheld.

The results include three measures: the number of false positive responses (pushing response to figure 3 – maximum number of errors is 25), the number of false negative responses (pushing response withheld to figures other than 3 – maximum number of errors is 200) and average response time for all responses. Prior to the formal test, the subjects had an opportunity to try and practice the response (with 16 untargeted figures and 2 figures 3). There is an association between the SART results and distraction and absentmindedness experienced on daily bases (2).

For the selection of PTSD patients, we relied on DSM IV classification system. PTSD evaluation was performed based on Mississippi scale (3). All the patients included into the study scored above 110 on the Mississippi scale. Thus, one of
the inclusion criteria was the duration of symptoms. For our group, we considered only chronic PTSD. Also, the subjects with head injury or surgical intervention during traumatic experience were excluded from the study. History of neurological disorders, psychotic disorders, and drug or alcohol addiction were also criteria for exclusion. The age of subjects ranged between 30 and 50 years. The groups were harmonized according to the age, education level and gender. Hence, it was a homogenous group of male subjects.

Testing Protocol and Informed Consent Forms were prepared specifically for this study. The study results were of confidential nature. Subjects’ identity can never be revealed. The applied method is neither aggressive nor detrimental to the subjects. Ethical component of this study was rather high.

### Results

The difference between the PTSD group and the control is statistically highly significant. Value of t – test is: \( t = 5,942; \) with significance threshold at \( p < 0,001. \)

The difference between the PTSD group and the control has high statistical significance. Value of t – test is: \( t = 4,485; \) with significance threshold at \( p < 0,001. \)

The difference in values between PTSD group and the control is not statistically significant. Value of t – test is \( t = 0,429. \)

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<thead>
<tr>
<th>Table 1. Sustained attention to response task – SART/false negatives</th>
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<td>1 - 9</td>
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Discussion

Our study was aimed at examination of cognitive function in individuals with diagnosed PTSD. The results of earlier studies and theoretical background clearly indicate the existence of deficit in cognitive functions such as memory, attention, initiation and inhibition.

Sonia et al. (4) report activation within or in the proximity of hippocampal region during the encoding phase of memorizing process. Memory encoding is the process that may be divided into two different sub-processes, which may also be related to the hippocampal activation. One of the first roles (functions) attributed to hippocampus is the encoding process. Actually, PET and fMRI studies demonstrate that hippocampus and neighboring (bordering) cortex participate in the encoding of facial information but not in their retrieval. Hippocampal region also encodes (records) meaningful response (5) with respect to the meaningless one. Other studies report activation of hippocampal region during recording – encoding of visual objects (6,7), visual images and in depth word processing (8). Certain fMRI memory studies suggest hippocampal region role during novel encoding (recording). Tulving et al. (9) demonstrated intense hippocampal activity during recognition task where subjects had to decide whether the displayed object was “new” (never displayed before) or “old” (displayed earlier). This potential involvement of hippocampus in the detection of “new” is a powerful inducer of stress reaction in people as well as animals (10). Golier et al. (11) explain the influence of trauma-dependent information on the memory in holocaust survivors.

PTSD group has significantly lower memory association compared to the PTSD-free group and unexposed group. This trauma-related connection with the explicit memory, joint with generally weaker explicit memory, may be explained by bi-directional nature of memory failure in PTSD.

Vermetten et al. (12) emphasize that animal studies demonstrate that stress associated with hippocampus injury inhibits neurogenesis and creates deficit and dysfunction in hippocampus-based memory. Studies on PTSD patients revealed deficit in hippocampus-based declarative verbal memory and reduced hippocampus volumes measured by MRI. Liberzon et al. (13) report different blood supply in amygdale, insula and medial prefrontal cortex in PTSD patients during emotional reactions. Preliminary results suggest that these neural substrates may be involved in the deficit of emotional process in PTSD on one side and trauma release on the other side. Zoellner et al. (14) indicate that recent research into posttraumatic sequelae suggests that intrusive rather than avoiding-dissociative models precisely represent encoding processes in the traumatized. Shin et al. (15) point out irregular regional cerebral blood supply in hippocampus during explicit remembrance of non-emotional material in individuals with PTSD.

Woike et al. (16) examine how personal motives influence the perception of traumatic event in the memory, and how such a perception may

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<th>RESPONSE TIME</th>
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Mean - $\bar{X}$  
PTSD GROUP: $\bar{X} = 451,07$ msec 
CONTROL GROUP: $\bar{X} = 464,51$ msec

Standard deviation - SD  
PTSD GROUP: SD = 143,37 
CONTROL GROUP: SD = 131,15
relate to psychological unrest. In both studies, general motives influence the shaping of perception and integrate stress-induced growth. The findings indicate that motives play significant role in the perception of traumatic and difficult experience, and that the perception may be related to psychological influences in different manner. Yovell et al. (17) suggest that survivors of trauma share short and irreversible blanks, while longer, progressive and potentially reversible amnesia is characteristic for survivors who develop PTSD. Failure in acquiring episode memory may coincide with stress-dependent reduction in the function of hippocampal memory system. Nixon et al. (18) underline that earlier exposure to intense stress (i.e. child abuse, abduction) significantly correlates with poor performance in memory tasks. Regressive analysis, dedicated to the assessment of IQ and psychopathological edge demonstrate the importance of earlier trauma exposure and anticipate poor performance in memory tasks, thus suggesting that in current sample, deficit in verbal memory may be related (partly) to the level of stressful experiences accumulated (deposited) over lifetime. Danckwerts et al. (19) suggest that PTSD may be related to the deterioration in cognitive function. However, anomalies may appear and develop from various levels, thus masking the true nature of the relationship. At one level, there is vagueness (fogginess) of emotional and physical case of cognitive dysfunction, in particular with memory tasks, which is similar to those in neurological diseases. At another level, the problem apparently develops directly from both specific and general population. Then, there is an issue of application of narrowly focused neuropsychological instruments which cannot make distinction among summarized components of memory that are not related to everyday situation. Yehuda et al. (20) estimated the most profoundly affected memory component. The most profound deterioration in PTSD was observed in verbal learning, which may be either a risk factor or a consequence of chronic PTSD. Nutt et al. (21) underline that PTSD represents highly weakened condition which is associated with intrusive remembrance of traumatic event, hyper-stimulated, characterized by the avoidance of trauma associated issues and psychological dullness. Authors emphasize that PTSD symptoms include exaggerated initial response to flashbacks which may be dependant on the weakening of higher neural regions (hippocampus, central frontal cortex). Silenced exaggerated excitation and anxiety symptoms mediate the response to memory of traumatic event through amygdale. Candel et al. (22) indicate that psychiatric references consider dissociative reactions at the moment of traumatic event (i.e. peri-traumatic dissociations) a risk factor for PTSD development. Also, it is established that the description of earlier emotional stress is hard to define. Restrictive factors play a role in the context of forgetting, functions and simulation.

