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Adolescent Delinquency and Psychopathology: Is Maysi-2 a Valid Instrument to Assess Psychopathology Risk among Turkish Adolescents?

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⁴Derince Teaching and Research Hospital, Clinic of Child and Adolescent Psychiatry Kocaeli, Turkey

Abstract

Introduction: In this study it was aimed to study validity and reliability of Turkish form of Massachusetts Youth Screening Instrument-Second Version (MAYSI-2).

Methods: Totally 387 adolescents, 333 boys and 54 girls participated to the study. Calculation of each subscale’s Cronbach’s alpha and inter subscales correlation coefficient has been performed to assess reliability of Turkish form of MAYSI-2. Exploratory factor analysis and Turkish form of Youth Self Report (YSR) have been used to assess validity of the scale.

Results: Cronbach’s alpha efficiency values were 0.84 for Alcohol/Drug Use, 0.78 for Anger/Irritability, 0.66 for Depression/Anxiety, 0.58 for Somatic Complaints, 0.84 for Suicidal Ideation, 0.15 for Thought Disturbance, 0.55 for Traumatic Experiences for boys and 0.66 for Traumatic Experiences for girls. Turkish form of MAYSI-2 consisted of seven factor structure as the original one in exploratory factor analysis. Statistically significant correlation coefficients which range between 0.27 and 0.69 were found in between all the subscales of both Turkish form of MAYSI-2 and Turkish YSR.

Conclusion: Results of this study showed that Turkish form of MAYSI-2 is valid and reliable to perform risk assessment with regard to psychiatric disorders among Turkish youth population who entered to the juvenile justice system.

Keywords: juvenile delinquency, reliability, validity, Maysi 2.

Introduction

Mental disorders seen in children and youths differ from those seen in adulthood and considerably higher incidence rates have been reported for children in detained children and youths for any reason. Some studies have indicated that 60-70% of the children and youths who were claimed to be involved in criminal acts had at least one psychiatric diagnosis (1,2), besides severe mental disorders were found in 20% of the children and youths who were driven into criminal behaviors (3). Additionally in nearly half of them substance abuse was detected. As authors reported the incidence rates of psychiatric disorders were as follows: psychotic disorders (1-6%), mood disorders (32-37%), anxiety disorders (7-15%), mental retardation (25-95%), specific learning disorders (19-46%), attention-deficit-hyperactivity disorder (50-90%) and conduct disorders (50-90%).

Mental evaluation of a detained child or a youth who was driven into criminal acts, appears to be important from two different perspectives. Firstly, mental disorders are intervened using appropriate treatment modalities so as to improve impaired functionality of a youth with the intention of preventing the youth from committing repetitive acts of crime. Secondly, it aims to detect risky conditions such as substance abstinence, suicidal thoughts and psychotic attacks, which require emergency treatment from the time of his/her detention (1,4,5). Use of validated methods, which evaluate precisely mental treatment, needs of the children/adolescents who were pushed to crime and their families constitute one of the key points. Assessment tools used should determine the risk and protective factors for the child and his/her family and allow the selection of more applicable and realistic interventional method to be used to that end. A healthy evaluation to be performed will guide the treatment in order to be able to decrease the risk and increase protective factors with the aim to prevent at least partially the adolescent from involving in criminal acts in the future (6).

In our country, a screening tool is not in use which will determine the need for mental help and emergency
treatment of every child and youth who are driven to commit a crime. The first assessments of the penal responsibilities of the children and youths who for the first time confronts judicial system may not encompass psychiatric examinations. In this study, we aimed to perform validation and reliability studies of Massachusetts Youth Screening Instrument-Second Version (MAYSI-2) among the children of our country. MAYSI-2 is one of the screening tools which is used frequently in foreign countries in order to be able to determine psychiatric symptoms seen in children and youths who are pushed to crime and provide guidance regarding their treatment requirements.

Methods

Sampling

The universe of the study consisted of youths aged between 12-17 years, who were sent from Kocaeli Branch Office of Juvenile Justice to Juvenile Prosecutor’s Office and finally to Juvenile Court with the accusation of getting involved in a crime and/or those included in the supervised release and/or rehabilitation programs. Individuals whose mental capacity is too low to understand and reply the questions directed to them were excluded from the study. The approval of the Kocaeli University Ethics Committee was obtained for the study.

Interviews with the participants were realized in institutions affiliated to İzmit Province judicial systems as Juvenile Court, Juvenile Prosecutor’s Office, Kandıra T type Prison, Supervised Release Bureau and Rehabilitation Bureau. The participants were informed about the study and the adolescents volunteered to participate in the study were evaluated within 2-3 days after they entered a juvenile justice setting. The participants were requested to fill up the sociodemographic information form, Turkish version of MAYSI-2 (Massachusetts Youth Screening Instrument-Second Version) and (YSR) Youth Self Report-Turkish Version. Illiterate youths who could understand the questions asked, filled up the scales with the aid of the investigators.

Sociodemographic Information Form

It was prepared by the investigator with the intention to get information about the participants including age, gender, educational level, family togetherness, number of siblings, medical, psychiatric personal and family history. It consists of 23 questions which can be completed by the participants with the aid of the interviewer who will read the questions to them.

Massachusetts Youth Screening Instrument-Second Version (MAYSI-2)

Massachusetts Youth Screening Instrument-Second Version was developed as a questionnaire form, which can be applied within 1-3 hours, also by non-clinicians on all youths aged 12-17 years when they are filed in the judicial system. MAYSI-2 does not assume a diagnostic function, but it aims to determine manifestations related to psychiatric disorders (thoughts, emotions, behaviors) It provides information about youths whose names were entered in the judicial system regarding crisis situations (risk of suicide, need for further evaluation and psychiatric support) related to mental health which might require emergency interventions. MAYSI-2, consists of 52 questions which evaluate thoughts, emotions and behaviors experienced within the previous few months as responses of “Yes” and “No.” It can be completed using pen, paper or a computer. Illiterate individuals may complete the form when someone read them its contents. MAYSI-2 can be administered within about 15 minutes. MAYSI-2 consists of seven subscales determined as a result of factor analyses. Since Thought Disturbance subscale is only for boys, so for girls only six subscales were used (Table 2). There is no MAYSI-2 total score. Each subscale is evaluated within itself and each “yes” answer is accepted as one point (7).

Youth Self Report

Turkish version of this scale which was developed by Achenbach is available (8,9). The scale consists of 17 “competence” and 112 “problem” items. The items related to competence include sportive and other activities the youth actively interested or participated in, his/her relevant skills and number and quality of his/her performances both at home or outside. Total Competency Score is the sum of the scores of Activity and Social Skill subscales. Second part of the scale consists of 112 “problem” items. Problematic behaviors are graded based on their incidence rates within the previous six months with 0.1 and 2 points and grouped in various subscales. From this scale, two behavior assessment scores as internal and external orientation are obtained. Internal orientation (internalizing) group consists of social introversion, somatic complaints, and anxiety-depression. While total external orientation (externalizing) score comprise the sum of the scores obtained with subtests of delinquent behaviors and aggressive behaviors. Besides this scale contains the items related to social problems, thought problems and attention problems which are not included.
Procedure
Priorly written permission was obtained from Dr. Thomas Grisso, who developed MAYSI-2 scale, then validation and reliability studies of the scale were realized in Turkish. A research assistant and an academician, with a good knowledge of English who were working in the department of pediatric mental health and diseases, translated the Maysi-2 scale into Turkish. Then, another academician reviewed the translated text. This revised text was back-translated from Turkish into English by an academician well-versed in English. Still another academician compared the translated text with its original version. For this study on detained children, required permissions were obtained from TR Ministry of Justice, Child Surveillance, Training and Communication Bureaus, Kocaeli Province Chief Public Prosecutor’s Office, Kocaeli Provincial Security Directorate, Social Services and Child Protection Agencies, Kocaeli Province Directorate of Social Services. The investigator provided participants, information about the study. The scales used in the study were filled up by youngsters who entered in youth detention centers under the surveillance of the personnel working in Kocaeli Provincial Court House, Kandira T-type closed prison, Kocaeli Province Supervised Release Center, Kocaeli Province Male Protection, Care and Rehabilitation Center. The participants were given written and verbal information about the study and then they were asked to undersign an enlightened consent form. After they had given their approval, the procedure of responding the items of the scales used in the questionnaires was demonstrated to them with examples.

Statistical Analysis
Study data were evaluated using statistical package program 16.0 for Windows (SPSS: Statistical Package for Social Sciences). The results were assessed at a significance level of p≤0.05 and within 95% confidence interval. While evaluating study data, descriptive statistical methods (mean, standard deviation, median), for parametric data Pearson correlation analysis, for non-parametric data, Spearman correlation analysis were used. In the analysis of internal consistency, Cronbach’s alpha coefficient was estimated. In the analysis of internal consistency, Cronbach’s alpha coefficients of ≥ 0.90, 0.79-0.89, 0.60-0.69, 0.50-0.59 and ≤ 0.49 were accepted as indicators of excellent, good, adequate, poor and unacceptable correlations, respectively (10,11). In the evaluation of sample size, Kaiser-Meyer-Olkin (KMO) test was applied. In the KMO test as the estimated value approaches 1, sample size for the investigation is assessed as excellent, when it drops below 0.5 it is deemed as inappropriate (12). Bartlett test was applied to test if the sample structure is suitable for factor analysis. A statistically significant result derived from Bartlett’s test demonstrates suitability of data for factor analysis (12). In the exploratory factor analysis, correlation analysis was subjected to principal components analysis and then a rotation analysis namely “Varimax Method with Kaiser Normalization was applied. Factors with eigenvalues greater than 1 were taken into consideration.

Results
General findings
A total of 187 patients were included in the study. Among organizations integrated with justice system, youths were interviewed in juvenile courts (n=178; 46.0%), in juvenile prosecutor’s offices (n=193; 49.9%), in prisons (n=11; 2.8%) in supervised release bureaus (n=4, 1%) and rehabilitation centers (n=1; 0.3%).

Sociodemographic Characteristics
The participants consisted of 333 (86.0%) boys and 54 (14.0%) girls. Mean age of the participants was 15.9±1.2 years (range 13-17 years). Educational level of the participants was estimated based on the years of training. The lowest educational status consisted of illiterates. The longest duration of education lasted 12 years. Mean length of training was detected as 8.6±2.2 years. Hundred and twenty (31.0%) participants had employments. Twelve (3.1%) adolescents did not respond to this question.

Findings related to MAYSI-2 Reliability Study
Internal Consistency
In the internal consistency analysis of 52-item MAYSI-2 scale, for each subscale Cronbach’s alpha coefficients were estimated as 0.84 for Alcohol-Substance Use, 0.78 for Anger-Irritability, 0.66 for Depression-Anxiety, 0.58 for Somatic Complaints, 0.84 for Suicidal Thoughts, 0.15 for Traumatic Experiences (boys), 0.66 for Traumatic Experiences (girls) and 0.90 for the whole scale (Table 1).
MAYSI-2 Subscale Correlations

Reciprocal correlation coefficients of subscale points of MAYSI-2 are seen in Table 1. All correlation coefficients were statistically significant and ranged between 0.23 and 0.94 (p<0.001) (Table 2).

<table>
<thead>
<tr>
<th>MAYSI-2</th>
<th>Alcohol-Substance Use</th>
<th>Anger-Irritability</th>
<th>Depression-Anxiety</th>
<th>Somatic Complaints</th>
<th>Thought Disturbance (Boys)</th>
<th>Suicidal Thoughts</th>
<th>Traumatic Experiences (Boys)</th>
<th>Traumatic Experiences (Girls)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol-Substance Use</td>
<td>0.38*</td>
<td>0.40*</td>
<td>0.23*</td>
<td>0.30*</td>
<td>0.43*</td>
<td>0.38*</td>
<td>0.37*</td>
<td></td>
</tr>
<tr>
<td>Anger-Irritability</td>
<td></td>
<td>0.75*</td>
<td>0.63*</td>
<td>0.40*</td>
<td>0.61*</td>
<td>0.62*</td>
<td>0.56*</td>
<td></td>
</tr>
<tr>
<td>Depression-Anxiety</td>
<td></td>
<td></td>
<td>0.62*</td>
<td>0.48*</td>
<td>0.47*</td>
<td>0.54*</td>
<td>0.60*</td>
<td></td>
</tr>
<tr>
<td>Somatic Complaints</td>
<td></td>
<td></td>
<td></td>
<td>0.43*</td>
<td>0.65*</td>
<td>0.40*</td>
<td>0.46*</td>
<td></td>
</tr>
<tr>
<td>Thought Disturbance (Boys)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.40*</td>
<td>0.37*</td>
<td>0.94*</td>
<td></td>
</tr>
<tr>
<td>Suicidal Thoughts</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Traumatic Experiences (Boys)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Traumatic Experiences (Girls)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Spearman correlation analysis, *p<0.001
MAYSI-2: Massachusetts Youth Screening Instrument -2
structur of the scale were taken into consideration and scale structure with 7 factors was deemed to be appropriate. Items with factor loadings more than 0.35 were included in the factor analysis and all items with factor loadings greater than 0.35 were considered under a single factor (Table 3). MAYSI-2 items integrated with factors, eigenvalues of factors and percent variances explained by each factor are shown in Table 4. Seven factors obtained account for 44.7% of the total variance.

