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USE OF PSYCHOACTIVE SUBSTANCES AMONG BELGRADE UNIVERSITY STUDENTS WITH DIAGNOSED SOMATIC OR MENTAL DISORDERS

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SUMMARY

Introduction/Objective The objective of this study was to examine the relationship between use of psychoactive substances among University students and diagnosed somatic or mental disorders.
Methods The cross-sectional study was conducted in a population of 2,000 students of the Belgrade University. Four faculties (Medicine, Geography, Economics, Electrical Engineering) from which the students participating in this research were chosen by the method of random choice (by computer listing), conducted in the period April - June 2010.
Results We observed that are more numerous students who used psychoactive substances among students with diagnosed somatic illnesses compared to those without them. Statistical significance was found among students who used tobacco (p=0.027), alcohol (p=0.002), sedatives (p<0.001) and cannabis (p=0.021). Mental disorders are also connected to use of psychoactive substances. The statistical significance was achieved for all psychoactive substances except for alcohol.
Conclusion Use of psychoactive substances is an important issue among University students with diagnosed somatic or mental disorder. Therefore, it is essential to recognize the symptoms and consequences of such behavior, and above all and connection thereof, the importance of prevention which may enhance better solution-seeking via proper education.

Keywords: Psychoactive substances, University students, somatic disorders, mental disorders

SRPSKI

UPOTREBA PSIHOAKTIVNIH SUPSTANCI MEĐU STUDENTIMA UNIVERZITETA U BEOGRADU, SA DIJAGNOSTIKOVANIM SOMATSKIM ILI MENTALNIM POREMEĆAJIMA

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SAŽETAK

Uvod /cilj Cilj ove studije je bio da se ispita povezanost između upotrebe psihoaktivnih supstanci među studentima Univerziteta i dijagnostikovanih somatskih i mentalnih poremećaja.
Metode Sprovedena je studija preseka u populaciji od 2 000 studenata Univerziteta u Beogradu .Četiri fakulteta (Medicinski, Geografski, Ekonomski, Elektrotehnički),čiji su studenti učestvovali u ovom istraživanju u periodu april-jun 2010. godine, bila su izabrana metodom slučajnog izbora (preko kompjuterskog listinga).
Rezultati Mi smo zapazili da je veći broj studenata koji su koristili psihoaktivne supstance bio među studentima sa dijagnostikovanim somatskim bolestima, u poređenju sa onima bez tih bolesti. Statistička značajnost je nađena među studentima koji su koristili cigarete (p = 0.027), alkohol (p = 0.002), sedative (p < 0.001) i kanabis (p = 0 .021). Mentalni poremećaji su takođe povezani sa korišćenjem psihoaktivnih
supstanci. Statistička značajnost je postignuta za sve psihoaktivne supstance izuzev alkohola.
Zaključak Upotreba psihoaktivnih supstanci je važno pitanje među studentima Univerziteta sa dijagnostikovanim somatskim ili mentalnim poremećajem. Stoga je neophodno prepoznati simptome i posledice takvog ponašanja, a pre svega i njihovu povezanost , kao i važnost prevencije koja može poboljšati bolje traženje rešenja putem odgovarajućeg obrazovanja.

Ključne reči: psihoaktivne supstance, studenti Univerziteta, somatski poremećaji, mentalni poremećaji