Based on the analysis of our results related to cognitive functions in the group of PTSD subjects and the control group we may establish the following:

PTSD patients made more errors of both types (false positive and negative) at Sustained attention at response task (SART) test (Table 1 and 2).

Statistically significant difference between PTSD group and the control group was not found only in the case of average response time in SART test (Table 3). Subjects with PTSD have shorter response time. This result may be associated with the excitation symptoms in PTSD subjects. Exaggerated excitation may cause these individuals to react faster but also to make more errors in such tasks.

Considering the information on cognitive functions obtained in neuropsychological tests and analyzing the results obtained in this study, we may establish that the deficits in our PTSD subjects are highly significant when compared with the control group. Such outcome may be explained by the type of trauma experienced by our participants. The issue is prolonged, constant stress induced by four-year long bestial war devastation. Also, along with fighting for their own life, our subjects protected bare lives of their loved ones.
Conclusions

In comparison with the control group, subjects with diagnosed PTSD achieve significantly poorer results in the tests that evaluate focused attention, sustained attention and cognitive flexibility. Significantly poorer achievement in SART test in PTSD subjects is related to the difficulties in the maintenance of vigilance over time. Reduced response time in SART test is associated with the increased intensity of PTSD symptoms.

Acknowledgments

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List of Abbreviations

PTSD - Posttraumatic stress disorder
SART - Sustained Attention to Response Task
fMRI - Functional Magnet resonance Image
PET - Positron emission tomography

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Re-affirmation of traditional values of space for the sake of healthier manner of life – analysis of traditional and modern materials, their influence to the human health and giving directions for future actions in the materialization of contemporary facilities

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Abstract

Background and goal: Neglecting of traditional values in the architectural heritage, has brought not only to the loss of the consciousness on the identity but also to the loss of the quality in using housing space. Negative aspects of globalization, especially at “small peoples” who haven’t affirmed themselves yet, out of unknown reason, brought into question their traditional specific characteristics under which we certainly place the traditional architecture. Development of urban structure of all traditional city compounds led towards the changes produced by different way of life including the utilization of space. Conditional-consequential relation of the living culture, as the expression of modern life trends and the formation of space which is the result of new technological knowledge, contemporary modeled ideas and innovation approaches, resulted with general change of urbanism of all levels of settlements but also with the change of loving space and general change of ambience. The goal of this work is to point out the values of traditional materials and forms, recognized as the Bosnia and Herzegovina traditional values, and by comparing it with modern materials and forms being classified into universal one, to point out the advantages of these traditional values in relation to the health of their users.

Methodology: By using the DeAngelis D Os-sat method it is common to analyze the overall facility, in detail and in relation to the ambience, but for this analysis the most important is to express the attitude on:
1. Cultural and historic aspects;
2. Artistic-esthetic aspect;
3. Constructive aspect and materials.

In this way, characteristics of traditional facilities, traditional ambience and traditional materials that were used for their construction will be defined. By comparing it to modern facilities, modern ambience and modern materials, the advantage and disadvantages of the both will be defined.
**Target Group:** On one side, those are traditional facilities out of which we chose the urban housing heritage of the Ottoman period in Sarajevo and rural heritage of the mountainous regions of the Sarajevo surrounding, and on the other side, it is modern housing construction from the year 1975 by today, whose characteristic are the block constructions from the prefabricated elements with cheap construction materials intended for the collective residence.

**Results:** The results of the research showed that from the urbane spaces almost disappeared the group of facilities that we call vernacular architecture which was the reflection of traditional values of the local national constructors, that we consider as the bearer of the elementary message of the identity of the space and of historic stratify. This architecture almost disappeared from rural ambiances thus only rear remains witness about their existence. The aspect of mental and physical health was analyzed through possible advantages and disadvantages which characterize the use of modern spaces, so as the advantages and disadvantages while using traditional facilities. The form of the space, materials the facility was constructed from and the ambience which was created by mutual relation of the facilities were taken into consideration. The concept of the contemporary use of traditional facilities is given through the overview of the characteristics of the rural and urban heritage and the values which additionally influence to one and another group of facilities were defined.

**Conclusion:** *The advantages of modern facilities are the designed and planned space, adjusted to modern needs – infrastructural network in the function of the facility, isolation characteristics of the facilities; and disadvantages are in the use of materials and construction elements harmful to health, alienation of the users, the form subject to the function and construction elements, non-identification with the residence place and lack of genius loci.*

*The advantages of traditional facilities are the standards adjusted to a man, the form providing the open communication with the surrounding, the use of healthy and ecologically acceptable materials, constructive elements subject to the form, function and form in harmonized relation, the feeling of the user to belong to the space, offering the sense of the identity to the users, mutual communication of the users and… Disadvantages are in insufficient infrastructural network, difficulties at maintenance of the facilities, isolation characteristics of the facilities, obsolete of mounted materials and insufficient capacity of traditional ambiences.*

By subliming the both, only at look confronted poles, we come to the conclusion that the defining of traditional values, their affirmation through modern life trends and determination of solid frameworks of actions in forming and conception of facilities, may contribute that modern construction with the reminiscence to traditional values would be a form of the expressing all modern needs through modeling and materialization directed towards mental and physical health of the user.

**Key words:** Traditional materials and forms, traditional values, restoration of traditional facilities. Healthy materials, ecology, vernacular architecture, physical and mental health.