**Table 3.** Loads of the items included in Massachusetts Youth Screening Instrument-Second Version in Factor Analysis

<table>
<thead>
<tr>
<th>Factor 1 (8 items)</th>
<th>Factor loadings</th>
<th>Factor 2 (9 items)</th>
<th>Factor loadings</th>
<th>Factor 3 (5 items)</th>
<th>Factor loadings</th>
<th>Factor 4 (9 items)</th>
<th>Factor loadings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Item 23</td>
<td>0.79</td>
<td>Item 33</td>
<td>0.75</td>
<td>Item 37</td>
<td>0.55</td>
<td>Item 26</td>
<td>0.48</td>
</tr>
<tr>
<td>Item 33</td>
<td>0.75</td>
<td>Item 45</td>
<td>0.71</td>
<td>Item 39</td>
<td>0.55</td>
<td>Item 20</td>
<td>0.48</td>
</tr>
<tr>
<td>Item 24</td>
<td>0.64</td>
<td>Item 40</td>
<td>0.61</td>
<td>Item 45</td>
<td>0.55</td>
<td>Item 50</td>
<td>0.45</td>
</tr>
<tr>
<td>Item 10</td>
<td>0.61</td>
<td>Item 37</td>
<td>0.55</td>
<td>Item 40</td>
<td>0.61</td>
<td>Item 21</td>
<td>0.43</td>
</tr>
<tr>
<td>Item 20</td>
<td>0.61</td>
<td>Item 19</td>
<td>0.49</td>
<td>Item 19</td>
<td>0.49</td>
<td>Item 43</td>
<td>0.41</td>
</tr>
<tr>
<td>Item 40</td>
<td>0.61</td>
<td>Item 37</td>
<td>0.55</td>
<td>Item 29</td>
<td>0.55</td>
<td>Item 48</td>
<td>0.40</td>
</tr>
<tr>
<td>Item 19</td>
<td>0.49</td>
<td>Item 37</td>
<td>0.55</td>
<td>Item 19</td>
<td>0.49</td>
<td>Item 21</td>
<td>0.40</td>
</tr>
</tbody>
</table>

The validity of a scale conceptually parallel to MAYSI-2

Statistically significant correlation coefficients ranging between 0.27 and 0.69 were found when all sub-dimensions of MAYSI-2 and YSR were compared (p≤0.001). Correlation coefficients between mean sub-dimension scores of MAYSI-2 and YSR scales are seen in Table 5.
Global evaluation of the scale

In order to be able to evaluate Turkish version of MAYSI-2, internal consistency of the scale and mutual correlations between subscales were analyzed. In the the analysis of internal consistency, Cronbach’s alpha coefficient was calculated. In the analysis of internal consistency of the 52–item MAYSI-2 scale, for the

Table 4. MAYSI-2 factor eigenvalues.

<table>
<thead>
<tr>
<th>Factor</th>
<th>Items contained in relevant factors</th>
<th>Eigenvalue</th>
<th>%</th>
<th>% (Cumulative)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Factor 1</td>
<td>M23, M33, M45, M24, M10, M40, M37, M19</td>
<td>4.55</td>
<td>8.75</td>
<td>8.75</td>
</tr>
<tr>
<td>Factor 2</td>
<td>M41, M34, M39, M17, M35, M42, M38, M46, M13</td>
<td>3.83</td>
<td>7.38</td>
<td>16.13</td>
</tr>
<tr>
<td>Factor 3</td>
<td>M22, M11, M18, M47, M16</td>
<td>3.72</td>
<td>7.17</td>
<td>23.30</td>
</tr>
<tr>
<td>Factor 4</td>
<td>M14, M51, M48, M26, M20, M50, M1, M43, M21</td>
<td>3.60</td>
<td>6.92</td>
<td>30.23</td>
</tr>
<tr>
<td>Factor 5</td>
<td>M5, M2, M7, M27, M44, M8, M4, M3, M28</td>
<td>3.28</td>
<td>6.32</td>
<td>36.55</td>
</tr>
<tr>
<td>Factor 6</td>
<td>M32, M6, M52, M15</td>
<td>2.24</td>
<td>4.31</td>
<td>40.87</td>
</tr>
<tr>
<td>Factor 7</td>
<td>M25, M30, M29, M31, M9</td>
<td>2.01</td>
<td>3.87</td>
<td>44.74</td>
</tr>
</tbody>
</table>

MAYSI-2: Massachusetts Youth Screening Instrument -2

Table 5. Correlation coefficients between median subscale scores of MAYSI-2 and YSR.

<table>
<thead>
<tr>
<th>YSR</th>
<th>Depression-Anxiety</th>
<th>Social Introversion</th>
<th>Somatic Complaints</th>
<th>Social Problems</th>
<th>Thought Problems</th>
<th>Attention Problems</th>
<th>Delinquent Behaviours</th>
<th>Aggressive Behaviours</th>
</tr>
</thead>
<tbody>
<tr>
<td>MAYSI-2 Alcohol-Substance Use</td>
<td>0.29*</td>
<td>0.28*</td>
<td>0.27*</td>
<td>0.40*</td>
<td>0.35*</td>
<td>0.37*</td>
<td>0.54*</td>
<td>0.44*</td>
</tr>
<tr>
<td>MAYSI-2 Anger-Irritability</td>
<td>0.59*</td>
<td>0.48*</td>
<td>0.54*</td>
<td>0.59*</td>
<td>0.54*</td>
<td>0.60*</td>
<td>0.55*</td>
<td>0.69*</td>
</tr>
<tr>
<td>MAYSI-2 Depression-Anxiety</td>
<td>0.66*</td>
<td>0.56*</td>
<td>0.61*</td>
<td>0.66*</td>
<td>0.60*</td>
<td>0.64*</td>
<td>0.48*</td>
<td>0.58</td>
</tr>
<tr>
<td>MAYSI-2 Somatic Complaints</td>
<td>0.54*</td>
<td>0.37*</td>
<td>0.51*</td>
<td>0.48*</td>
<td>0.48*</td>
<td>0.48*</td>
<td>0.41*</td>
<td>0.48*</td>
</tr>
<tr>
<td>MAYSI-2 Thought Disturbance (Boys)</td>
<td>0.37*</td>
<td>0.31*</td>
<td>0.36*</td>
<td>0.39*</td>
<td>0.42*</td>
<td>0.36*</td>
<td>0.32*</td>
<td>0.35*</td>
</tr>
<tr>
<td>MAYSI-2 Suicidal Thoughts</td>
<td>0.60*</td>
<td>0.39*</td>
<td>0.41*</td>
<td>0.57*</td>
<td>0.52*</td>
<td>0.52*</td>
<td>0.46*</td>
<td>0.52*</td>
</tr>
<tr>
<td>MAYSI-2 Traumatic Experiences (Boys)</td>
<td>0.44*</td>
<td>0.36*</td>
<td>0.47*</td>
<td>0.49*</td>
<td>0.47*</td>
<td>0.48*</td>
<td>0.41*</td>
<td>0.49*</td>
</tr>
<tr>
<td>MAYSI-2 Traumatic Experiences (Girls)</td>
<td>0.41*</td>
<td>0.33*</td>
<td>0.44*</td>
<td>0.45*</td>
<td>0.44*</td>
<td>0.44*</td>
<td>0.40*</td>
<td>0.44*</td>
</tr>
</tbody>
</table>

Spearman correlation analysis, *p<0.001
MAYSI-2: Massachusetts Youth Screening Instrument -2
YSR: Youth Self-Report Scale

Discussion
sum of all the items of the scale, Cronbach’s alpha coefficient was 0.90, while for the sub-dimensions of the scale (excl. subdimension of Thought Disturbance for boys) coefficients ≥ 0.55 were obtained. Data related to the validity of MAYSI-2 support the assertion which indicates MAYSI-2 as a valid scale for the urgent risk evaluations of mental disorders in detained youths. In the studies on original scale, Velicer’s “Minimum Average Partial Factor Analysis” method was used and factor structures with 7, 8 and 9 items were deemed to be appropriate (7, 13). Sample size and competency, were analyzed using Kaiser-Meyer-Olkin (KMO) and Bartlett tests before factor analysis, as was done for the original scale and suitability of the sample for factor analysis was determined. In the exploratory factor analysis, items for the scale were seen to be mostly fitted to a factor structure of seven items similar to other studies. Structure with seven factors accounted for 44.7% of the total variance. This outcome is very much similar to other outcomes (7, 14).

Alcohol-Substance Use subscale
Cronbach’s alpha coefficients for Alcohol-Substance Use subscale in original MAYSI-2 study were detected to be 0.88 for girls, 0.85 for boys and 0.86 for the whole sample (7). In other studies performed on the same subscale, for instance in a study by Archer et al., Cronbach’s alpha coefficient was 0.90 for white and 0.86 for black girls, while it was 0.83 for boys in both races (14). When the whole sample was analyzed, it was 0.87 and 0.84 for girls and boys, respectively. In a study by Ford et al., Cronbach’s alpha coefficient was reported as 0.84 for both genders (15). Since our study did not contain adequate number of girl participants, we did not calculate Cronbach’s coefficients separately for girls. For all participants Cronbach’s alpha coefficient of alcohol-substance use subscale was detected as 0.84. In our study factor 1 with 8 items was loaded similarly both in the original scale study and in the study by Archer et al., under the factor 1 (7,14). This factor corresponds to Alcohol-Substance use subscale. Items 10, 19, 23, 24, 33, 37, 40 and 45, which were loaded in Factor 1, had very similar characteristics in all three scales.

Anger-Irritability Subscale
Cronbach’s alpha coefficients for Anger-Irritability subscale in the original MAYSI-2 study were 0.79 for girls and 0.80 for boys and 0.80 for all participants (7). When other studies related to the same factor were considered, in the study by Archer et al., (2004) Cronbach’s alpha coefficients for the white and black girls were 0.84 and 0.83, respectively (14). The corresponding values for boys were 0.78 and 0.82, respectively. While for the whole sample, it was 0.83 for girls and 0.81 for boys. In a study by Ford et al., it was found to be 0.80 in both genders (15). In our study, Cronbach’s alpha coefficient of Anger-Irritability subscale was detected to be 0.78 for all participants. In our study factor 5 with 9 items, in the original scale factor 2 with 8 items and in Archer’s scale with 9 items were similarly loaded (14). This factor corresponds to Anger-Irritability subscale. In all three scales, items 2, 7, 8 and 44 were loaded in the Anger-Irritability subscale. As indicated before, items 1, 3, 39 and 42, which were loaded in Anger-Irritability Subscale of the original scale and Archer’s scale, were included in the Anxiety – Depression subscale in our study (14). In youths, symptoms of anxiety and depression can manifest themselves as anger management difficulty and nervousness. (16,17). Presumably for this reason, these items might be loaded in Anxiety-Depression subscale. Therefore, we speculate that revision of the terminology used in the questionnaires and then application of these revised items on larger-scale sample group will be more appropriate.