INTRODUCTION

Risky behaviors have negative influence on the physical health of adolescents. In connection to vulnerable populations, the effects can even be of a large-scale, such populations being patients with somatic diseases [1,2]. Unfortunately, problems associatedwith the drug abuse in the mentioned population have partly been explored in the contemporary academic resources. The same relates to the rate of substance misuse in the general population, with insufficient data [3]. Mental problems are also connected to the drug use, therefore commonly referred to as "the dual diagnosis" as a combination of severe mental disorder and substance use disorder [4,5]. As an example, a case in the USA shows that approximately 7–10 million people suffer from at least one psychiatric disorder followed by a substance use disorder [6]. There are four hypotheses on the causes for the dual diagnosis, as follows: "common factors (risk factors common to both disorders), secondary mental disorder (substance use precipitates mental disorder), secondary substance use ('self-medication hypotheses) and bidirectional (presence of either mental illness or substance use disorder can contribute to the development of the other)" [6]. Another example reveals that approximately at least 10% of the American population use prescribed psychopharmacological medications, which represent approximately 20% of all prescriptions in the USA. In addition, other substances, such as psychoactive drugs, including narcotics, psycho stimulants, and central nervous system depressants are widely used [7,8].

Referring to chronic illnesses, a closer correlation can also be found between health status and quality of life with psychosocial factors than physical disease severity [9]. Moreover, a strong relationship between chronic somatic diseases and mental disorders were established [10-12]. In spite the notion that a variety of patients with chronic somatic diseases have experienced mental disorders, the exact extent of such correlation and the increased risk thereof cannot yet be determined [10]. In the USA, anxiety disorders and mood disorders are the most common mental disorders [13].

METHODS

The cross-sectional study was conducted in a population of 2,000 students of the Belgrade University, in the period April - June 2010. Four faculties (Medicine, Geography, Economics, Electrical Engineering) from which the students participating in this research were chosen by the method of random choice (by computer listing). From each of the faculties an equal number of students per academic year was examined who have received practical training on test day. Students filled out voluntarily an anonymous self-administered questionnaire designed at the Institute of Epidemiology, Faculty of Medicine in Belgrade and has been used in similar studies [14, 15]. The questionnaire included questions related to demographics (gender, age, faculty and year of study, place of residence), social (education and occupation of parents, social status) and behavioral (reasons for starting practising this habit, attitudes related to knowledge of its harmfulness) characteristics. A second part of the questionnaire included questions about whether or not (yes/no) students have diagnosed somatic (diabetes, hypertension, heart disease, chronic bronchitis, bronchial asthma, neurological diseases, gastric or duodenal ulcer, skin diseases) and mental diseases. The third part of the questionnaire included questions about whether or not (yes/no) students have ever used the following psychoactive substances: tobacco, alcohol, sedatives, tramadol, methadone, marijuana, hashish, amphetamine, ecstasy, LSD, cocaine and heroin. Researcher was in charge to provide the questionnaires to respondents in person.

For the evaluation of depression and anxiety the Hamilton Rating Scale for evaluation of depression (HAMD) [16] and Hamilton Anxiety Rating Scale (HAMA) [17] were used and assessed by psychiatrist.

The Institutional review Board approved the study. Informed consent forms were assigned by all students who agreed to participate.

Statistical analysis was performed using descriptive statistics and Chi-square test, Fisher exact test and Student t-test to test group differences. For testing association between variables the Spearman rank correlation coefficient was calculated. The collected data were analyzed using SPSS Statistics Software 24.0 for Windows.

RESULTS

Data were collected from 2,000 students of University of Belgrade, 860 (43%) males and 1,140 (57%) females. The average age of the participants was 21.5 years. From each of the faculties an equal number of students (500) per academic year was examined. Response rate was 99.8%.

Out of 2,000 students, 270 of them (13.7%) have somatic disease. Among them, 123 (14.6%) are males and 147 (13.1%) are females.

There are 20 (1%) students with diagnosed mental disorder.

The distribution of psychoactive substances in relation to diagnosed somatic diseases is shown in table 1. We observed that are more numerous students who used psychoactive substances among students with diagnosed somatic illnesses compared to those without them. Statistical significance was found among students who used tobacco (p=0.027), alcohol (p=0.002), sedatives (p<0.001) and cannabis (p=0.021). According to Fisher's exact test, p-value did not quite achieve the conventional levels of significance for tramadol (p=0.056) and for methadone where was close to being statistically significant (p=0.051).