**Introduction**

Relation towards heritage reflects also the relation towards own identity but also the level consciousness on the characteristics of traditional values and level of civilization. Actual situation in architecture opens confuse and non-articulated situation in society, thus it is not unusual that people for very long time have stopped to take care of healthy way of life and universal values of residing in architectural facilities. Construction is in greatest extent directly towards the economic aspect of sustainable development while very often social and ecological aspects are only formally present. Contemporary architecture, especially one of the residing character, is modeled in way that the form follow the function, so according to all known theoretic postulates, architecture does not exist at all. It is not our goal for this research to have the character of the critic of contemporary residing architecture, but to point out its disadvantages and to give propositions for its improvement. The aspect of traditional construction is unfortunately confronted to contemporary construction, mostly from the fact that once more care was directed to the final ser of the space, that is to a man. Actual situation is such that architectural approach to the
housing space is reduced to simple satisfaction of basic human needs which I certainly caused by numerous socio-economic factors which are not subject to this research. These same factors influence not only the modeling but the choice of materials, so it is not rare that the house becomes the source of mental and physical diseases for their tenants. Reasons for these problems are numerous and may be caused by wrong disposition, use of unhealthy or even toxic materials, bad bio-climate conditions and not adequate position of the facility on the ground. Contrary to the actual construction, traditional facilities were carefully located on the ground with special care to isolation “rose of winds”, the position of facility in relation to neighboring facilities, selection of materials and their combination and mutual interaction, disposition of anterior and people loved the space they lived in, used very often gardens or yards and communicated with nature, traditional city blocks of the Ottoman period “Mahala” same as actual new city blocks were exclusively zones of residence but the people there did not feel alienated. The reason is in the fact that once the public place in those zones was reduced only to the street or small narrow street, and private space, separated by high wall, was divided to opened and closed, but those private units mutually communicated by some internal communicational ways. Enclosed porches on the upper floors of the houses were surpassed over the street and on three sides opened with windows, thus the visual communication was established with outer “world” which existed outside this private oasis. All this was dimensioned according to human standards so that all views to those facilities, but also those internal towards outside, were subject to the feeling of closeness to the space. The use of material was reduced of stone, unbaked brick and wood. Construction form coming out from the characteristics of materials from one side and technological knowledge from the other side resulted in a solution which produced specific traditional form.

Second example talking about harmonized interaction of architectural form, its materialization and surrounding ambience, is the rural traditional architecture. Its bio-climate characteristics is expressed much stronger than at urban architecture, but here also, it is possible to talk about the modeling of space that is subordinated to its final user and the use of the material which is ecological, but also in construction sense, a clear answer of a local builder to all stimulus of natural environment. The observer has a feeling that all facilities are surfacing from the landscape joining with it. Dominant accent is a monolith four leaned roof, covered with shingle, which we consider as the bearer of the traditional picture of the space but also the characteristic location of the facilities on the inclined terrain with the stone supportive wall on the front house representing the storage dig into the terrain. The only floor is in the proportion 1:2,5 to 1:3 in relation to the roof and is constructed from stones or woods depending on the disposed materials in the environment. These characteristics of the traditional rural construction stand opposite to the contemporary rural construction which has no characteristics, it is no more formed by bio-climatic and geo-morphological conditions of the region but is confronting to them by technological and technical achievements, providing to their users bigger comfort, which price is, in this case, extremely high. It is paid in healthy life in new projected space, under the loosing of identity and the spirits of the space atmosphere they live in.

Elaboration

Cultural-historic aspect

For this research which I referred to the man’s health, cultural-historical aspect of the space he lives in has a strong spiritual value. The feeling of alienation or the feeling of belonging, are the characteristic emotions of the users towards the space they live in. Globalization is, with strong and aggressive urbanization, affected the accelerated development and uncontrolled construction. Consequences of these influences are seen at constructed spaces but also from the relation of the users towards that space. City blocks without identity, which remind one to another, and which remind to any other in any other city in the world, are the picture of today’s architectural urbane reality. Reasons for these relations towards the space are found in insensible society but also the authors, architects, for traditional values. Their inspirations
are widely accepted clichés, universalized on the level of the whole planet. Unification of values in the formed sense, is a result of the unification within mental scope, and transitional countries, we belong to, are mostly fond to these influences. Lack of self-awareness and non articulated globalization, jeopardize the harmony of the relation between a man and his surrounding space. Existential space, has outgrown the constructed architectural space, which has jeopardized his own existence, and the question of modern construction brought to an absurd. This aspect, is far more important when we speak about the protection of the construction heritage, where the research and documentation is the starting point for the final conservation and restoration practice. When talking about the utilization of this traditional space, we will only say that it is created as a result of the traditional living culture ad such, even though old, is still more humane and better solution, for its many characteristics than it is today’s concept of living.

**Artistic-esthetic aspect**

According to Kant, esthetic is a science which treats the conditions of the emotional perception. May we the thing considered as non-esthetic pronounce unemotional, or is non-esthetic suppression of emotions. Just such definition is corresponding to the spirit of the users of contemporary living space in new city blocks. Here it is important to mention that all of our analytic critics towards contemporary housing construction is directed to non care of its final users, so the conclusion is that it is about self purpose, and that it reduced the housing standards to the minimum. In neither case, it is not appropriate to talk about artistic character of the facility because in the first case it is related to the housing vernacular architecture, so, about the architecture without the architect, whose task is not to express itself with its exceptionality, but to, collecting previous knowledge and experience, present construction skills, as well as to improvise with empiric knowledge and produce a form which will provide satisfaction of the needs for shelter, and create the pleasant residence. This position that we have described, is related to rural heritage, and urban vernacular architecture will differ by the fact that its goal is to create a beautiful and pleasant home for its family. Contemporary architecture itself, which we have defined within target group, can also be treated as vernacular, neglecting the fact that it has its own authors and because it is a result of planned architectural project. It evaluated very much in its form, which can be seen on these facilities facades, with notable interventions of the users, and which has transformed uniformed facilities into colorful and non-attractive spaces with differently closed balconies, inadequate annexes, non unified windows openings, inadequate attics, and… All those subsequent interventions, significantly devastated original look of the facility, but these examples clearly witness to the contribution of our thesis that the tenants of these facilities are non sensible towards them in emotional sense an it is completely not important what external impression their house gives. They have introvert perception of that space and they are solely interested in their own micro space. It is clear that then we can talk about the alienation from the space in which people live and about lack of the interest for the wider space in which they reside.

Both those aspect certainly have strong influence to the level of human consciousness, which then provoke changes in behavior, depressive states, expressed aggressiveness…

**Materials and constructive aspect**

All traditional architecture of this region is based upon three elementary materials of natural origin:

Stone, woods and brick (which in the Ottoman architecture appeared in the form of blocks made of unbaked dirt, so called čerpić).