Depression-Anxiety Subscale
In the original MAYS-2 study, Cronbach’s alpha coefficients for Depression-Anxiety subscale were 0.73 for girls, 0.72 for boys and 0.73 for all participants (7). In a study by Archer et al., for the same subscale Cronbach’s alpha coefficients for white and black girls were 0.84 and 0.83, while for white and black boys it was 0.78 and 0.82, respectively (14). For the whole sample, it was 0.74 for girls and 0.73 for boys. In a study by Ford et al., Cronbach’s alpha coefficient was calculated as 0.74 (15). In our study Cronbach’s alpha coefficient of Depression-Anxiety subscale was found to be of sufficient level (0.66) for all participants. Though this Cronbach’s alpha coefficient estimated for this subscale was sufficient, still it is apparently lower when compared with original scale study and other studies. In various studies performed, the authors have reported that among youths driven into delinquency, depression was seen more frequently in girls rather than boys (1,4). It might be thought that since the number of our girl participants were lower than those of other studies and we did not perform statistical evaluations separately for boys and girls, our Cronbach’s alpha coefficient was remained at that level. In our study factor 2 which consisted of 9 items and factor 4 which comprised of 7 items in the original scale (7) and factor 5 with 6 items in a study by Archer et al., display similarities
Somatic Complaints subscale
According to literature data on Somatic Complaints subscale, in the original MAYSI-2 study Cronbach’s alpha coefficients were found to be 0.77 for girls and 0.75 for boys and 0.77 for the whole study population (7). In a study by Archer et al., Cronbach’s alpha coefficients for white and black girls were 0.80 and 0.77, respectively, while the corresponding values for boys were 0.81 and 0.76, respectively (14). For the whole sample, it was reported as 0.87 for girls and 0.86 for boys. However, in a study by Ford et al., Cronbach’s alpha coefficient was 0.73 for the whole study population (15). Cronbach’s alpha coefficient of Somatic Complaints subscale was found to be 0.58 for all participants. When six items of Somatic Complaints scale were analyzed individually, Cronbach’s alpha coefficient did not increase. It has been suggested that it would be appropriate to elaborate items included in the Somatic Complaints subscale among sample groups with equal number of participants from every judicial unit together with review of the terminology used. In our study, factor 7 consisted of five items. It was loaded similar to factor 5 with 5 items in the original scale and factor 4 with 5 items in the Archer’s scale (14). This factor is included in the somatic complaints subscale. In all three scales, items 29, 30 and 31 were loaded under this factor. In the other two studies, items 27, 28 and 43, which were included in the Somatic Complaints subscale, were loaded in different factors (7).

Suicidal Thoughts subscale
In the MAYSI-2 original study for the suicidal thoughts subscale (7) Cronbach’s alpha coefficients were reported to be 0.83 for girls and 0.80 for boys and 0.83 for the whole sample. However in a study by Archer et al., Cronbach’s alpha coefficients for the same subscale were 0.89 for white and black girls, respectively (14). The corresponding Cronbach’s alpha coefficients for white and black boys were 0.87 and 0.86, respectively. While for the whole sample, Cronbach’s alpha coefficients were 0.78 for girls and 0.73 for boys. However, in a study by Ford et al., it was reported as 0.88 (15). In our study Cronbach’s alpha coefficient of Suicidal Thoughts subscale was detected as 0.84 for all participants. In our study, factor 3 with 5 items, factor 5 in the original scale and factor 2 in Archer’s scale were loaded similarly (14). This factor was included in the Suicidal Thoughts subscale. Items 11, 16, 18, 22 and 47 have very similar factor loadings (7).

Thought Disturbance Subscale
In our study Cronbach’s alpha coefficient of Thought Disturbance subscale was 0.15 for boys. Our results are not sufficient to establish reliability of this subscale. The items included in this subscale should be revised and reorganized in further studies in compliance with the characteristics of the population of our country. In the original study by Grisso Cronbach’s alpha coefficient of Thought Disturbance subscale for girls was not determined, while for boys it was calculated to be 0.61 (7). In a study by Archer et al., Cronbach’s alpha coefficients for white and black boys were 0.56 and 0.55, respectively, while it was 0.55 for the whole sample (14). In a study by Ford et al., Cronbach’s alpha coefficient was found to be 0.59 for both genders (15).

Traumatic Experiences Subscale
In original s3udies with MAYSI-2 scale, Cronbach alpha coefficient of Traumatic Experiences subscale was found to be 0.63 (7). Other studies performed for the same subscale were also taken into consideration and in a study by Archer et al., Cronbach’s alpha coefficients were found to be 0.61 for the white and 0.67 for the black races, while for the whole sample it was 0.65 (14). In a study by Ford et al., male and female participants were not analyzed separately and Cronbach’s alpha coefficient related to the Traumatic Experiences scale for both genders was determined as 0.58 (15). In our study Cronbach’s alpha coefficient for Traumatic Experiences scale for boys was 0.55. Traumatic Experiences subscale for boys consists of five items. Analysis of individual items did not increase total Cronbach’s alpha coefficient. Though our findings demonstrated similarities with the outcomes of the study performed by Ford, our study results demonstrate that it will be appropriate to elaborate items of the Traumatic Experiences subscale for boys with further studies (15).

In the original MAYSI-2 study, Cronbach’s alpha coefficient for Traumatic Experiences subscale for girls was found to be 0.70. (7). In a study by Archer et al., Cronbach’s alpha coefficients were 0.70 for the white, 0.79 for the black races (14). While for the whole sample it was 0.77. In our study Cronbach’s alpha coefficient was 0.77 for both genders (7).
alpha coefficient of Traumatic Experiences subscale for girls was found to be 0.66. In our study factor 4 which consists of 9 items and factor 6 which contains 4 items correspond to Traumatic Experiences and Thought Disturbance items in the original scale and Archer’s scale (14). However, these items contained in scales do not demonstrate homogenous distribution, as is the case in the original scale. This difference between scales was thought to be related to intercultural differences in the expression of trauma and thought disturbance or heterogeneity of samples. Similarly, Thought Disturbance subscale in the original scale is not assigned for women. Similar to our study, in a study by Archer et al., Thought Disturbance and Traumatic Experiences subscales (especially for boys) demonstrated lesser similarities to the original scale (14).

**Conclusion**

In this study, evaluation of validity and reliability of Turkish version of Massachusetts Youth Screening Instrument-Second version were aimed. Data related to the reliability of MAYSI-2 have supported reliability of this scale in urgent risk evaluation regarding mental disorders of youths who entered judicial system. In order to perform validation studies of a scale resembling MAYSI-2, the correlations between MAYSI-2 and YSR subscales were investigated. Between all MAYSI-2 and YSR sub-dimensions, statistically significant correlations were found. For the evaluation of validity of MAYSI-2, exploratory factor analysis and conceptually similar scale validation analyses which evaluated scale structures were performed. In addition data obtained related to the validity of MAYSI-2 have demonstrated that it is a valid scale in the emergency evaluation of mental disorders in detained youths. To evaluate and elaborate whether the items placed in sub-dimensions different from those specified in the original scale and sub-dimensions with lower alpha values are specific to our sampling require conduction of further studies with different sampling groups.

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Patient Characteristics, Locations and Histopathological Features of Pilomatrixomas in Erzurum/Turkey

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Abstract

Introduction: The aim of this study is to examine the patient characteristics, locations, presentations and histopathological features of pilomatrixomas in a group of patients.

Methods: We analyzed 41 patients that histopathologically diagnosed as pilomatrixoma in Erzurum Regional Training and Research Hospital between 2009 and 2014, retrospectively.

Results: Patient’s mean age was 30 years (age range: 3–78 years), with a female to male ratio of 26:15. There were 12 patients in the pediatric age group (<16 years). The average diameter of the lesion at presentation was 18.5 mm (range: 2–55 mm). A total of 36 out of 41 (87.8%) patients presented with solitary lesion, while 5 patients (12.2%) had two lesions. Most common location in our patient group was head and neck region and second most common location was limbs. The most common clinical presentation was a painless solitary skin lesion which was noticed incidentally. All cases more or less shared the same microscopic features of pilomatrixoma such as basophilic cells, eosinophilic shadow cells, calcification and foreign body type giant cells.

Conclusion: Pilomatrixoma is not an uncommon benign lesion. It is more common in female gender, adult age group and at the head and neck region.

Keywords: pilomatrixoma, histopathology, epithelioma of Malherbe

Introduction

Pilomatrixoma (pilomatricoma, calcifying epithelioma of Malherbe), which accounts for almost 20% of pilar tumors, is a benign lesion with differentiation toward the matrix of the hair follicle (1). It is found particularly on the head and neck and upper extremities (1,2). It was first described in 1880, by Malherbe and Chenantais (3). It was believed to be a rare tumor, but increasing reports in the literature show that it is not uncommon (4).

Etiology has been linked to mutations such as β-catenin and bcl-2 (5-7). Epidemiology shows bimodal peaks in presentation, with up to 60 percent of cases occurring in the first two decades and a secondary peak in the sixth decade (3,5). Most cases are occurred as single nodules, but multiple occurrences have been reported (3,5,8). There is a slight female predominance in reported cases (2,4).

The aim of this study is to examine the patient characteristics, locations, presentations and histopathological features of pilomatrixomas in Erzurum/Turkey with a group of patients.

Materials and methods

We analyzed 41 patients that histopathologically diagnosed as pilomatrixoma in Erzurum Region Training and Research Hospital between 2009 and 2014, retrospectively. The data such as patients’ characteristics, site of lesions, lesions characteristics, histopathological features collected from patients’ pathology reports. Data analysis performed using the SPSS 20.0 program. Descriptive statistics for the evaluation of results have shown in the form of mean, the nominal variables have shown as the number of cases and (%).

Results

Patients’ mean age was 30 years (age range: 3–78 years). There were 12 patients in the pediatric age group (<16 years) and 29 in the adult age group. There was slight female predominance, with a female to male ratio of 26:15.

The average diameter of the lesion at presentation was 18.5 mm (range: 2–55 mm), although 15 cases (35.7%) were less than or equal to 10 mm in size. A total of 36 out of 41 (87.8%) patients presented with solitary lesion, while 5 patients (12.2%) had multiple lesions.
Most common location in our patient group was head and neck region such as scalp, cervical, pre-auricular or face areas. 21 out of 41 cases’ lesions was occurred in head and neck region (51.22%), and it was more common in face than others. Second most common location was limbs. In 36.58 % of cases lesions was localized in limbs and in 12,20 % of them localized in trunk (Table 1).

Table 1. Locations of cases.

<table>
<thead>
<tr>
<th>Location</th>
<th>Number of cases</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Head and neck region</td>
<td>51.22%</td>
<td>21</td>
</tr>
<tr>
<td>-Preauricular</td>
<td>3</td>
<td>7.31 %</td>
</tr>
<tr>
<td>-Scalp</td>
<td>5</td>
<td>12,20 %</td>
</tr>
<tr>
<td>-Cervical</td>
<td>5</td>
<td>12,20 %</td>
</tr>
<tr>
<td>-Face</td>
<td>8</td>
<td>19,51 %</td>
</tr>
<tr>
<td>Limbs</td>
<td>15</td>
<td>36,58 %</td>
</tr>
<tr>
<td>-upper extremity</td>
<td>12</td>
<td>29,26 %</td>
</tr>
<tr>
<td>-lower extremity</td>
<td>3</td>
<td>7,32 %</td>
</tr>
<tr>
<td>Trunk</td>
<td>5</td>
<td>12,20 %</td>
</tr>
</tbody>
</table>

The most common clinical presentation was a painless solitary skin lesion which was noticed incidentally. The mass was almost always well-circumscribed and had a hard structure.

Histologically, all cases had almost the same microscopic features of pilomatrixoma such as basophilic cells, eosinophilic shadow cells, calcification, fibrosis and foreign body type giant cells (Figure 1,2).

**Discussion**

Pilomatrixoma is slightly more common in females (2,4). Similarly, 26 of 41 our patients were female. It is more common in childhood, but it can occur at any age (2,3,9). 29 of 41 our patients were adults which is different than literature.

They were most commonly seen in the head and maxillofacial location (2,4). Analogously, 52% of our patients had lesions in the head and neck region.

Pilomatrixomas are usually solitary nodules, but multiple lesions have been seen in 4% of cases (3). In a study performed on 205 cases of pilomatrixoma multiple presentations were seen in 2.43% of cases (2). In our study12.2 % out of cases had multiple lesions.

Pilomatrixomas that diameters ranging between 0.5-3 cm are solid nodules (1,10). Also, large or giant cases (>5.5 cm) were reported (10-12). Gongidi et al. reported a case of pilomatrixoma measuring 24 cm arising from the posterior thorax (12). In our cases mean of lesions size was 18.5 mm. Only in one patient’s lesions size was 5.5 cm.

Histologically, pilomatrixoma is a deep, subcutaneous tumor occurring between the dermis and hypodermis, with medial displacement of pilosebaceous glands and follicles. The tumor is separated from the epidermis by a layer of fibrous tissue (3).

There are two basic cell types in pilomatrixomas, basophilic cells and eosinophilic shadow cells. The basophilic cells tend to be at the periphery of the cell islands and have little cytoplasm, indistinct cell borders, hyperchromatic nuclei and mitotic figures. The eosinophilic shadow cells in the usual form are found toward the central areas of the cell masses and they are enucleated. They have more cytoplasm and distinct cell borders (1).

Malignant change of pilomatrixoma is rare. The principal indicators of malignancy are cellularity pleomorphism, frequent abnormal mitotic figures or atypia, central...
necrosis, and infiltration of the soft tissues, skin and lymphatic or vascular elements (1,4,13).

Histopathologic differential diagnosis include calcified trichilemmal cyst and malignant pilomatrixoma (matrical carcinoma). In calcified trichilemmal cyst, cyst lined by epithelial cells abundant eosinophilic cytoplasm and there is no shadow or ghost cells. In malignant pilomatrixoma infiltrative growth pattern, marked nuclear atypia, frequent abnormal mitosis and areas of necrosis is seen, which specified in the previous paragraph (14).