The distribution of psychoactive substances in relation to the diagnosed somatic diseases is shown in table 2. Our data revealed that students with diagnosed diabetes mellitus used more psychoactive substances compared to students without this illness with significant difference for smoking (p=0.004). For cannabis, according to Fisher's exact test, p-value did not quite reach acceptable levels of statistical significance (p=0.051). Regarding hypertension no significant difference was found. When it comes to heart disease, just for alcohol, LSD, amphetamine and heroin was not found significant difference. For lung diseases no statistical difference was found. Regarding neurological diseases the significant difference was found for smoking (p=0.037), sedatives (p<0.001), tramadol (p<0.001), cannabis (p=0.006), amphetamine (p=0.039), LSD (p<0.001) and heroin (p=0.002).

For gastric and duodenal ulcer, the significant difference was found for sedatives (p=0.014), tramadol (p<0.001), methadone (p<0.001), amphetamine (p=0.027), LSD (p=0.002), cocaine (p=0.009) and heroin (p=0.001). Concerning skin diseases the significant difference was found just for sedatives (p<0.001).

Degrees of depression among students with and without somatic disease are shown in Table 3. Students with diagnosed somatic disease are more depressed compared to students without it, but no significant difference was found.

Degrees of anxiety among students with and without somatic disease are shown in Table 3. Our data revealed that the percentage of students with somatic disease and mild or moderate anxiety is higher than percentage of students without somatic disease, but the percentage of students with expressed anxiety is higher among students without somatic disease with significant difference (p=0.012).

The distribution of psychoactive substances in relation to the diagnosed mental disorders is shown in table 4. The statistical significance was achieved for all psychoactive substances except for alcohol.

Table 1. The distribution of psychoactive substances in relation to diagnosed somatic diseases

Psychoactive substances	Somatic Disease Yes	Somatic Disease No	*P*
Smoking	74 (27.8)	366 (21.7)	0.027
Alcohol	231 (87.8)	1336 (79.8)	0.002
Sedatives	53 (19.6)	175 (10.3)	<0.001
Tramadol	5 (1.9)	11 (0.7)	0.056*
Methadone	2 (0.8)	1 (0.1)	0.051*
Cannabis	49 (18.1)	220 (12.9)	0.021
-Marijuana	48 (18.3)	217 (13.2)	0.026
-Hashish	13 (4.9)	52 (3.2)	0.308*
Amphetamine	8 (3.0)	24 (1.5)	0.071*
Ecstasy	9 (3.4)	35 (2.1)	0.192
LSD	3 (1.1)	15 (0.9)	0.727*
Cocaine	5 (1.9)	20 (1.2)	0.375*
Heroin	5 (1.9)	12 (0.7)	0.071*

p - According to $\chi 2$ test

*According to Fisher's exact test

Table 2. The distribution of psychoactive substances in relation to the next diagnosed somatic diseases