All these three basic materials belong to the group of ecologically acceptable materials even those considered as extremely recommendable for the extern and intern use, because they are not harmful to health. Construction forms are characteristic for the time of the construction, as well as in traditional architecture so as today, they are the reflection of the characteristic level of technical and technological knowledge.
Talking about healthy and unhealthy materials, or more precisely about constructive forms which make living space, we will see that it is about physical and psychological causes which produce disturbances or have negative effect to the space users. Physical causes may be divided into small particles of the smallest structures and into radiation produced by the materials. These causes result in negative effects of the construction materials. Psychological causes are provoked by structuring of inner and outer space and mutual relation of the facilities in the space, surroundings and spirit of the space (genius loci).

Physical causes are divided into live and non live, where the live ones are divided into: microbes, eggs, cocoons and…, and non live to: atoms, molecules or basic forms of some substances in solid, liquid and gas conditions.

Radiation understands emission of harmful waves and the activity of energetic radiation on to the people being in the constructed pace.

Harmful influences produced by physical causes are predictable and known, but the very radiation represents huge danger for the users of the space. Some authors classify radiation to one which can be registered by the apparatus and the one which is difficult to be registered, even thou it is known that they exist. In the first group we place: electro magnetic, ionization, radio active and cosmic radiation, while in the second one we place: radiation from earth, houses and appliances – radio etesian radiation.

Modern materials made in chemical manner, which characteristics are closely directed to salvation of some constructive task, mostly those materials which composition is of the mineral origin, contain radon, radio active gas causes lung cancer.

Up to day researches of the harmful influences of the construction materials separated six most dangerous space polluters: asbestos, toxic materials, dissolvent, radon, biological polluters and the means for the protection against them.

Radiation of radio etesian origin, were known even in the traditional construction, and the successor constructers based upon some forgotten and neglected knowledge, such as oarlock, plumb line and similar methods, which in this moment look in ephemeris way. However, we consider these influences extremely harmful and we divide them into:

- natural waves originating from composition and physical features of the soil;
- telluric stream – influences being the consequence of all soil movements;
- underground constructions;
- technological facilities;
- buildings, depending on the materials they are build from and the type and the amount of installations;
- geo-biological (Hartman) net;
- own radiation from individual objects and living beings;

Beside these usual or some more concrete divisions we made, definition of the harmfulness of some materials in architecture is still hardly realistic, but according to the results from the Engineer R. Kovačević, generally we can conclude the following:

- metals are principally not suitable, especially if used on the surface (tins, nets);
- concrete is not suitable specially when reinforced or when the aggregate originates from not suitable source;
- artificial materials are principally non suitable;
- stone is suitable depending on the finding place;
- wood is suitable;
- brick is suitable.

Given this analysis provides only partial insight of harmful influences of the construction materials to the humans, using the table from R. Kovačević, we will give the preview of the individual materials and their features.

After one such review of harmful influences, it is clear by itself, that for each individual material we try to determine its features from the point of view of the healthy house, being the subject of the following text.
Features of the construction materials being the most common in contemporary construction

- **Concrete** – We consider it as the material of all choices for all construction and construction forms. It becomes definition sine qua non in civil engineering, and at complicated static constructions. Given the concrete non consistent behavior at low temperatures and at temperature changes, so as at humidity presence, it is not recommended in hosing spaces. Its harmfulness is increased while introducing reinforced concrete in its construction and while using aggregates of the volcano send or in combination with pucoaine cement it becomes extremely harmful for health. Modest use is recommended and the avoidance of this construction material. In traditional housing architecture this material has never been used, although in its original form it has been known for centuries.

- **Steel and other metals** – Characteristics of these materials are very applicable in construction and with time they became one of the basic constructive elements. However, their conductivity features and a possibility of producing electro-magnetic fields and waves on this basis including negative emission in space, declares this material as highly not suitable for its use in housing construction. Only the usage of copper foils and led connectors, which is normally the part of traditional construction, has no harmful influence to the space.

- **Brick** – This is one of the three traditional materials which do not have any harmful influence to the humans. One of its derivates, čerpić - non baked brick mixed with straw, is considered as the safest material for life, not taking into consideration its bad physical characteristic, because it’s very sensitive to humidity and it is not slid enough to pressure and movement. To the contrary, brick has outstanding physical characteristics, it is solid, resistant to the temperature changes and it is only one having the feature of thermo isolation and accumulation at the same time. For this material we may say that it can be harmful if the clay the brick is made from is extracted from radio active finding place, even thou in such situation radiation is decreased during baking time.

- **Stone** – We consider stone as historic material, which is, because if it persistence, preserved artifacts of many historical facilities up today. Architecture is, mostly because of the stone and its persistence, become an element of historic remembrances. However, stone does not have even closely the features of the brick, so it is bad isolator, and it is hard to be manipulated during the construction. Its basic characteristic, besides esthetic, is solidness. It is not principally harmful for the health but depending on its volcano origin, it may radiate. Even its granulation used in mortar, in such way may represent potential danger to health. In housing construction, sediment and metamorphic stones are recommended, that is, lime stone and marble. Lime stone is mostly used in urban and rural traditional architecture and granulate for mortar is made of it.

- **Wood** – It appears through history as the faithful partner of brick and stone in the unity of the construction form, and represents a unique connection f healthy and useful construction material. Depending on the sort, we have different wood characteristics, so that we have soft and less resistant sorts and those solid and in static sense extremely resistant sorts. Some of them are resistant to humidity so they are used in exterior, although the key shortage of this material is non resistance to living organisms, pests, which may be removed by certain protections, but at this procedure the wood becomes harmful for the environment. Given these protective coats are chemically based and intended to the elimination of living pests attacking the wood, their use is not recommended in interior of living facilities.

- **Artificial coats for wood** – As it was already said, coats for the wood act against the insects and fungus who habitat in and on the wood surface. These insecticide and fungicide may cause severe damages to humans, especially during their application, so we should prefer
organic coats or adequate techniques of the wood processing and avoid the others. In traditional architecture, the wood was exposed to smoke, so that soot may the protective layer which was impenetrable for all the pests, while the extern surfaces were coated by different sorts of oils and waxes thus being protected from humidity.