Surgical excision is the usual method of treatment because of spontaneous regression is never observed. Most tumors, even if inadequately excised, will not recur. However, local recurrence and aggressive forms have been documented (1,3,4). After an average follow-up of 26.65 months we didn’t observe any recurrence in our cases.

Conclusion: Pilomatrixoma is a benign lesion which is not rare. In Erzurum/Turkey, it is more common in female gender and the head and neck region similar to literature on the other hand it is more common in adult age group which is different than literature.

References

An Independent Risk Factor for Quality of Life in Cancer Patients: Urinary Incontinence

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Abstract

Introduction: Urinary incontinence impacts the lives of older individuals and it is considered one of the most important and recurrent geriatric syndromes. The aim of this study is to determine the prevalence of urinary incontinence in cancer patients and to evaluate its association with age and quality of life.

Method: One hundred and thirty three patients with cancer were assessed at hematology/oncology outpatient clinic. The validated form of the Turkish version of the International Consultation on Incontinence Questionnaire-Short Form was used to evaluate urinary incontinence and quality of life (QOL). Descriptive statistics were used. The association between urinary incontinence and age, gender, cancer type and quality of life were evaluated with chi square.

Results: A total of 133 patients including 84 male and 49 female were evaluated. The mean age of patients was 62.5±12.3. While 45.9% of patients are older than 65, 54.1% of them are less than 64. The rate of urinary incontinence was found 40.6% (n=54). The association between urinary incontinence and age, quality of life has been shown statistically significant with chi square (P<0.001, P<0.001 respectively). The mean of ICI-Q and QOL score is 7.6±3.1 and 3.2±1.7 respectively. The most common type of urinary incontinence is urge incontinence following by stress, mix and overflow (12.8%, 12%, 11.3% and 4.5% respectively).

Discussion And Conclusion: Our results suggest that urinary incontinence is a significant problem which is underdiagnosed and undertreated in cancer patients. It inversely affects the quality of life. While focusing on cancer and chemotherapy, this important problem should not be underestimated. This leaves incontinent patients with unresolved physical, functional, and psychological morbidity, and diminished quality of life. The study suggests that awareness and education regarding incontinence should be increased among cancer patients and screening of Urinary Incontinence is an important part of their assessment.

Keywords: Quality of Life, Cancer, Urinary Incontinence, Elderly

Introduction

Cancer is increasing rapidly in the elderly population. Approximately 50 percent of cancers and 70 percent of deaths due to cancer occur in those ≥65 years old, and this is expected to increase (1-3). The patient’s life change dramatically from the moment cancer is diagnosed. Dealing with cancer is a life-changing event for most people. Patients with cancer face complex physical, psychological and social consequences of disease and its treatment.

Urinary incontinence (UI) is the involuntary loss of urine, in the absence of urinary tract infection. The International Continence Society defines urinary incontinence as ‘involuntary loss of urine that is a social or hygienic problem’ (2). Urinary incontinence impacts the lives of elderly individuals and it is considered one of the most important and recurrent geriatric syndromes (2-5). Its occurrence increases exponentially as age advances due to functional and structural changes occurring in the urinary system and with impaired functional independence. There are four major types of urinary incontinence associated with lower urinary tract dysfunction: urgency incontinence, stress incontinence, mixed incontinence, and incontinence due to incomplete bladder emptying.

Urinary incontinence (UI) usually under diagnosed and undertreated in elderly people. Some of the complications of UI include sexual dysfunction, stress, major depression and diminished quality of life (6-9). Quality of life was found to significantly decrease with increasing urinary incontinence severity (10). Many patients are reluctant to initiate discussions about
their incontinence which leaves these patients with unresolved physical, functional, and psychological morbidity, and diminished quality of life (11). Detection of this problem is essential for preventing complications and improving the quality of life. In cancer patients, urinary leakage can be controlled and many of the problems associated with urinary incontinence can be prevented to the patient’s satisfaction with a multidisciplinary approach.

The aim of this study is to determine the prevalence of urinary incontinence in cancer patients and to evaluate its association with age and quality of life.

Method

One hundred and thirty three patients with cancer were assessed at oncology/hematology outpatient clinic. Patients with urogenital cancers and pelvic surgery are not included in the study. The validated form of the Turkish version of the International Consultation on Incontinence Questionnaire-Short Form (ICIQ-SF) was used by physician to evaluate urinary incontinence and quality of life (QOL). ICIQ-SF is composed of six questions, which evaluate the frequency and severity of urinary loss and how much UI interferes in daily life. It also presents a sequence of eight self-diagnosis items related to the causes or situations of UI that are not scored. To be considered incontinent, the patient should present a score equal to or above three. For the statistics of the study SPSS.20 software was used. The association between urinary incontinence and age, gender, cancer type and quality of life was evaluated with chi square statistical analysis. The association between the variables were considered significant when p <0.05.

Results

A total of 133 patients including 84 male and 49 female are evaluated. The mean age of patients was 62.5±12.3. While 45.9% of patients are 65 and older, 54.1% of them are younger than 65. The rate of urinary incontinence was found 40.6% (n=54). The association between urinary incontinence and age, quality of life has been shown statistically significant with chi square (P<0.001, P<0.001 respectively). While 72.2% of patients with UI are older than 65 years, 27.8% of them are less than 64. While the number of patients with hematologic cancer was 31, 102 of the patients have solid malignancy. 96.3% of the patients with UI have been stated that the quality of life was affected negatively. No association between UI and gender, cancer type has been shown (p=0.147, p=0.094).

Table 1: The association of Urinary Incontinence with age, gender, cancer type and QOL

<table>
<thead>
<tr>
<th></th>
<th>% (n=133)</th>
<th>UI (40.6%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>AGE</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;65 y/o</td>
<td>45.9%</td>
<td>72.2%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>&lt;65 y/o</td>
<td>54.1%</td>
<td>27.8%</td>
<td></td>
</tr>
<tr>
<td><strong>GENDER</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>36.8%</td>
<td>44.4%</td>
<td>0.147</td>
</tr>
<tr>
<td>Male</td>
<td>63.2%</td>
<td>55.6%</td>
<td></td>
</tr>
<tr>
<td><strong>CANCER TYPE</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hematologic cancer</td>
<td>23.3%</td>
<td>31.5%</td>
<td>0.094</td>
</tr>
<tr>
<td>Solid cancer</td>
<td>76.7%</td>
<td>68.5%</td>
<td></td>
</tr>
<tr>
<td><strong>QOL (IN PATIENTS WITH UI)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Affected</td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Not affected</td>
<td>96.3%</td>
<td>3.7%</td>
<td></td>
</tr>
</tbody>
</table>
Discussion

Urinary incontinence is an important problem especially in geriatric population which negatively affects the quality of life. Identifying this comorbid condition in cancer patients who frequently face the complex consequences of cancer and its treatment is important in order to improve the cancer care. To our knowledge, this is among the few studies that investigate the prevalence of UI as a comorbid condition in cancer patients, and determine the impact of UI on QOL. The provision of cancer care should consider the medical, psychological and social consequences of the disease in each individual patient. Assessment of the needs, goals and preferences of patients with advanced cancer has been identified as a necessary step toward tailoring the care delivered to these individuals (12). In that sense it is important to recognize the comorbid conditions that might affect the quality of life and individualize the management.

The urinary incontinence rate was found 40.6% among cancer patients which is similar to general population. Since UI would be a predominant feature of genitourinary cancer these patients were excluded from the study. In older women, the prevalence of urinary incontinence is 17 to 55 percent and in younger and middle-aged women it is 12 to 42 percent. In general, the prevalence of urinary incontinence in men is approximately half that in women (13,14). No association has been shown between UI and cancer type.

In present study; 96.3% of the patients with UI have been stated that the quality of life was affected negatively to some degree. Quality of life was found to significantly decrease with increasing urinary incontinence severity (10). QOL might be described as the effect of an illness and its treatment as perceived by patients and is modified by factors such as impairments, functional stress and perceptions (15). QOL has been introduced as an endpoint for treatment comparisons in many cancer types and as an early indicator of disease progression that could help the physician to closely monitor the patients (16,17). In that sense; the comorbidities affecting the QOL in cancer patients should be evaluated and treated accordingly both to improve the life quality and to evaluate the impact of cancer treatment adequately.

There are also a few studies that have investigated the impact of urinary incontinence (UI) on quality of life among cancer survivors. One study has been shown that UI is highly prevalent, in bladder, endometrial/uterine and prostate cancer survivors and QOL measures were negatively associated with UI (18). Also a recent study showed that cancer survivors with urinary incontinence and major depressive disorder experiences diminished quality of life (19). Stress urinary incontinence and voiding dysfunction were found prevalent in gynecologic cancer survivors after hysterectomy. However, no association has been found with quality of life (20).

Our finding has been shown an association between UI and age. 72.2% of the patients with incontinence are older than 65 years old. Urinary incontinence increases by age due to functional and structural changes occurring in the urinary system and with impaired functional independence. It is estimated that approximately 15% of community-dwelling elderly individuals and 50% of institutionalized elderly persons have significant urinary incontinence (21). In older persons, UI can cause significant morbidity and functional impairment. Risk factors for UI in older persons include impaired mobility, falls, medications, depression, transient ischemic attacks and stroke, dementia, congestive heart failure, fecal incontinence and constipation, and obesity. Comprehensive geriatric assessment evaluation should be an integral part of cancer management (22,23).

In our study urge incontinence has been shown the most common UI type following by stress, mix and overflow. Urge incontinence becomes more prevalent with age, with urge and mixed incontinence explaining the majority of urinary incontinence in older women (24). Urge urinary incontinence constitutes a much larger portion of total urinary incontinence in men than in women. Mixed incontinence is relatively rare in men, although it is the most common type in women. Stress incontinence is the primary type of urinary incontinence reported among younger women (25).

Conclusion

Cancer itself and the side effects of treatment affect the quality of life dramatically. This study shows that urinary incontinence is another challenge in the lives of cancer patients. Clinicians should be aware of this problem in order to offer their patients adequate treatment options. Therefore awareness and education regarding UI as a disease in cancer patients needs to be increased to avoid underdiagnosis and lack of treatment especially in elderly cancer patients. The understanding of UI
prevalence and QOL impact of UI among cancer patients may assist in focusing to improve the QOL. Further long term well controlled studies are needed to identify the risk factors associated with UI in this specific population.

References


Serum Level of suPAR and YKL-40, a New Biomarker in Patients with Acute Myocardial Infarction?

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Abstract

Introduction: Low grade inflammation plays an important role in the several development process of coronary artery disease. The soluble urokinase plasminogen activator receptor (suPAR) and chitinase 3-like protein 1 (YKL-40) are the new potential biomarkers of inflammation. We intended to test the hypothesis whether the inflammatory biomarker YKL-40 alone or in combination with suPAR could be the new diagnostic biomarkers for acute myocardial infarction (AMI).

Material and Methods: Fifty-five patients with AMI and seventy control subjects were included in the study. The diagnosis of AMI was based on the current 3rd standard universal definition criteria. Serum YKL-40 and suPAR levels were measured at the first and second days of AMI by using ELISA method.

Results: Serum YKL-40 levels were significantly higher in the first (69.10±16.58 ng/mL) and second day (60.64±16.01 ng/mL) of AMI patients than those of the control subjects (37.11±4.30 ng/mL) (p<0.001). Serum YKL-40 levels in the first day of AMI patients also were significantly higher than those of second day of AMI patients (p<0.01). Serum suPAR were significantly higher in the first (6.58±3.24 ng/mL) and second day (5.86±4.56 ng/mL) of AMI patients than those of the control subjects (2.26±1.92 ng/mL) (p<0.001).

Conclusion: Serum suPAR and YKL-40 can be considered strong inflammatory markers of AMI. We concluded that serum suPAR and YKL-40 levels at the first day and second day of AMI could be used as a clinically useful marker for diagnosis of AMI.

Key words: Inflammation, the inflammatory biomarker, ischemic heart disease

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Introduction

Acute myocardial infarction (AMI) is the important cause of death worldwide. Systemic and local inflammatory response plays an important role in AMI (1). Atherosclerosis is concerned throughout all stages of the development of AMI, from endothelial dysfunction and plaque formation to plaque disruption with superimposed thrombosis (2-4). Early atherosclerotic lesion development is initiated by endothelial dysfunction and the local deposition of lipids (e.g. low density lipoprotein) (4).