Psychoactive substances	Diabetes Yes - N (%) No - N (%) *p*	Hypertension Yes - N (%) No - N (%) *p*	Heart disease Yes - N (%) No - N (%) *p*	Chronic bronchitis Yes - N (%) No - N (%) *p*	Bronchial asthma Yes - N (%) No - N (%) *p*	Neurological diseases Yes - N (%) No - N (%) *p*	Gastric or duodenal ulcer Yes - N (%) No - N (%) *p*	Skin diseases Yes - N (%) No - N (%) *p*
Smoking	7(63.6) 434(22.3) 0.004*	16(26.2) 425(22.4) 0.483	13(40.6) 428(22.2) 0.014	19(30.6) 422(22.3) 0.120	15(18.3) 426(22.7) 0.346	5(50.0) 436(22.4) 0.037	4(44.4) 436(22.4) 0.114	15(27.3) 426(22.4) 0.395
Alcohol	11(100) 1560(80.8) 0.138*	53(86.9) 1519(80.7) 0.224	26(86.7) 1545(80.8) 0.415	54(90.0) 1518(80.6) 0.068	70(87.5) 1501(80.6) 0.123	7(87.5) 1564(80.8) 0.632	7(87.5) 1564(80.8) 0.632	45(84.9) 1527(80.8) 0.453
Sedatives	3(27.3) 225(11.5) 0.125*	11(17.5) 217(11.3) 0.134	10(31.3) 218(11.2) 0.002*	9(14.3) 219(11.4) 0.487	9(10.8) 219(11.6) 0.840	6(60.0) 222(11.3) 0.000*	4(44.4) 224(11.4) 0.014*	15(26.8) 213(11.1) <0.001
Tramadol	0(0.0) 16(0.8) 1.000*	0(0.0) 16(0.9) 1.000*	2(6.5) 14(0.7) 0.026*	0(0.0) 16(0.9) 1.000*	0(0.0) 16(0.9) 1.000*	3(30.0) 13(0.7) <0.001	2(22.2) 14(0.7) <0.001	0(0.0) 16(0.9) 0.503
Methadone	0(0.0) 3(0.2) 1.000*	0(0.0) 3(0.2) 1.000*	1(3.2) 2(0.1) 0.048*	0(0.0) 3(0.2) 1.000*	0(0.0) 3(0.2) 1.000*	0(0.0) 3(0.2) 0.900	1(11.1) 2(0.1) <0.001	0(0.0) 3(0.2) 0.772
Cannabis	4(36.4) 266(13.5) 0.051*	12(19.0) 258(13.5) 0.205	10(31.3) 259(13.3) 0.008*	7(11.1) 263(13.7) 0.550	15(18.1) 255(13.5) 0.232	5(50.0) 265(13.5) 0.006*	3(33.3) 267(13.6) 0.113*	8(14.3) 262(13.7) 0.892
Marijuana	4(36.4) 262(13.8) 0.054*	11(17.5) 255(13.8) 0.405	10(32.3) 255(13.5) 0.007*	7(11.3) 259(14.0) 0.547	15(18.8) 251(13.7) 0.200	5(50.0) 261(13.7) 0.001	3(33.3) 263(13.8) 0.091	8(15.4) 258(13.9) 0.755
Hashish	1(9.1) 64(3.4) 0.577*	5(7.9)/ 60(3.2) 0.126*	4(12.9) 61(3.2) 0.013*	0(0.0) 65(3.5) 0.319*	3(3.8) 62(3.4) 0.963*	0(0.0) 65(3.4) 0.836	1(11.1) 64(3.4) 0.439	2(3.8) 63(3.4) 0.974
Amphetamine	0(0.0) 32(1.7) 1.000*	3(4.8) 29(1.6) 0.085*	2(6.5) 30(1.6) 0.093*	0(0.0) 32(1.7) 0.623*	1(1.2) 31(1.7) 1.000*	1(10.0) 31(1.6) 0.039	1(11.1) 31(1.6) 0.027	2(3.8) 30(1.6) 0.225
Ecstasy	1(9.1) 43(2.3) 0.226	3(4.8) 41(2.2) 0.173*	3(9.7) 41(2.2) 0.032*	0(0.0) 44(2.4) 0.399*	0(0.0) 44(2.4) 0.258*	1(10.0) 43(2.3) 0.103	1(11.1) 43(2.3) 0.077	1(1.9) 43(2.3) 0.840
LSD	0(0.0) 18(0.9) 1.000*	0(0.0) 18(1.0) 1.000*	0(0.0) 18(1) 1.000*	0(0.0) 18(1.0) 1.000*	0(0.0) 18(1.0) 0.374	2(20) 16(0.8) 0.000	1(11.1) 17(0.9) 0.002	0(0.0) 18(1.0) 0.476
Cocaine	0(0.0) 25(1.3) 1.000*	2(3.2) 23(1.2) 0.197*	3(9.7) 22(1.2) 0.007*	0(0.0) 25(1.3) 1.000*	1(1.2) 24(1.3) 0.965	0(0.0) 25(1.3) 0.716	1(11.1) 24(1.3) 0.009	0(0.0) 25(1.3) 0.401
Heroin	1(9.1) 16(0.8) 0.094*	1(1.6) 16(0.9) 0.435*	1(3.2) 16(0.8) 0.243*	0(0.0) 17(0.9) 1.000*	0(0.0) 17(0.9) 0.390	1(10.0) 16 (0.8) 0.002	1(11.1) 16(0.8) 0.001	0(0.0) 17(0.9) 0.489
Alcohol and drugs	2(50.0) 112(25.3) 0.270*	4(26.7) 110(25.4) 1.000*	2(18.2) 112(25.7) 0. 737*	1(7.7) 113(26.0) 0.199*	5(26.3) 109(25.4) 0.929	1(20.0) 113(25.5) 0.779	1(25) 113(25.5) 0.984	3(33.3) 111(25.3) 0.583