- **Light concrete** – Its application in contemporary construction is of extreme importance considering that it is about the material which weight has decisive importance in construction forms, and is eagerly used because they do not burden bearing construction making the construction cheaper. However, these materials do not have physical stability, so they radiate small particles in physical sense, but even in chemical sense, they radiate unstable general structures. Development of these materials is ongoing thus it may be expected the improvement of their characteristics, but in this moment the caution is necessary while using them.

- **Artificial wall coats** – It’s completely illusory to expect these materials to be excluded from the usage because in relation to the natural one, they are much more economic and have good characteristics. Objective, it is about material which completely prevents the circulation through the walls thus preventing micro circulation between inside and outside space. Circulation process enables eventual exit of negative particles fro the space, but thanking to this coat, it is prevented. Among others, these materials contain toxic metals and their dissolvent by its toxic activity directly jeopardize human health and causes many diseases.

- **Materials made from mineral fibers** – Thermo isolation materials are made out of this material. Their exceptional isolation features have become inevitable, because of the fact that the isolation aspect, in construction sense, is one of the main advantages of the contemporary in relation to traditional construction. There are different types of the mineral fibers processing and their origin. People mostly know about glass and stone wool, both may be found in various forms. There are pressed fibers, which are mounted in compact blocks as isolation, but there are also densities structures, which are the most harmful for their small particles which never stop to radiate into the space. Still, there are those which are ecologically certified and which are completely acceptable or at least less harmful. In any case, this material should be mounted with protection.

- **Plastics** – his material produces static electricity by which, on one side, it attracts small particles from the air, but it leases them during movements in space, thus it is not recommended for the emplacement on the floor surfaces. It has indirectly harmful effect, because it is constantly emitting micro particles into space.

Table review shows the behavior of the quoted materials and their harmful features

Still, we may not neglect the usage of the materials for the construction of the architectural details, openings, windows and doors. This paper will treat characteristics of plastic and wood carpentry.

Common opinion that the plastic carpentry may have harmful influence to the human health, mostly have no basis except in two cases. Because of good isolation provided by plastic carpentry, humidity may appear in houses and apartments, which at some persons may cause respiratory problems, and damages on the facilities related surface works on the walls because of condensates being the place for fungus and molds. Other problem appears in the case of fire because during melting the gases are released being very harmful for human health.

Wood as material has been already elaborated, and its usage in carpentry s traditionally present in this region for centuries. As the material suitable for processing, with good technical characteristics, this carpentry, varying in its technical characteristics was changed during the existing period of the facility, but always with the same functional value. It is, expressing the characteristics of the wood as a material and responding to temperature changes and changes of the air humidity, creating the final barrier between inner and outer space, micro movements characteristic to wood, always have had a small dosage of semi-conductivity, so it enables the breathing of space thus ventilating...
and airing the living space. In judging over the advantages and disadvantages between the two types, wooden carpentry is recommended.

Upon reviewing the characteristics of quoted materials, it is clear how difficult is to choose those which combination can reach suitable construction of the living house. Architect R. Kovačević offers a schema of the construction, which is mostly acceptable and which we present here.

Analysis of the construction form of the traditional living house differed in different periods of construction and such form element is a true reflection of the technological conscious of the local builders. Getting knowledge on the materials and their characteristics will not be difficult to choose adequate construction for design. These are concrete quoted examples which speak about harmfulness of construction materials to human health, but also the designing of the space influences human organism, thus making the responsibility of the creator bigger, and in such way we will point the possible mistakes, while we have already determined which are the advantages of traditional spaces in relation to those newly designed. Nowadays, from the construction of the facility it is expected: bearing, thermo isolation, sound isolation, steam conductivity (breathing), accumulation, water proof, non hydroscopic, ecological fitness, acceptable price and rapid construction. It seems that construction profession puts before itself high demands, but not fulfilling them not in the smallest percentage. Not taking care of final users and their health, demands are finally reduced to acceptable price and rapid construction.
Except physical damage to human health, ambiance, atmosphere that ambience carries, memory of the place, socio-economic aspect of the space, they can all influence the psycho-physical condition of people in one specific environment.

Aggression, conflict and anxiety can often be the consequence of small or confuse space. These conditions are caused by different reasons, but the space in which such persons reside very often has the role of a trigger, which provokes such behavior. On the other hand, the ambience being pleasant for living, which by its form, presence of the green or water, for example, is calming and soothing. Just to recall the rooms of the dervish tekia, which were among the first to cure mentally ill with
poetry, music, silence, murmuring of water and birds singing inside their gardens, inside the walls of tekia or zavija. Some of the most known such dervish hospitals were placed in Sarajevo (Hadži Sinanova Tekia in Sagrdžije and Mevlevijska Zavija on Bentbaša).

Picture 5. Review of typical urban block in the city
There are certainly many different situations coming from the influence from construction phenomenon to the behavior and experiences of people and such phenomenon analysis will demand much wider research. We may put the consideration that in today’s moment many factors represent more important dominants of human behavior from the surrounding ambience we move inside, but it is non-doubtful that just architectural space, as the part of the general existence space, represents the framework of the individual and social life. It would be an interesting example the space ruined by war, which in the same moment, for that place inhabitants, represents the memory of the place, remembering of some horrible moment from the past, and then, when the place is reconstructed, rehabilitated and returned to the previous condition, a man start to forget horrible images the place reminded him of. Historic memory is always connected to constructed space, although natural landscape may represent a part of the place memory, if it is about important, accented points in space. We have already talked about the need of the space user for recognizing the own identity through the space identity in which he permanently resides and the alienation from the own surrounding on the other side. Presumption is that even such conditions affect mental health of people moving in their own defined space. Such detailed analysis would be useful for architectural and medical practices, because by this mutual interaction, the results would be followed up and compared.