Endothelial dysfunction causes the local inflammatory response. Activation endothelial cells express several adhesion molecules that facilitate leukocyte recruitment to the vessel wall (4,5) via binding of the integrin. Monocytes that take in excess lipids are transformed into macrophages and foam cells (4). These foam cells generate the initial lesions leading to advanced atherosclerosis (5). Foam cells secrete pro-inflammatory cytokines, growth factors, matrix metalloproteinases and tissue factor (3). Neutrophils, lymphocytes, monocytes, and macrophages initiate the inflammatory response through the secretion of numerous growth factors, cytokines (including tumor necrosis factor-α (TNF-α) and interleukin-1β) (2), proteolytic enzymes, integrins and cell adhesion molecules in patients with unstable angina and myocardial infarction (3,4). Proteolytic enzymes, including metalloproteinases and cysteinyl cathepsins can degrade extracellular matrix proteins (4-6) and convert a stable atherosclerotic plaques to unstable plaques called “vulnerable” plaque (2, 5, 7).

Acute rupture of vulnerable plaques frequently leads to myocardial infarction or stroke (4).

Chitinase 3-like protein 1 (YKL-40) is a 40 kDa heparin and chitin-binding glycoprotein (8-10). The acute phase protein YKL-40 is an inflammatory biomarker in both early and late phases of the atherosclerotic process and coronary artery disease (CAD) patients, which is produced by macrophages, neutrophils, and vascular smooth muscle cells (9-11). It was demonstrated that YKL-40 levels were elevated in patients with myocardial infarction (8). YKL-40 is association with migration, chemotaxis, remodeling of the extracellular matrix, proliferation,
differentiation and adhesion of vascular endothelial cells. It may also participate in angiogenesis, inflammatory processes, tissue destruction/remodeling, and apoptosis (12-14).

The urokinase-type plasminogen activator receptor (uPAR, CD87) is glycosylphosphatidylinositol (GPI)-anchored cell membrane glycosylated protein (15). uPAR is cleaved from the cell surface by elastase, matrix metalloproteinases, proteases and becomes to the soluble form of the receptor, suPAR, which has been detected in blood, urine and cerebro-spinal fluid (7,16-18). suPAR takes part in various immunological functions, including the plasminogen-activating pathway, inflammation (17), cell adhesion, migration, chemotaxis, proteolysis, tissue remodeling (18). uPAR accumulates in the atherosclerotic lesion, and plasma levels of suPAR have been associated with increased incidence of cardiovascular events (7).

Blood levels of sensitive and specific biomarkers, such as cardiac troponin and the MB fraction of creatine kinase (CK-MB), myoglobin and hsCRP are increased in AMI (19). New biomarkers is need assessed for AMI. YKL-40 and suPAR, which is secreted primarily from inflammatory cells, was associated with increased risk of developing cardiovascular events (7,8). Therefore, YKL-40 and suPAR could potentially be a new useful biomarker of disease severity, prognosis and survival in patients with ischemic heart disease. The inflammatory biomarker YKL-40 has been shown to be significantly increased in patients with ST-elevation myocardial infarction (STEMI) and stable chronic coronary artery disease (CAD) (20). The importance of inflammatory biomarkers in both diagnosing and determining the prognosis for AMI are established. Furthermore, several newer biomarkers have recently been determined and may soon be used clinically. Therefore, in this study we will evaluate whether the inflammatory biomarker YKL-40 alone or in combination with suPAR could be a new biomarker for diagnosis, monitoring the treatment and prognostic biomarker in patients with AMI. Furthermore, the aim was to study whether there was an association between plasma YKL-40 and suPAR markers of inflammation in AMI.

Methods

Participants

The protocol of this study was approved by the Ethics Committee. All of the patients were informed of the details of the study, and the written consent of each patient was received. The ethic number was 2013/89. The diagnosis of AMI was based on the following criteria: 1) Symptoms of ischaemia, 2) New or presumed new significant ST-segment–T wave (ST–T) changes or new left bundle branch block, 3) Detection of a rise and/or fall of cardiac biomarker values [preferably cardiac troponin (cTn)] with at least one value above the 99th percentile upper reference limit (URL), 4) Development of pathological Q waves in the ECG, 5) Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality, and 6) Identification of an intracoronary thrombus by angiography or autopsy. (21). The exclusion criteria for the cases comprised the following: a) patients with renal disease, b) thyroid disease, c) with a body mass index (BMI) more than 35, d) chronic inflammatory diseases, e) major surgery in last 6 months, f) malignancy. Control subjects were volunteers recruited from the hospital staff. All subjects were assessed by clinical examination and some laboratory tests including electrocardiogram (ECG) and routine biochemical tests. BMI was calculated as kg/m². History of smoking and alcohol consumption was noted in details. All participants were also investigated for conventional risk factors (BMI, serum lipid profile).

Sample Collection and Preparation

A venous blood sample was collected simultaneously from each patient on the first 24 hr and first 48 hr after occurrence of AMI. Venous blood samples were obtained from the antecubital fossa of the arm. Serum samples were obtained after suitable centrifugation and samples, stored in aliquots at −20°C until the time for analysis.

Biochemical Analysis

We measured serum lipid profile, aspartate aminotransferase (AST), alanine aminotransferase (ALT) activities. High-density lipoprotein cholesterol (HDL-C) levels were determined with direct enzymatic method without precipitation (Randox, UK). Low-density lipoprotein cholesterol (LDL-C) levels were calculated with Friedewald formula. Estimation of other parameters was done by routine methods using autoanalyzer (Synchron LX20 system, Beckman Coulter, CA, USA). The serum concentrations of CK-MB and cTnI were determined by using UniCel Dxi 800 analyzer (Beckman Coulter, CA, USA). The cut-off values for CK-MB and cTnI were set at 6. 3 ng/ml and 0.04 ng/ml, respectively. The measurement of all the cardiac markers using the analyzer in each sample was completed within 50 min.
suPAR Analysis

Serum suPAR levels were detected in serum samples using the AssayMax Human Urokinase Receptor (uPAR) ELISA Kit (Assaypro, St. Charles, MO, USA) in accordance with the manufacturer’s guidelines. This assay employed a quantitative sandwich enzyme immuno assay technique that measured suPAR. Serum samples were diluted 1: 4 in the supplied buffer and measured. Absorbance was measured at 450 nm on an ELx800 Absorbance Microplate Reader (Biotek, Winooski, VT, USA).

YKL-40 Analysis

Serum YKL-40 levels were detected in serum samples using the Assayprotech Human chitinase-3-like protein 1 ELISA Kit (Assay Biotechnology, USA), in accordance with the manufacturer’s guidelines. This assay employed a quantitative sandwich enzyme immuno assay technique that measured YKL-40. Serum samples were diluted 1: 50 in the supplied buffer and measured. Absorbance was measured at 450 nm on an ELx800 Absorbance Microplate Reader (Biotek, Winooski, VT, USA). The results were expressed for serum suPAR and YKL-40 levels as ng/mL for both.

Statistical Analysis

Statistical analyses were performed using SPSS version 16.0 (SPSS Inc., IL). To compare the ratio of categorical variables, we used the Chi-squared test. The normality of the variables was evaluated using the one-sample Kolmogorov–Smirnov test. Total cholesterol (TC), LDL-C, BMI and age, were distributed parametrically but HDL-C, triglycerides (TG), AST and ALT were not normally distributed nonparametrically. Independent Samples T-test and Mann–Whitney U test were used for comparing mean and the median values, respectively. We performed (intergroup comparisons) independent samples T-test to compare the difference in the levels of serum suPAR and YKL-40 between healthy subjects and AMI patients. In addition, intragroup comparisons (first day and second day) were performed by paired-sample T-test. The correlations between variables were tested by Pearson’s correlation test. All data are expressed as mean ± standard deviations (SDs). Differences were considered significant at a probability level of p < 0.05. The YKL-40 and suPAR values were analyzed using ROC (Receiving Operating Characteristics) curve analysis. When a significant cut-off value was observed, the sensitivity, specificity were presented.

Results

Clinical characteristics and biochemical parameters of the subjects were presented in table 1. TC, TG, AST, ALT, and LDL-C levels of the AMI patients were significantly higher, whereas HDL-C level was significantly lower than those of the healthy subjects. In addition, no significant differences were observed in age, gender and BMI in AMI patients and healthy subjects.

Serum suPAR and YKL-40 levels of the groups were presented in table 2. Serum suPAR and YKL-40 levels were significantly higher in the first and second day of AMI patients than the healthy subjects (p < 0.001 and p < 0.001, respectively). In addition, intragroup comparisons (first day and second day) were presented in Table 3. Serum YKL-40 levels were significantly higher in the first day of AMI patients than second day of AMI patients (p < 0.01). In addition, there were no different between serum suPAR levels in the first day and second day of AMI patients (p = 0.34).

We were presented ROC analyses to compare the diagnosis in the first day and prognosis in the second day value of suPAR and YKL-40 levels of AMI patients in figure 1 and 2. We therefore, tested whether the predictive value of YKL-40 was equal or superior to suPAR by using ROC curve. We found that first day suPAR value is an AUC of 0.92 (cutoff value 3.16 ng/mL, sensitivity 91 %, specificity 81 %) and first day YKL-40 value is an AUC of 0.99 (cutoff value 44 ng/mL, sensitivity 95 %, specificity 94 %). In addition, second day suPAR value is an AUC of 0.81 (cutoff value 3.08 ng/mL, sensitivity 75 %, specificity 83 %) and second day YKL-40 value is an AUC of 0.94 (cutoff value 42 ng/mL, sensitivity 90 %, specificity 93 %). YKL-40 did show superiority compared to suPAR in predicting AMI.

Simple correlation analysis was performed to investigate the association between serum suPAR and YKL-40 levels. There were no correlation between serum suPAR and YKL-40 levels in AMI patients. Serum suPAR and YKL-40 levels in AMI were independent of each other biomarker in diagnosing for AMI.
**Table 1.** Clinical and demographic characteristics of the patients and controls.

<table>
<thead>
<tr>
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<th>Control Subjects n=70</th>
<th>AMI n=55</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>54.03 ± 6.89</td>
<td>55.85 ± 11.26</td>
<td>0.321</td>
</tr>
<tr>
<td>Sex (male/female)</td>
<td>48M/22F</td>
<td>45M/10F</td>
<td>0.069</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>26.96 ± 2.57</td>
<td>28.00 ± 3.29</td>
<td>0.062</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>-</td>
<td>21.66</td>
<td>-</td>
</tr>
<tr>
<td>Current smoking (%)</td>
<td>-</td>
<td>80</td>
<td>-</td>
</tr>
<tr>
<td>Diabetes mellitus (%)</td>
<td>-</td>
<td>16.66</td>
<td>-</td>
</tr>
<tr>
<td>Total Cholesterol (mg/dL)</td>
<td>178.15 ± 16.88</td>
<td>196.86 ± 46.57</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Triglycerides (mg/dL)</td>
<td>90.55 ± 28.89</td>
<td>170.45 ± 124.54</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HDL-C (mg/dL)</td>
<td>46.69 ± 9.74</td>
<td>33.01 ± 6.38</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LDL-C (mg/dL)</td>
<td>115.59 ± 21.14</td>
<td>126.92 ± 30.63</td>
<td>0.032</td>
</tr>
<tr>
<td>AST (U/L)</td>
<td>18.60 ± 3.11</td>
<td>72.73 ± 54.46</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ALT (U/L)</td>
<td>15.95 ± 3.54</td>
<td>29.95 ± 13.99</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>cTnI (ng/mL)</td>
<td>-</td>
<td>30.31 ± 35.83</td>
<td>-</td>
</tr>
<tr>
<td>CK-MB (ng/mL)</td>
<td>-</td>
<td>114.17 ± 113.60</td>
<td>-</td>
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</table>

*Serum samples were obtained at the time of hospitalization.
BMI, body mass index; HDL-C, high-density lipoprotein-cholesterol; LDL-C, low-density lipoprotein cholesterol; AST, aspartate aminotransferase; ALT, alanine aminotransferase; cTnI, cardiac troponin I;
CK-MB, creatine kinase MB.

**Table 2.** Serum biomarkers of the patients and controls.

<table>
<thead>
<tr>
<th></th>
<th>Control Subjects n=70</th>
<th>AMI patients First day n=55</th>
<th>AMI patients Second day n=55</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>suPAR (ng/mL)</td>
<td>2.26 ± 1.92</td>
<td>6.58 ± 3.24***</td>
<td>5.86 ± 4.56***</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>YKL-40 (ng/mL)</td>
<td>37.11 ± 4.30</td>
<td>69.10 ± 16.58***</td>
<td>60.64 ± 16.01***</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

1 All values are mean ± standard deviation.
2 suPAR: Soluble urokinase plasminogen activator receptor
3 YKL-40: Chitinase 3-like protein 1
4 *** p<0.001 compared with control group (Independent samples T-test;)

**Discussion**

AMI has high mortality rates, therefore accurate and rapid diagnosis of AMI is essential. Researching new biomarkers that could be more sensitive or shorter time periods for testing. Our results have demonstrated that, both on the first and second day, serum suPAR and YKL-40 levels were increased in patients with AMI compared to the healthy subjects. In addition, serum YKL-40 levels were significantly higher in the first day of AMI patients than second day of AMI patients.