p - According to $\chi 2$ test

* According to Fisher's exact test

Table 3. Degrees of depression among students with and without somatic disease

Degrees of depression	Somatic disease		Total	*P*
	Yes - N (%)	No - N (%)		
No	131 (50.4)	916 (56.8)	1047 (55.9)	0.196
Mild	89 (34.2)	502 (31.1)	591 (31.6)	
Moderate	23 (8.8)	122 (7.6)	145 (7.7)	
Expressed	17 (6.5)	73 (4.5)	90 (4.8)	
Total	1613 (100)	260 (100)	1873 (100)	
Degrees of anxiety	Somatic disease		Total	*P*
	Yes - N (%)	No - N (%)		
No	215 (86.0)	1459 (92.0)	1674 (91.2)	0.012
Mild	32 (12.8)	118 (7.4)	150 (8.2)	
Moderate	3 (1.2)	7 (0.4)	10 (0.5)	
Expressed	0 (0.0)	2 (0.1)	2 (0.1)	
Total	250 (100)	1586 (100)	1836 (100)	

p - According to $\chi 2$ test

Table 4. The distribution of psychoactive substances in relation to the diagnosed mental disorders

Psychoactive substances	Mental disorders		*p*
	Yes - N (%)	No - N (%)	
Tobacco	9 (45)	432 (22.3)	0.016
Alcohol	14 (77.8)	1556 (80.9)	0.740
Sedatives	11 (55.0)	217 (11.1)	<0.001*
Tramadol	5 (26.3)	11 (0.6)	<0.001
Methadone	2 (10.5)	1 (0.1)	<0.001
Cannabis	11 (55.0)	259 (13.2)	<0.001*
Marijuana	10 (52.6)	256 (13.5)	<0.001
Hashish	5 (26.3)	60 (3.2)	<0.001
Amphetamine	5 (26.3)	27 (1.4)	<0.001
Ecstasy	4 (21.1)	40 (2.1)	<0.001
LSD	3 (15.8)	15 (0.8)	<0.001
Cocaine	4 (21.1)	21 (1.1)	<0.001
Heroin	4 (21.1)	13 (0.7)	<0.001
Alcohol and drugs	7 (63.6)	107 (24.5)	0.003

p - According to $\chi 2$ test
*According to Fisher's exact test

DISCUSSION

There is little research about how drugs affect young people with somatic diseases [18]. In the current study presented results are for University students. According to our survey, among Belgrade University students, even 100% of them with the diagnoze of diabetes reported drinking alcohol, since in one research conducted on the population of adolescents with diabetes mellitus in USA, 39% of the sample reported a drinking episode [2]. In comparison with that research, our students with diabetes reported higher rate of tobacco (34%:64%) and marijuana use (11%:36%) [2]. In the same study 10% of adolescents reported drug use [2], since in our study, among students with diagnosed diabetes, about 9% of them used hashish, and the same number used heroin and ecstasy.