**Conclusion**

We may conclude that forming and materialization directly participate to the process of the protection and preservation of human health, mental and physical. Application of traditional materials and their careful selection for the sake of structuring new facility with the reminiscence of traditional construction values, will produce good results. Contemporary construction today is based on cheap and non quality materials, which represent danger to human health, thus the caution is recommended while selecting them. Traditional materials are not binding today’s constructors to traditional constructions, if there is creative desire to create new values, but traditional constructions represent tried out and always balanced concept of building, where for the centuries almost nothing has been changed. Forming of architectural space represents the form in which we move and live. That form is a parameter by which all its inhabitants are recognized, by which they are identified and with whom they sympathize. Emotional bonds between inhabitants and the location at certain way are mutual, and equally as a harmony which is seen and measurable, so as disharmony between the tenants and space is promptly noticed. Negative manifestations are aggression, depression, anxiety and …. while ambience is neglected, devastated, confused and…

Research and adoption of traditional value of space, its authenticity in form, materials, content and ambience, would contribute to better physical and mental health of people, the users of the space.
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New information about Von Willebrand’s factor?

ŠTA JE NOVO O VON WILLEBRANDOVOM FAKTORU?

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Abstract

The Von Willebrand factor (vWf) is a multi-metric plasma glycoprotein that participates in the adhesion and aggregation of the platelets at the blood vessel injury sites. The vWf serves as a coagulation factor VIII carrier. The vWf is synthesized in endothelial cells and megakaryocytes, in the form of large polymers, composed of identical subunits. The size of a circulating vWf multimer is determinant of its function in the adhesion of platelets, and is controlled by proteolytic actions of a specific protease. Reduced synthesis or reduced functional activity of the vWf causes a hemorrhagic diathesis. Elevated vWf levels indicate an increased risk of arterial and venous thrombosis. The vWf is an acute phase reactant. Its level may increase due to inflammation, stress, physical exercise, and following a surgery. The vWf is also a marker of endothelial dysfunction.

This article intends to illustrate the current methodical findings about the structure, the biosynthesis and the role of the vWf at various physiological and pathophysiological states.  

Key words: von Willebrand factor (vWf), multimers, platelets, endothelial dysfunction

Introduction

Von Willebrand factor (vWf) was named after dr. Erik von Willebrand, a Finnish doctor. Dr. Willebrand first described the hereditary bleeding disorder with cutaneous and mucosal bleeding, including menorrhagia in 1926. The vWf was isolated in 1970.  
The vWf, as a large adhesive glycoprotein was confirmed in the Weibel-Palade bodies of endothelial cells, the α-granules of platelets and megakaryocytes, in plasma and in the subendothelial connective tissue (1).  
The vWf plays an important role in primary hemostasis, supporting adhesion and aggregation of the platelets at the site of blood vessel injury under
A high shear stress. The vWF also participates in a secondary hemostasis, as a protein carrier and stabilizer of blood coagulation factor VIII. The vWF is considered an indicator of endothelial dysfunction and in determining of a level of activity of the atherosclerotic process.

**A Structure of vWF**

The circulating vWF is one of the largest soluble proteins with a molecular mass of 520 to 20,000 kDa. The mature vWF protein is a multimeric glycoprotein molecule, composed of numerous identical subunits (M 260,000), monomers, which are connected by disulfide bonds. Their number in the vWF molecule may range from only two to a very large number, where it forms the so-called ultra-large multimer vWF (UL vWF).

Each vWF monomer contains many specific domains with specific functions: the D1/ D3 domain (which binds to factor VIII), the A1 domain (which binds to platelet gp I bα receptor, heparin, heparin-like molecules, proteoglycans, sulfatides, and possibly collagen), the A3 domain (which binds to collagen), the C1 domain (containing Arg-Gly-Asp (RGD) sequence which binds to platelet integrin αIIbβ3 when this is activated), the “cysteine knot” domain at C-terminal end of protein, which vWF shares with platelet growth factor (PDGF), transformed growth factor β (TGFβ) and β-human chorionic gonadotropin (βHCG) (2).

Small, medium and very large multimers of vWF exist in the plasma.

**Synthesis of vWF**

The Von Willebrand factor is synthesized primarily by vascular endothelial cells and also in small quantities, by megakaryocytes (3). Only 10-20% of the vWF in humans have a platelet origin.

The synthesis of the vWF is a complex process, involving multiple steps. The vWF is synthesized as a precursor, polypeptide of 2813 amino acids (pre-pro-vWF), including the 22-residue signal peptide, the 741-residue propeptide, also known as von Willebrand antigen II, and the 2050 residue mature vWF protein. After cleavage of a signal peptide in the endoplasmic reticulum, the pro-vWF molecules forms C-terminal dimers, then undergoes intense posttranslational modifications. This includes glycosylation, sulfation, then polymerization, multimerization, and finally splitting the pro-vWF in vWF multimer (mature vWF) and propeptide. Both aminoterminal multimerization and propeptide cleavage are thought to occur in the trans-Golgi network, where the furin was detected, as the vWF proteolytic processing enzyme (4). After the proteolytic action of furin, the propeptide remains noncovalently associated with vWF, and is transmitted along the secretory granules: The Weibel-Palade bodies of endothelial cells, and the platelet α granules.

The propeptide plays an active role in targeting, sorting and storage of the vWF in secretory granules (5). The connection between the vWF and the propeptide is pH-dependent. At a low pH and at the presence of calcium ions, as in the trans-Golgi network, these two proteins are noncovalently associated. However, at pH 7.4, this interaction is not sustained (6). The secretory granules have a lower pH than the Golgi apparatus, so the vWF and propeptide are constantly connected. Both proteins are found in an equimolar ratio in the Weibel-Palade bodies. The vWF propeptide facilitates multimerization of vWF, as one of the most characteristic post-translational event, which takes place in the secretory granules. It remains unknown what is the influence on the final length and on the number of dimers in the Ul vWF multimer. The Weibel-Palade bodies contain only the high-molecular vWF multimers, whereas vWF released constitutive composed of dimers and small multimers. A degree of polymerization of the vWF directly correlated with its prothrombotic activity. High-molecular weight vWF multimers are most effective in hemostasis.

Michaux and al. (7) have shown that vWF is stored in the secretory granules in the form of tubules, giving a characteristic elongated shape of Weibel-Palade bodies. The tubular conformation of vWF is essential for a rapid unfurling of 100 micrometers long vWF filaments, when exposed to neutral pH after exocytosis in cell culture or in living blood vessels. The increase in pH (from pH 5.5 in Weibel-Palade bodies to pH 7.4 in the blood) causes release of vWF propeptide, after which the chain of vWF multimer unfold (7).
Stored vWF plays an important role in the secretion of other proteins from Weibel-Palade bodies (P-selectin, interleukin-8), and may modulate inflammatory processes (8).