It was shown that highest YKL-40 mRNA expression is seen in macrophages in the early lesion of atherosclerosis (9,14). Serum YKL-40 levels have been increased in patients suffering AMI. YKL-40 could a possible screening or diagnostic marker for coronary atherosclerosis (8,9) and be used for monitoring the efficiency of medical treatment of patients with CAD (8).
Our findings were in agreement with previous studies. Wang et al. (20) and Hedegaard et al. (22) have found that plasma YKL-40 was significantly increased in patients with MI during the first 24 hour after admission compared to controls. The increased YKL-40 level decreased over time, but remained significantly elevated one month after MI compared to controls. Moreover it has been concluded that level of YKL-40 was positively correlated with the severity of patients with non-ST segment elevation acute coronary syndrome. YKL-40 was lower after treatment, when compared with the control group (23). In patients with CAD, it has been reported that plasma YKL-40 was increased (24, 25). In another study, Michelsen AE et al. (26) have found that serum YKL-40 level was significantly elevated in patients with carotid atherosclerosis. Nøjgaard C et al. (27) have found that Serum YKL-40 at the time of admission was higher in patients with AMI than in patients with stable coronary artery disease and healthy participants.

uPAR, known to be present on such inflammatory cells as monocytes and macrophages. When exposed to proteases, metalloproteinases, and elastases released from activated monocytes and macrophages, cell-surface–bound uPAR is cleaved, resulting in the release of suPAR (7). Cytokines released from activated monocytes and lymphocytes stimulate the release of suPAR from neutrophils (IL-8), endothelial cells (IL-1β), and monocytes (TNF-α) (7,28). Enhanced uPAR expression on monocytes from patients with AMI [29] was associated with increased cell adhesion to the uPAR ligand vitronectin (15,29). uPAR has a regulatory role in integrin-mediated cell adhesion (15) in AMI (29). Soluble factors (probably inflammatory cytokines) in plasma from patients with AMI can directly activate integrin-mediated and uPAR-mediated adhesion (29).

In our study, we found that serum suPAR level was increased in patients with AMI compared to the healthy subjects. In the previous studies; Edsfeldt A. et al. (7) reported that plaque levels of uPAR and suPAR correlate with levels of macrophages and lipids in the plaque. Persson M. et al. (30) found that suPAR is associated with increased occurrence of carotid plaque and increased incidence of ischemic stroke and CAD. Lyngbæk S. et al. (31) reported that suPAR is a strong predictor of adverse long-term outcomes and improves risk stratification beyond traditional risk variables in chest pain. Ascitto G. et al. (32) found that the reduced level of suPAR in human carotid plaques of subjects on long-term treatment with beta-blockers suggests their possible

<table>
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<th>Table 3. Serum biomarkers in the first and second day of AMI patients.</th>
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<tr>
<td>AMI patients</td>
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<tr>
<td>n=55 First day</td>
</tr>
<tr>
<td>suPAR(ng/mL)</td>
</tr>
<tr>
<td>YKL-40 (ng/mL)</td>
</tr>
</tbody>
</table>

1All values are mean ± standard deviation.
2 SuPAR: Soluble urokinase plasminogen activator receptor
3 YKL-40: Chitinase 3-like protein 1
4 p; paired sample t test

**Figure 1:** For first day suPAR and YKL-40 roc curve below.

**Figure 2:** For second day suPAR and YKL-40 roc curve below.
protective role in plaque inflammation. Lyngbæk S. et al. (33) reported that suPAR is a stable plasma biomarker after ST-segment elevation myocardial infarction. Beside these findings same author also found that suPAR provides prognostic information of CVD risk beyond Framingham Risk Score (34). Persson M. et al. (35) found that elevated level of suPAR is, independently of established cardiovascular risk factors, associated with an increased incidence of CVD in elderly subjects. Chavakis T. et al. (36) found that suPAR from vascular cells is upregulated by proangiogenic as well as proatherogenic growth factors and cytokines, is preferentially released towards the basolateral side of endothelial cells and accumulates in the vessel wall. Pawlak et al. (28) found that suPAR correlated with several of the main proinflammatory cytokines and chemokines, in plaque tissue, involved in the atherosclerotic process, including IL-6, IL-1β and TNF-α.

Study Limitations

The present study has some limitations. We did not measure the serum suPAR and YKL-40 levels in the first few hours after the onset of AMI and after second day of AMI. Further studies are needed for the assessment of serum suPAR and YKL-40 levels on the time of admission and in larger study groups.

Conclusion

In the present study, we determined higher serum suPAR and YKL-40 levels on the first and second day of AMI in patients as compared to the healthy subjects. In addition, serum YKL-40 levels were significantly higher in the first day of AMI patients than second day of AMI patients. The increased YKL-40 level decreased on the second day of AMI in patients. We suggest that serum YKL-40 and suPAR are a clinically useful marker for myocardial ischemia, remodelling and may be prognosis.

Funding

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References


Longitudinally Giant Left Ventricular Thrombus after Anterior Wall Myocardial Infarction

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Abstract

Incidence of post-infarction left ventricular (LV) thrombus is reduced by modern methods of revascularization and treatment with intensive antithrombotic agents. LV thrombus may be an important cause of morbidity and mortality due to relatively high risk of embolization. Therefore, the diagnosis and appropriate management is crucial. The paper introduces a successful treatment of massive, mobile LV thrombus originating from the apical aneurysm and extending to the left ventricular outflow tract.

Keywords: Acute myocardial infarction, thrombosis, apical aneurysm.

Introduction

Nowadays incidence of post-infarction left ventricular (LV) (1,2) is greatly reduced by routine primary percutaneous intervention and intensive anticoagulant therapy (1,2). The risk of LV thrombus formation is higher within the first few weeks after acute myocardial infarction (MI), on the other hand spontaneous resolution also may occur (1). Likewise the risk of thrombus formation is higher in anterior MI than other infarct locations (3). Two-dimensional echocardiography has high sensitivity (95%) and specificity (85-90%) in the diagnosis of LV thrombus (4,5). LV thrombus is often located within the apical, rarely septal (11%) and inferoposterior wall (3%) (5). We want to introduce a case of MI with mobile and massive LV thrombus which was originated from the apical aneurysm and extending to LV outflow tract and was successfully treated with oral anticoagulant therapy.

Case

54-year-old man was admitted with shortness of breath and chest pain, for a week. There was a heavy cigarette use in medical history. Physical examination revealed resting tachypnea and tachycardia. Electrocardiogram showed sinus rhythm and anteroseptal MI age undetermined. Transthoracic echocardiographic examination demonstrated a mobile and massive LV thrombus (63 x 18 mm) which was originated from the apical aneurysm and extending longitudinally to LV outflow tract. Transesophageal echocardiographic examination confirmed longitudinal LV thrombus that occupied half of the cavity (figure 1A-1B). Coronary artery angiography showed critical stenosis in the proximal of left anterior descending artery (figure 2A-2B). Surgery (aneurysmectomy, thrombectomy and coronary artery bypass graft surgery) was recommended but the patient refused all treatment.

Figure 1. Transesophageal echocardiographic images show longitudinal left ventricular thrombus that occupying a half of the cavity.
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Figure 2. Coronary artery angiography demonstrates critical stenosis of the proximal of left anterior descending artery.

options. Thus oral acetyl salicylic acid and vitamin K antagonist were started. Eighth week follow-up examination by transthoracic echocardiography revealed that the thrombus was completely disappeared (figure 3A-3B). Any embolic event was not observed during follow-up period.

Discussion

LV thrombus is clinically important because of the risk of embolism. Previously the risk of embolization is nearly 10% but today has decreased to 2-3% (5). It has been suggested that the thrombus extending ventricular cavity and mobile has a greater risk for embolization (5).

Similarly, increased thrombus size, central echoluceny and hyperkinetic myocardial segment adjacent the thrombus are associated increased risk of embolism (5). On the other hand, there is no consensus on the most appropriate treatment option for the LV thrombus. Thrombectomy, thrombolysis and anticoagulant therapy are options (6). Surgery is preferred especially if thrombus large, mobile and extending into LV cavity (7). Treating with fibrinolytic agents is not preferred because of the high risk of embolization. The oral anticoagulation with vitamin K antagonist therapy is regarded as a standard therapy option especially for mural thrombus (5). Furthermore there are some case reports about the successful treatment with the new oral anticoagulants (NOAC) for LV thrombus (8,9).

As a conclusion LV thrombus is a rare complication of myocardial infarction. Embolization of thrombus can cause severe morbidity and mortality. Therefore early diagnosis and proper management are important.

References

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Coexistence of Ectasia and Myocardial Bridge on the Same Coronary Artery Segment

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Abstract

Coronary artery ectasia (CAE) is the dilatation of coronary artery segment just about 1.5 times than normal adjacent segment. Myocardial bridge (MB) is rare congenital anomaly of coronary arteries, characterized by systolic compression of the vessel segment. In this article, we report on a case of the coexistence of CAE and MB in the same segment of left anterior descending artery (LAD) in an 82 year old patient with acute coronary syndrome.

Keywords: Coronary artery ectasia, myocardial bridge, acute coronary syndrome

Introduction

Coronary artery ectasia (CAE) is the dilatation of coronary artery segment just about 1.5 times than normal adjacent segment (1). CAE is an uncommon disorder diagnosed in one to 4% of patients undergoing coronary arteriography (2). There are various causes of CAE as atherosclerosis, connective tissue diseases and iatrogenic trauma (3). The most common among them is the atherosclerosis. Myocardial bridge (MB) is defined as an anomalous course of a coronary artery, in which an epicardial vessel penetrates intramyocardially, with occurring compression during systole (4). The angiographic prevalence of MB in the general population is between 0.15% and 25% (4,5). The proximal left anterior descending artery (LAD) is the main site affected by MB, occurring with a reported relative incidence of 46% of the MB cases (5,6). The length of MB can range from 10 to 50 mm (7).

Case

An 82-year-old male admitted to our emergency department with the complaint of chest pain in an unstable manner. His medical history included only hypertension. He had been treated in another hospital for non-ST-elevation myocardial infarction (NSTEMI) in the previous week but had no improvement. Physical examination when he was transported our department, his temperature was 36.8 °C; pulse rate, 82 beats/min; blood pressure, 144/81 mmHg; respiratory rate, 18 breaths/min; and oxygen saturation, 99% on room air. His jugular venous pressure was approximately 6 cm H₂O. Cardiovascular examination had no-significant findings. Lungs were clear on auscultation bilaterally, and no peripheral edema was present. There were dynamic ST-segment and T-wave changes in his serial electrocardiogram (ECG) especially on anterolateral precordial derivations. The measured troponin level was 0.265ng/ml. The other biochemical parameters were unremarkable except mild anemia and mild thrombocytopenia. Systolic function of the left ventricle was found to be normal in two-dimentional echocardiography. Patient was taken emergently to the coronary angiography laboratory. Coronary angiography was performed and three-vessel disease was detected. Additionally, LAD was found to be ectatic especially in the middle segment (Figure A-B). Also a severe MB (causing a stenosis of 90 % during systole) was noticed in the same region.

Figure 1. A. Selective left coronary angiogram demonstrating ectasia of the middle segment of the LAD in diastolic phase; B. The left coronary angiogram shows lesions of 80%-90% systolic narrowing at the middle of LAD, and ectasia is not seen. There is a hint of LAD systolic compression.
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Discussion

CAE have been defined as a dilatation in a coronary artery segment to more than 1.5 times the diameter of adjacent normal coronary segments (2). Markis and colleagues (8) designed a classification system in a study of 30 patients with coronary artery ectasia; diffuse ectasia of 2 or 3 vessels was classified as type I, diffuse disease of 1 vessel and localized disease in another vessel as type II, diffuse ectasia of 1 vessel only as type III, and localized or segmental ectasia as type IV. The reasons of CAE are multifactorial: approximately 50% of CAE are thought to be caused by atherosclerosis; other risk factors are congenital causes, inflammatory or connective-tissue disorders (9). Postmortem histologic assessment of these patients with CAE showed underlying changes that were similar to those in patients with atherosclerotic lesions diffuse hyalinization, together with intimal and medial damage which supported an overlapping pathophysiologic mechanism (10,11).