An example from the UK shows that twenty-nine percent of diabetic patients – respondents have admitted that they were using street drugs [18]. In our survey, the reported lifetime prevalence of cannabis use in persons with diabetes mellitus was around 36% and it is the highest one in comparison to other studies in USA: 11% [2], 13% [19], 10% [20], in Chile almost 10% [1], in UK 28% [18]. In research in USA the reported lifetime prevalence for cocaine in patients with diabetes mellitus was 1% [19]. In another research, rates for cocaine were 5% [20], in Chile almost 3% [1], in UK 12% [18], since our subjects with diabetes mellitus didnot use cocaine at all.In research in USA the reported lifetime prevalence of amphetamine in persons with diabetes was 6% [19], in Chile around 3% [1], in UK 8% [18], since our students with diabetes didnot have experience with this psychoactive substance. In research on the population of adolescents in Chile, around 1% used Ecstasy [1], in UK 5% [18], since in our study rates for ecstasy were 9%. In UK among young patients with diabetes mellitus, reported rates for LSD were 2% [18]. As distinct from, in the current study, our students with the same disease didnot use this drug at all. In the same study in UK, 15% of patients reported poly-drug use [18], while in our research that percentage was 50%. In the current study our respondents didnot use cocaine and amphetamine at all, but they reported prevalence rates for heroin and ecstasy of 9%.

Surveys conducted in 19 countries showed that alcohol consumption was significantly associated with heart disease onset [21].In our survey, among subjects with hypertension the rates of using psychoactive substances were less than in the study in USA(18%:23% for marijuana; 3%:7% for cocaine; 5%:9% for amphetamines; 2%:4% for heroin) except the rates for psychedelics (5%:3%) [22].

When it comes to subjects with respiratory illnesses, in research in USA, among subjects with asthma, 8% of them reported substance use [23], since in Canada 4% with asthma and 8% with bronchitis reported the same [24]. In that country among respondents with no respiratory condition, 2.8% of them used substances [24] and in our research is the opposite, among students without chronic bronchitis, the number of users was higher, but no significant difference was found.

In our investigation 18% of students with asthma reported cannabis use, about 1% reported amphetamine use and the same number cocaine use. In Canada, in the research among study subjects with respiratory illnesses, among patients with asthma, about 4% used substances, almost 8% among patients with chronic bronchitis [24]. In our survey students with chronic bronchitis used next substances: about 11% used cannabis, about 31% smoked cigarettes, 90% used alcohol, and around 14% used sedatives. In the study from 19 of the World Mental Health surveys alcohol abuse had specific associations with respiratory diseases. That investigation found similar prevalence rates of 1.7 % of alcohol use among persons with respiratory disease and without them (1.7%:1.6%) [25]. Regarding alcohol, in the research in Canada, the prevalence rates were higher (almost 4%:2.5%) [26]. In the present study alcohol users were much more numerous, about 88% of students with diagnosed respiratory disease used alcohol, compared to almost 81% without it.

Data from general population surveys over 17 countries showed significant relationship between neurological disease and alcohol [27]. In our study, data revealed that subjects with a history of neurological diseases had high rates of alcohol use (87.5%) as those without it (80.8%) what is consistent with one Canadian survey [28]. Another Canadian survey doesnot corroborate this association [29].

There is a strong relationship between gastrointestinal symptoms and alcohol consumption, as our survey observed [30, 31]. In our study population, among respondents who had diagnosed ulcer, almost 88% of them drank alcohol.

Alcohol consumption seems to be greater in patients with skin diseases than in the general population [32]. Our research corroborates this association.

People with mental disorders are more likely to smoke than people without it [33, 34]. In the USA, 68% of schizofrenia patients were smokers compared to 35% of age matched controls [33]. Persons with mental illness are about twice as likely to smoke as other persons [35] what is consistent with our study (45% of students with mental disorders were smokers, compared to 22% without it with statistically significant difference). Some authors have suggested that such persons use cigarettes as a means of self-medication of psychiatric symptoms [35]. However, in our research, students with diabetes and neurological disease reported a higher rate of tobacco use in comparison with students with mental disorders (67%:55%:45%).