The vWF Secretion

Quantitative analysis of secretion, both in resting and in stimulated cultured endothelial cells, found that the vWF is released together with propeptide at 1:1 ratio. The propeptide has a circulating half-life of only 2-3 hours compared to the vWF, whose half-life is approximately 18 hours (9).

The vWF is secreted by two pathways: constitutive, requiring no cellular stimulation and regulated pathway, responsive to secretagogues. The most of vWF from unstimulated, resting cells are secreted constitutively, continuously in small amounts (9). This type of secretion is found in endothelial cells and platelets during thrombogenesis. Megakaryocytes do not constitutively secrete vWF. Endothelial cells constitutively secrete the vWF both into the circulating blood and the subendothelial matrix. This secreted low molecular weight of the vWF was detected on the basal membranes and is free in plasma (10). Functionally, this vWF is less competent. It shows little affinity for binding to subendothelial structures. In regulated secretion, the vWF is released only through luminal membranes in the lumen of blood vessels. Secretion of vWF from specialized storage granules of the endothelial cell is triggered by several substances, some which are important mediators of thrombosis and inflammation (11, 12).

Vischer et al. (12) investigated the pattern of release and the cytoskeletal requirements for secretion in response to Ca²⁺ raising agents or to cAMP-raising agents. Thrombin and histamine induced rapid vWF release (less than 5 minutes), which is dependent on a rise in concentration of ions Ca²⁺ in the cytosol. It involves released from central and peripheral secretory granules and is accompanied by cell retraction. On the other hand, adenosine, adrenaline and prostacyclin induced a slower response (more than 10 minutes), dependent on the rise c-AMP with the release of only peripheral secretory granules, without cell retraction (12).

Giblin et al. (13), in experiments on human endothelial cells pointed to a third pathway of the vWF secretion, which the authors call basal secretion (also called constitutive-like secretion). They demonstrated that most of the vWF secreted by the unstimulated cells was not a product of constitutive secretion but a basal release of post-Golgi storage organelle, presumably the Weibel-Palade bodies. Their findings sparked considerable public interest in science in this area (14) and generated a huge interest.

The Physiological Functions of the vWF

The primary function of the vWF is binding with different proteins. Its function in thrombogenesis is to promote a thrombus formation by creating adhesion of platelets to the injured vessel wall and to one another, under flow conditions, especially under high shear rate as arterioles in the normal circulation and in stenosed arteries. In plasma, vWF forms noncovalent complex with coagulation factor VIII, whose is essential for normal survival of factor VIII. It protects factor VIII from proteolytic inactivation and appears to prolong this half-life about 5 times. Factor VIII is separated from the vWF by a thrombin activity.

Dong et al. (11) showed that UL vWF multimers secreted from the stimulated endothelial cells remained anchored onto the endothelial surface, in form several millimeters long chains. Shear stress enhances binding of UL vWF with platelets, potentially accelerating a platelet aggregation and thrombus formation. Platelets had no measurable interaction with the soluble vWF in the circulation but adhered promptly to the exposed immobilized vWF. The platelets adhered to the long strings attached to stimulated endothelial cells as “beads on a string”. These structures moved together back and forth, in the blood stream (11).

The first contact between platelets and immobilized vWF, under high flow conditions, is mediated by the binding of platelet GP Iba receptor to
the A1 domain of vWF (15). The connection is achieved fast, by the multimetric nature of the vWF and a high density of the active A1 domain sites. However, this relationship has a limited half-life and cannot provide bonds supporting irreversible platelet adhesion. The platelets, tethered to the vessel wall, move constantly in the direction of flow. During the slow translocation platelets become activated. Activated platelet integrin αIIbβ3 binds to the RGD sequence in the vWF C1 domain, and create an irreversible platelet adhesion. This interaction plays a role in platelet accumulation during the thrombus growth (16).

The vWF in Pathophysiological Conditions

When the endothelium is damaged, the vWF binds to the collagen in subendothelial tissue. In areas with small and slow blood flow, the platelets bind to the walls of blood vessels, as an independent entity from the vWF. The fibrinogen stimulates platelet aggregation at low shear levels. The vWF is essential for platelet adhesion in the areas with high shear force caused by changing the size of a blood flow.

There is evidence that vWF in different anatomical locations participates in hemostatic processes (16). Although the vWF originating from subendothelial tissue directly supports an adhesion of platelets. Its distribution is inhomogeneous and is lacking a protein in many vessels where it is necessary for platelet function in hemostasis, as the subendothelium of arterioles and arterial capillaries. The plasma vWF is well suited to mediate early adhesion because it is adapted to quickly binds to collagen, particularly the proteoglycans, at the site of vascular damage. For optimum adhesion and aggregation of platelets, the additional vWF, released from endothelial cells or platelets, is required (17).

The vWF secreted from the endothelial cells also rapidly binds to the collagen fibers at the site of a vascular injury. It is exposed to high levels of shear stress, deformation of endothelial cells in the direction of blood flow, which unfold the conformation of vWF from globular to an elongated form, providing the substrate to support platelet adhesion and aggregation. Under normal flowing conditions, the vWF multimers circulate in a globular form. However, when the vWF is exposed to increased shear forces, these molecules unravel into a “stringlike” conformation. This increases the number of exposed platelet/matrix binding sites and thus enhances the platelet tethering potential of the vWF molecule. The vWF is also released by the activated platelets and is active in platelet aggregation under conditions of high shear stress and has a contribution at a later stage of creation of thrombus (18).

Fibrin is actively involved in platelet reactions essential for thrombus growth. Keuren et al. (21) have shown that the C domain of vWF is critical determinant of platelet adhesion to fibrin under conditions of high shear stress. This authors suggest that fibrin-bound vWF present at an injured vessel wall or disrupted atherosclerotic plaque may critically contribute to thrombus growth by tethering (nonactivated) platelets from fast flowing blood.

Deficit of vWF, especially in large multimers and also reduced activities of the vWF causes the von Willebrand’s disease, a bleeding diathesis of skin and mucous membranes, including menorrhagia. Increase in the vWF levels observed in several clinical conditions such as diabetes mellitus, hypertension, renal failure, liver diseases and malignant tumors poses a significant risk factor for development of thrombosis (19,20). Persons with increased cardiovascular risk: smokers, people with hypertension, hypercholesterolemia, diabetes mellitus have higher values of vWF.