Myocardial bridge (MB) occurs when a band of myocardial fibers overlies a segment of the coronary artery, which results in mechanical stenosis secondary to systolic compression. It is described by the following functional signs; systolic compression of the bridge segment of the coronary artery; accelerated flow velocity at early diastole (finger-tip phenomenon); no or reduced systolic antegrade flow; decreased diastolic/systolic velocity ratio (5). Polacek and Kralove (12) found that the relative frequency of MB involving the LAD was 70%, the circumflex artery 40%, and the right coronary artery 36%; Macroscopic observations on a total of 1056 hearts showed that 23% of MB involved the left anterior descending artery and only 5.7% involved the right coronary artery (13).

Conclusion

In this manuscript, coexistence of myocardial bridge and coronary artery ectasia in the same segment of left anterior descending artery is presented. We considered the atherosclerotic process added on the congenital muscular bridge leaded to the formation of ectatic muscular bridge in this patient, because, our patient did not have the other possible causes CAE. In the angiography, significant difference in the diameter of LAD during systole and diastole drew our attention, so we called LAD as ambivalent. This association between CAE and MB is a phenomenon that warrants further study to determine its incidence and possible causes. According to the best of our knowledge, coexistence of muscular bridge and ectasia in the same segment has not been reported previously.

References

Introduction

Dermatofibrosarcoma protuberans (DFSP) is a rare, locally aggressive cutaneous mesenchymal skin tumor (1). Typically it presents as a solitary, slowly growing, painless cutaneous nodule. After a period of inactivity it can grow slowly and then cause characteristic protuberant nodules. Most cases are observed in the third and fourth decades of life, but newborns and children can be affected (2). Several histological variants of DFSP have been described (3, 4). Here we report a patient with myxoid DFSP, rarely reported in the literature.

Case Report

A 35-year-old man was presented with a 5x2 cm in size, violaceous, painless, enlarging nodular lesion on the lower abdomen (Figure 1). The lesion had been present for approximately nine years and was gradually increasing in size. In the affected area there had been no history of trauma or any preexisting skin lesions. Clinical examination showed erythematous to brownish nodule, with reddish plaque on lower abdomen. He denied any treatment of the lesion in the past. No other lesion was noted. The lymph nodes in the head and neck region and the axillae were nonpalpable. A skin biopsy was performed. On microscopic examination, the tumor consisted of spindle-shaped cells that were strongly positive for CD34 with a typical storiform pattern and myxoid stromal changes.

Discussion

DFSP is a low grade spindle cell neoplasm of fibroblastic differentiation of the dermis and underlying soft tissue. Estimates of the overall incidence of DFSP in the United States are 0.8 to 4.5 cases per million persons per year (1, 2). It can be seen in all races. DFSP is found in similar distribution in men and women, although some large series suggest a slight male predominance (5). DFSP most commonly occurs between 20 and 50 years of age, although its can appear at any age. It occurs less frequently in children, and congenital forms of DFSP have been reported (2). Pathogenesis of dermatofibrosarcoma protuberans (DFSP) is unknown. Laboratory studies have shown that chromosomal aberrations (translocation of chromosomes 17 and 22) may contribute to the pathogenesis of DFSP (6, 7). In 10-20% of patients with this tumor, trauma at the site seems to be incriminated. Surgical and burn scars, radiodermatitis, vaccinations and sites of central venous lines have all been reported as sites of DFSP (8-10). In our patient, in the affected area there had been no history of trauma or any preexisting skin lesions.

DFSP most commonly presents as a slow growing, asymptomatic, erythematous, flesh-colored, or violaceous plaque that slowly enlarges over months.
to years. It becomes raised, firm, and nodular (1). It also can present as a nonprotuberant, atrophic, violaceous lesion resembling morphea, sclerosing basal cell carcinoma, lipoma, dermatofibroma or scar (5).

The most common location for a DFSP is on the trunk and proximal extremities, generally on the chest and shoulders followed by the proximal extremities, head and neck. Lesion size usually ranged from 1-5 cm but can reach up to 20 cm in advanced cases (1).

The low-grade DFSP (85-90 %) is the most common condition. The remaining 10-15% constitute the high-grade variant, which is more frequently associated with local recurrence and metastasis (11, 12). The potential for distant metastasis is low (< 5%), most often to the lung, also to regional lymph nodes, bone, heart, and brain (5, 13, 14).

Definitive diagnosis requires a core needle or incisional biopsy. The correct diagnosis can be made by review of hematoxyline and eosin-stained sections, combined with immunohistochemical staining. DFSP is composed of dense, monomorphic cells with spindle-shaped nuclei that are arranged in a storiform or matlike pattern in the center of tumor nodules, and infiltrate the dermal stroma peripherally. Immunohistochemical expression of CD34 has been considered characteristic for the diagnosis of DFSP. Approximately 80%-100% of DFSP express this marker, although between 10% and 20% are negative. Factor XIIIa is very useful in the differential diagnosis between DFSP and cellular fibrous histiocytomas, as it is usually negative in DFSP (13, 15).

Several histological variants of DFSP have been described including the Myxoid, Fibrosarcomatous, Pigmented (Bednar tumor), Giant cell fibroblastoma, Atrophic DFSP, Sclerosing DFSP and Granular cell types (3, 4). Myxoid DFSP doesn’t differ from conventional DFSP in terms of clinical characteristics or prognosis. It’s contain an abnormal type of connective tissue that is called myxoid stroma. Almost all cases are positive staining for CD34, and negative for other markers, such as S-100, desmin.
and actin (16). Our histopathology also showed typical features, characteristic of DFSP.

Treatment is primarily surgical, with chemotherapy and radiation therapy sometimes used. Wide surgical excision is the standard treatment in localized, resectable cases. Mohs micrographic surgery is the treatment of choice for recurrent tumors. The high recurrence rate for conventional Radiotherapy has been used as an adjuvant therapy after wide surgical excision or in those patients who have inoperable macroscopic disease. Imatinib is a tyrosine-kinase inhibitor used in the treatment of multiple cancers. It is gold standard for treatment of inoperable, recurrent and/or metastatic DFSP (17).

We presented a case of myxoid DFSP, rarely reported in literature. Dermatologists should be aware of this rare entity and should make wide excision and reduce risk of recurrence.

References

Dear Editor,

Breast cancer in the opposite breast diagnosed within a year after initial breast cancer is known as synchronous breast cancer. The incidence of synchronous cancer in both breasts is 2%, with very rare observation of different histological types (1). Lobular carcinoma histology, young age, family history, multicentric disease, positivity for progesterone receptors and nulliparity are among factors increasing the risk of bilateral breast cancer (2).

A 73-year old woman with no family history of breast cancer applied to our clinic due to a mass felt in the left breast and mammography found a spiculated contoured mass, one in each breast. After mammography breast ultrasound (US) found two heterogeneous hypoechoic solid mass lesions with irregular edges and posterior acoustic shadowing: 15 x 12 mm in the lower outer quadrant of the left breast and 10 x 9 mm on the midline of the upper quadrant of the right breast. The lesions in both breasts were marked with wire accompanied by US and excised. After excision histopathological investigation reported the lesion in the right breast as compatible with grade 2 invasive lobular carcinoma while the lesion in the left breast was compatible with grade 2 invasive ductal carcinoma. The patient later had bilateral radical mastectomy.

The diagnosis of synchronous cancer in both breasts can easily be missed owing to unawareness of selecting the appropriate imaging method and low index of suspicion. Delay in diagnosis of breast cancer decreases the duration of life expectancy. As a result the assessment of unilateral breast cancer patients for development of synchronous bilateral breast cancer becomes very important. Consequently, correct diagnosis of different histological types in bilateral breast cancer allows for appropriate treatment protocols to be applied and increases the duration of life expectancy. In our case mammography and ultrasound were used efficiently in the diagnostic stage and were helpful in directing the treatment stage.

Figure 1. Craniocaudal mammography of right breast (a), ultrasound of the spiculated mass in right breast (b), invasive lobular carcinoma (x200 hematoxylin-eosin) in right breast (c).
Letter to the Editor

Figure 2. Craniocaudal mammography of left breast (a), ultrasound of the spiculated mass in left breast (b), invasive ductal carcinoma (x200 hematoxylin-eosin) in left breast (c).

References


Is Sodium Bicarbonate Therapy Still Up To Date?

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Abstract

Sodium bicarbonate (SB), which has a vital role in the regulation of acid-base balance of all tissues and organs, is one of the most important buffering systems of the body. SB plays an important role in the treatment of poisoning caused by numerous agents including mainly salicylate and tricyclic antidepressants. In metabolic acidosis (MA) occurred in patient with systemic and metabolic diseases, first, the primary disease should be treated and in the case of low bicarbonate levels such as diarrhea and renal tubular acidosis, missing SB should be recovered. As the kidney has an important role in acid-base balance, SB is widely used in the treatment of acute and chronic renal failure. Although there is no conclusive evidence to prevent contrast nephropathy, SB comes to the fore compared to other agents. SB is used due to MA and its effects occurring in acute renal failure. In addition, SB treatment applied to reduce the increased acid levels in chronic kidney failure may reduce mortality. While SB can be used as individualized in lactic acidosis and cardiac arrest cases, it can be used safely as a performance enhancer for athletes. SB is used widely in gastrointestinal tract diseases due to its antacid effects and its routine use is not recommended in diabetic ketoacidosis. These data demonstrate that SB is still popular and it will retain its popularity in the near future.

Keywords: Sodium bicarbonate, metabolic acidosis, toxicology, contrast induced nephropathy, lactic acidosis.

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Introduction

Acid-base balance is vital for the body as all the tissues and organs are very sensitive to pH shift. Acid-base balance in the organism is kept through the major chemical buffering system, mechanisms for respiratory adjustment and renal adjustment. Particularly, the kidney has a crucial role for keeping acid-base balance by means of many mechanisms. Bicarbonate reabsorption and regeneration, and acid excretion are some of these mechanisms. When blood pH level is high, kidneys increase excretion of bicarbonate through urine. However, it reduces urinary bicarbonate excretion when blood pH is low. Carbonic acid/ bicarbonate buffer systems, commonly available in the body, are generally extracellular liquid buffer systems and it is the most rapid buffer system of the body. When pH is 7.4, bicarbonate/carbonic acid ratio is 20, and this ratio is stable under normal conditions. Once bicarbonate/acid ratio rises above 20, acidosis develops, whereas alkalosis occurs when it reduces lower than 20. In this ratio, bicarbonate affects kidneys, while carbonic acid demonstrates its effect on the lungs. On the other hand, changes in bicarbonate levels lead to changes in metabolic blood gas levels, and changes in carbonic acid levels cause changes in respiratory blood gas.

Sodium bicarbonate (SB) is being used therapeutically in many areas (1, 2). Treatment of metabolic acidosis (MA), occurring when bicarbonate concentration is missing, are provided through the replacement of the SB. Additionally, SB plays an important role in the treatment of poisoning which occurs due to mainly tricyclic antidepressants (TCA), and a large number of agents. SB is widely used in the treatment of acute and chronic renal failure because of its important role in maintaining acid-base balance. In this review, both the treatment areas in which SB is used will be evaluated and the actuality of SB will be discussed.

Metabolic acidosis

MA is formed when the anion load exceeds the cation load in the plasma. In the normal arterial blood, pH level varies between 7.35 and 7.45. Plasma bicarbonate concentration is generally estimated through using blood gas from pH and plasma partial carbon dioxide pressure (pCO₂) values. Blood gas measurements include three parameters as total blood carbon dioxide concentration (tCO₂), pCO₂ and plasma bicarbonate concentration (HCO₃⁻) (3). Treatment for primary disease should be applied first as MA is a biochemical parameter of systemic diseases and metabolic disorders. Ensuring electrolyte and volume balance in cases of MA including high anion gap is often sufficient. The degree of arterial
pH and the presence of symptoms due to acidosis are important in the SB treatment. Decreasing pH level in diabetic ketoacidosis (DKA), lactic acidosis (LA) and the development of acute conditions such as septic shock is associated with the severity of the disease and requires immediate treatment. SB treatment is required if, apart from MA, symptoms of severe hyperkalemia, hypotension not responding to volume treatment, coma, respiratory depression, respiratory acidosis and congestive heart failure are existed. There has been no clear evidence that MA, which occurs in humans, causes serious damage. (4). So, a successful treatment approach can only be possible with the treatment of underlying causes.

SB replacement is useful in cases such as diarrhea and renal tubular acidosis cases which have low bicarbonate level. On the other hand, no effect of SB, which is used symptomatically, on clinic and mortality, has been demonstrated (5, 6). However, further studies are needed to prove the beneficial effects of SB, which is used symptomatically (7, 8). In the most recent studies, it is estimated that MA worsens the kidney failure and it is just recommended to apply because of renoprotective effects (9).

**Toxicology**

While alternative treatment strategies in toxicology exist, SB is still the most important treatment option in several toxic actions. With SB treatment, serum alkalinization, alkalization of urine, and sodium ions load occur (10). SB is widely used in over-dosage of drugs that cause sodium channel blockade. As a result of poisoning with sodium channel blockers (SCB), seizures and ventricular arrhythmias occur. Cardiotoxicity is the most important cause of mortality related to SCB. Electrocardiography (ECG) has a vital role in the emergency diagnosis of poisonings caused by SCB and ECG plays a more important role than of serum concentrations of the drugs. SB is the most commonly used agent in the treatment of TCA and salicylate poisoning. In TCA poisoning, with fast sodium channel blocking, it has been indicated that ECG abnormalities have occurred in the early phase and it has returned to normal with SB infusion (11). Additionally, SB treatment was reported to normalize cardiac rhythm and be effective in the treatment of cardiac rhythm disorders such as cocaine-induced ventricular dysrhythmia (12, 13). However, SB is used actively in many drugs and substance poisoning. These drugs are mainly; type 1 and type 1C antiarrhythmics, local anesthetics, antimalarials, dextropropoxyphene, propranolol, carbamazepine, phenobarbital, chlorpropamide, salicylate, diphenhydramine, propranolol, amantadine, cocaine, phenothiazine, quinine, thioridazine, chlorophenoxy herbicides, venlafaxine, and chlorine gas (1, 14). There is no other accepted alternative treatment agent except SB in SCB poisoning. Alternatively, some researchers suggested sodium acetate as an agent. However, the routine use of sodium acetate is not recommended in the case where SB can be used. Although inexpensive sodium acetate has been asserted as an alternative agent, further prospective studies which verify this issue are needed (10). There are studies indicating that alternative treatment is possible by giving high dose inotropic, vasopressin or terlipressin to the patients who have hypotensive shock due to TCA intoxication. However, these studies suggested that SB treatment should be used primarily (15-16). Antidotes application is not commonly recommended in the literature (10). There are some studies indicating that SB can be used in the treatment of drug and substance poisoning even if acidosis does not exist. Indeed, it has been reported that a patient who developed arrhythmia due to TCA intoxication and had alkalis was successfully treated by giving SB (17). In another study, however, 2 patients had deep alkalosis due to aggressive SB treatment and hyperventilation and those patients were then lost (18). Thus, pH target is important for alkalis. 62% of the SB members of the United Nations Poisoning Center said to believe that minimum pH value should be 7.45, and 66% said that maximum pH should be 7.55 to start SB treatment (19). For the treatment of life-threatening poisoning, 50-100 ml from 8.4% SB is applied. Doses can be repeated to keep pH level between 7.45-7.55 by following blood gas. However, in the patients who are in extravasation and have more stable condition, 500 ml from 1.26% SB is recommended due to low skin necrosis risk (20).

**Contrast induced nephropathy (CIN)**

Due to the increasing chronic diseases, radiocontrast procedures are becoming increasingly common in diagnosis. Therefore, physicians have difficulty in taking the decision of radiodiagnostic contrast imaging in high-risk patients. So, to protect those patients, risk assessment in terms of CIN should be done and prophylaxis protocols should be used where necessary. As well as intravenous contrast media administration, contrast-induced acute kidney injury (CI-AKI) is the most prevalent iatrogenic reason of acute kidney injury. On the other hand, in patients who have normal renal function, the incidence is generally known to be low (21).
In studies related to the pharmacological treatment protocols used for protection from CIN in the emergency room, sodium chloride and hydration, N-Acetyl Cysteine (NAC), and SB are the foremost agents. The effectiveness of those protocols has been examined under different dosing schedules. The doses can be applied at varying times between 6-24 hours. Even if some of the patients are admitted to hospitals, an important part of them are discharged. Those protocols cause a loss of considerable time and resources. In the studies, it has not been demonstrated with certainty whether the protocols are superior to each other (22, 23). In the randomized controlled study conducted by Barr et al., 353 patients including patients with diabetes mellitus, congestive heart failure, hypertension or older than 75 years old, who took coronary angiography and had glomerular filtration rate (GFR) lower than 60 ML/min, were examined. Those patients were given sodium chloride infusion or SB to protect them from CIN. In the study, after a contrast agent was given, decrease in GFR more than 25% in the following 1-4 days was accepted as CIN. Thus, the study shows that SB was not superior to sodium chloride (22). In another prospective randomized clinical study conducted by Kama et al., 107 patients who were in at risk of CIN were given NAC, sodium chloride and SB. No significant difference was found among those agents in preventing CIN (23). Koomian et al. discovered that SB and sodium chloride which were given before contrast agent had a protective effect on kidneys and affect the quality of life (24). On the other hand, fenoldopam was found to be ineffective in a large-scale randomized study (25). Likewise dopamine was shown to be ineffective in terms of prevention strategies (26). As for hemofiltration, although it was shown to be useful, it was limited by high cost of implementation and impracticality (27). Dabarca et al. suggested that SB should be added to treatment hydration with sodium chloride after examining 266 studies including patients with cardiovascular disease who had direct contrasting agent exposure (28). However, in a meta-analysis of 19 studies, Jang et al. investigated 3609 patients and asserted that SB was superior to sodium chloride (29).

**Acute renal failure (ARF)**

ARF is a common, serious, but potentially treatable condition which is often accompanied by acidosis. SB treatment is a highly preferred method for patients with ARF due to MA and developing symptoms. Moreover, in people with acute acidaemia (arterial ph<7, 15), myocardial depression and systemic vasodilatation may be developed by decreasing oxygen delivery. And so, the implementation of SB can improve cardiovascular function and tissue perfusion by increasing extracellular pH (30). SB treatment is controversial in patients with ARF as MA may be caused by shock and LA occurring after the deterioration of tissue perfusion. In a review carried out by Hewitt et al., the answer to the question “what are the potential benefits and harms of SB treatment applied orally or intravenously in ARF?” was sought. Due to the lack of randomized controlled trials regarding the use of SB treatment in ARF, no claim was asserted regarding the advantages and disadvantages of SB (31). Although there is not enough evidence in favor of the use of SB, it is still widespread for the treatment ARF related acidosis, and is suggested as a supportive treatment in many nephrology textbooks (32).

**Chronic renal failure (CRF)**

In the treatment of many MA, which include renal tubular acidosis, SB is utilized, which has been suggested by many textbooks of nephrology. Moreover, in order to relieve symptoms and prevent uric acid stones in the kidney, SB is used with the aim of alkalizing urine in patients with cystitis (33). As increased acid levels accelerate CRF progression, low SB level is considered as an independent risk factor of CRF progression (34). In elderly patients with CRF, high level of SB within the normal range is effective to prevent the CRF progression. Kanda et al. discovered that low (<25th percentile) SB level was related to CRF progression, and a 1-mEq/L increase in SB level (in normal range) lowered the risk of CRF progression (35).

The advantages of SB treatment in patients with CRF are being inexpensive, popular and easily accessible. On the other hand, the disadvantages are causing volume overload and the risk of high blood pressure due to the inclusion of sodium. Studies revealed that SB treatment can reduce serum potassium, which may be benefited in patients with CRF that possess the hyperkalemia risk, and get angiotensin-converting enzyme inhibitors (36). Although there is no certain scientific evidence that supports the alkalization therapy done with SB in patients with CRF, SB is commonly used for MA associated with CRF. Additionally, to keep serum bicarbonate in ≥ 22mmol/L level, SB is strongly recommended in current guidelines (36, 37).

**Cardiac surgery**

ARF associated with cardiac surgery occurs in 50% of patients after surgery and it increasingly causes...
mortality and morbidity (38). In a double-blind randomized controlled study, Haas et al. examined 350 adult patients who underwent cardiopulmonary bypass surgery and were given sodium chloride and SB. In addition, SB was seen not to reduce the incidence of, and found to be associated with increased mortality in patients undergoing open heart surgery (39). McGuinness et al. investigated whether perioperative blood and urine alkalinization done with SB reduces acute renal failure associated with cardiac surgery. In that study conducted with 427 patients, it was discovered that SB infusion did not reduce the acute renal failure (38).

Diabetic Ketoacidosis

For many years, SB treatment has been recommended in order to keep pH level in a reliable range. However, it should be noted that the first aim of DKA treatment should not to keep pH level balanced, but to make up for the insulin, which is deficient. Studies in recent years show that bicarbonate treatment does not improve acidemia, and may even be harmful. Duho et al. found that SB treatment did not reduce glucose and ketone levels and did not increase pH (40). In a study compiling 44 works systematically, Chua et al. asserted that SB had no clinical benefit (41). In a recent study, the use of SB was claimed to cause cerebral edema in children with DKA (42). In literature, the studies related to the use of SB on patients with DKA were generally conducted on patients who had between 6.9-7.1 pH levels. No studies on patients having <6.9 pH have been carried out. However, some researchers defend the use of bicarbonate in patients with severe acidemia who have <7, 0 pH (43, 44).

Cardiac Arrest

SB was advised as a first line drug in first Standards for Cardiopulmonary Resuscitation and Advanced Cardiac Life Support written by the American Heart Association (45). In the guidelines published later, restrictions on the use of SB were imposed. In the latest one published in 2010, the use of SB was not recommended. However, SB may be advised to be used in prolonged cardiac arrest after enough alveolar ventilation and effective cardiac compression are performed. Additionally, SB may be useful in some cardiac arrest situations such as MA, hyperkalemia, and TCA overdose.

Lactic acidosis

Exogenous bicarbonate therapy in patients with LA is controversial. Although there is not any negative and positive evidence about SB in patients who have <7.1 pH, the use of SB is recommended. Because, use of the SB prevents various side effects of LA such as decreased left ventricular contractility, arrhythmia, arterial vasodilatation, venoconstriction and impaired response to vasopressors (47). The potential hazards of bicarbonate therapy are increase in arterial and tissue capillaries PCO2, increase in lactate production, decrease of ionized calcium, hypernatremia and an increase in the extracellular fluid volume (48, 49). In a study conducted with 103 patients whose mean age was 66.1, the group having LA and given SB had higher mortality rate. In this study, independent factors affecting mortality were found to be as Sequential Organ Failure Assessment score and SB treatment (50). Because of the limitations and potential side effects of bicarbonate therapy in patients with LA, efforts to find an alternative agent have been accelerated. These agents are Tromethamine, Carbicarb, and Dichloroacetate. No clinical benefit of these substances in terms of mortality could be demonstrated (51, 52). In animal studies on acute LA, it has been demonstrated that selective sodium-hydrogen exchanger 1 inhibitors help to improve hemodynamics and reduces mortality (53). As a result, correction of the underlying cause is always better than bicarbonate replacement. Bicarbonate that was given to patients may become carbon dioxide. Especially in patients with ventilation problems this situation creates serious problems. Although there is no definitive proven benefits of bicarbonate, it is recommended if pH <7.1 in LA. However, it is more effective than other alternatives.

Septic shock

In the studies conducted on patients with septic shock, SB was found to have no effect on mortality and hemodynamic changes in those patients (54). Surviving Sepsis Campaign guidelines, for patients with hypoperfusion-induced lactic acidemia with pH ≥7.15, do not recommend bicarbonate treatment to improve hemodynamic status or to reduce vasopressor requirements (55).

Rhabdomyolysis

SB is often used in preventing the destruction of myoglobin by doing urine alkalinization and its nephrotoxic metabolites (56). There has been little evidence related to the routine use of bicarbonate, mannitol and loop diuretics in rhabdomyolysis. On the other hand, today, aggressive fluid resuscitation with isotonic fluid is used in the majority of the
patients to prevent acute renal failure due to rhabdomyolysis (57).

**Oral use:** SB is widely used in digestive system diseases due to its antacid properties. In a randomized controlled study conducted with 92 patients, it was found that the combination of the use of SB and proton pump inhibitor had a significant effect on reflux esophagitis (58). In another study, SB with omeprazole was found to be very effective in Barrett esophagus (59).

SB is also used as a performance enhancer for athletes. In a meta-analysis examining the effects of SB, sodium citrate and ammonium chloride on performance, it was reported that SB was effective to increase performance and was recommended in short-term high-intensity exercises (60). On the other hand, in another study, SB, which was given before intermittent exercises, was found to have no significant effect on performance even if it induced metabolic alkalosis. However, individual bicarbonate intake based on the time and density of the exercises was recommended as individual performances of the subjects significantly differ from each other (61).

Consequently, SB is still used safely in especially toxicology, MA, some gastro-intestinal diseases and athletes as performance enhancers. Although, there is no conclusive evidence that SB prevents contrast nephropathy, it comes to the forefront compared to the other agents. In LA and cases of cardiac arrest, its use should be individualized. On the other hand, its routine use in DKA is not recommended. In the light of these findings, SB is still a central topic of discussion.

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