Degradation of the vWF

The proteolytic cleavage of the endothelial cells derived from the Ul vWF multimers is a rapid (one second to 2 minutes) physiological process that occurs on endothelial cell surfaces. The metalloprotease ADAMTS-13 (a disintegrin and metalloprotease with a thrombospondin type 1 Motif, member 13) enzymatically converts the prothrombotic UL vWF multimers to smaller and much less adhesive, but hemostatically active forms (22).

Thus, ADAMS-13 appears to be a key physiologic regulator of the vWF platelet functions. Shear stress facilitates Ul vWF proteolysis by stretching the UL vWF multimers to an open, elongated conformation. ADAMS-13 cleaves vWF whenever
one or more of its cleavage sites are exposed by shear stress (11). Cleavage of the UL vWF strings under shear stress is up to a thousand fold faster than under static condition (22). Smaller vWF fragments were degraded by the other peptidases after separation from the endothelial cells.

An ADAMS-13 deficiency or has been inhibited by antibodies directed at the enzyme, the uncleaved, or only partially cleaved, the UL vWF will accumulate on the endothelial surface and in plasma. This results in systemic thrombotic microangiopathies, as seen in the thrombotic thrombocytopenic purpura. The patients with ADAMS-13 deficiency have an increased risk of thrombosis.

Factors and Conditions Affecting Concentration and Activity of the vWf in Plasma

Concentration and activity of the vWf in plasma are influenced by many factors. In addition to age, estrogen levels, blood type, medication effects and the impact they have; it can cause some physiological (pregnancy, physical exertion) and pathological conditions (inflammation, proteolysis with ADAMS13, genetic variations, stress and malignant diseases).

Previous studies have shown that there is no difference in the concentration of the vWf in relation to gender. The vWf concentration increases with age in both sexes (23). The vWf concentration increases 2-3 times in the second and third trimester of pregnancy. There is a connection between a blood group type and a vWf concentration. Persons with blood type 0 have the lowest concentration and activity of the vWf, while the persons with blood type AB have the highest values of the vWf (24). There are disagreements about the effect of statins in reduction of the vWf concentration. Some studies show that the statins do not reduce level of the vWf, However, level of the vWf is reduced when using statins, as demonstrated in patients with hyperlipidemia, coronary artery disease (25), cerebrovascular disease and diabetic dyslipidaemia. Recent studies have shown that the fluvastatin inhibits a regulated secretion of the vWf in endothelial cells, in response to diverse secretagogues (26). In patients with the acute coronary syndrome, an early rise in the vWf levels can be reduced by a low molecular weight heparin and by thienopyridines, such as the clopidogrel. In patients with the coronary syndrome, who do not have diabetes, the level of vWf is reduced by applying of the oral antihyperglycaemic agent. Damin and al. (27) have found the increased concentrations of the vWf in patients with colorectal cancer, and these values tend to increase, in accordance with progression of a disease.

The vWf as a Marker of Endothelial Damage

Boneu et al. (28) were the first to propose measuring of plasma vWf as an indicator of endothelial damage in vascular diseases. The circulating vWf originates mainly from endothelial cells. The increased levels of this factor in plasma, probably indicates endothelial dysfunction and damage. However, the vWf is an inflammatory plasma reactant in acute phase, so that the increase of its concentration may indicate activation and endothelial stimulation, without primary damage.

Increased concentrations of the vWf were detected in the peripheral, cerebral and atherothrombotic coronary arterial disease. Increased shear stress on the stenosis arteries accelerates vWf binding to platelets and making thrombus formation. Whincup et al. (19) showed that increased concentrations of circulating vWf may be associated with an incident coronary heart disease. Constanst et al. (29) while examining several biological markers, found that the vWf was found as the best indicator of endothelial biomarkers and indicator of risk of ischemic heart disease and stroke. Kiki et al. (30) determined the vWf activity in patients with acute myocardial infarction. They compared these values with the efficiency of a thrombolytic therapy. They found that the activity of the vWf was significantly lower in patients with a successful recanalization of thrombolytic therapy, applied within 6 hours of the myocardial infarction, compared to patients in whom the recanalization was unsuccessful. The patients with acute myocardial infarction and a high vWf activity had significantly less successful fibrinolitic therapy. According to these findings, the vWf can be used as an indicator of the performance impact of thrombolytic therapy.
vath et al. (31) point out that activity of the vWF may be an indicator of the progression of vascular disease. The vWF activity is higher in patients with acute than chronic vascular disease (31). The vWF is increased in patients with diabetes, especially in those with microalbuminuria and macroalbuminuria (32,33) and positive history of coronary artery disease (34). Significantly higher level of vWF has been proven in patients with diabetic than in patients with nondiabetic claudication (35). Dejanov et al. (36) have found a significant increase in biological activity of vWF in patients with venous thrombosis, diabetes mellitus, chronic renal disease, ischemic coronary disease and, according to the type of hemodialysis membrane, in hemodialysis patients. Also, these authors have highlighted the importance of vWF as markers of endothelial damage, possible markers of biocompatibility hemodialysis membrane, and markers of the risk of thrombosis, AV fistula.

Lu Guo-yuan et al. (37) found that the vWF concentration increased significantly and the activity ADAMS13 significantly reduced in patients with chronic renal disease (lupus nephritis, diabetic nephropathy, nephrotic syndrome, and chronic glomerulonephritis). Other authors had similar findings (increase of the vWF and decrease of ADAMS13) in patients with myocardial infarction, thrombotic thrombocytopenic purpura and stroke (38,39,40).

**Conclusion**

The Von Willebrand factor (vWF) plays a critical role in adhesion and aggregation of platelets in the blood vessels, occurring in places of a large shear stress. The vWF participates in the secondary hemostasis, extending a half-life of a coagulation factor VIII in plasma. The increased levels of the vWF in plasma possibly indicate damage to the endothelial dysfunction, because the circulating vWF comes mainly from the endothelial cells. Increase in the vWF concentration may indicate activation and endothelial stimulation, without his primary damage, because the vWF is an inflammatory acute phase reactant. The future clinical research should focus on examining importance and role of the vWF, as an indicator of the endothelial damage, and the potential markers of atherosclerotic development and thrombotic process.
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