When it comes to anxiety and depression, our survey is in line with other researches. Our respondents with somatic disease diagnoses are more depressed compared to healthy respondents, but no significant difference was found. The explanation may be found in a small number of respondents with medical illness given the subject of the study is a student population with expected low prevalence of chronic health disorders. In Canada, among diabetic patients, depression has been shown to be a common co-morbidity [36], affecting 10% to 30% of the diabetic population [37]. Regarding anxiety, opinions are polarized. Some researchers showed that anxiety is higher among these patients [38], but the others think the opposite [39]. Interesting data from our research showed that subjects with mild and moderate anxiety were more numerous among somatic patients, while subjects without this illness were expressed anxious with statistical significance. In Canadian and Italian researches, somatic diseases were associated with both depression and anxiety [27,28,40].

Our study has several limitations. First, the cross-sectional nature of the study precludes any causal inferences. Second, the study is based on self-reported data without access to medical records. Third, even the students were asked to fill in the questionnaire independently, mutual influences among respondents cannot be fully excluded. Fourth, information bias should be taken into consideration, because students with substance use disorders often face the challenges of stigma [15]. Fifth, even with a large sample of 2,000 students and comparative groups from different faculties, the somatic and mental disorders were confirmed only with a small number of them. Despite the presented limitations, the findings of the study have suggested substantive correlation between somatic or mental disorders and the use of psychoactive substances, which may properly be treated by introducing the prevention education.

CONCLUSION

Use of psychoactive substances is an important issue among University students with diagnosed somatic or mental disorder. Both psychiatrist and somatic doctors who work with student population should bear in mind that young people explore and experiment with different life styles regardless of whether they are healthy or sick. Even the student's determined diagnosis does not constitute a guarantee that they will stop using psychoactive substances. Therefore, it is essential to recognize the symptoms and consequences of such behavior, and above all and connection thereof, the importance of prevention which may enhance better solution-seeking via proper education.

Competing interests: All authors have completed the Unified Competing Interest form and declare they have no competing interests to report.

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METOD ULTRAZVUČNOG MERENJA TEŽINE MOKRAĆNE BEŠIKE

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SAŽETAK

Cilj: Istražiti korelaciju između težine, odnosno mase mokraćne bešike koja je izmerena ultrazvukom i simptoma donjeg urotrakta (LUTS).

Metod: Merenje 2D i 3D ultrazvukom parametara koji su potrebni za izračunavanje mase mokraćne bešike-unutrašnji i spoljašnji radijus mokraćne bešike ispunjene sa minimalno 200 ml urina, u pacijenata sa LUTS.

Rezultati: Prosečna težina mokraćne bešike u muškaraca bila je 53,8 g, a kod žena-45,2 g. Nije bilo statistički značajne razlike u masi bešike između muškaraca i žena sa LUTS.Pacijenti sa LUTS, bez obzira na pol, imaju hipertofisan zid mokraćne bešike, što rezultira povećanjem spoljašnjeg i unutrašnjeg radijusa bešike i posledičnim povećanjem bešične mase koje se može precizno izmeriti ultrasonografski, ali bez statistički značajne razlike u odnosu na predeterminisane vrednosti iz tablica indeksa telesne mase.

Zaključak: Merenje težine mokraćne bešike možemo smatrati neinvazivnim pristupom pacijentima sa LUTS. Korisnije i jednostavnije je samo merenje debljine zida mokraćne bešike u odnosu na kalkulaciju mase-težine kod aparata koji nemaju ugrađen softver za težinu organa.

Ključne reči: Težina mokraćne bešike, ultrasonografija.

SUMMARY

THE METHOD OF ULTRASOUND URINARY BLADDER WEIGHT CALCULATION

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Objective: To investigate correlation between ultrasonically calculated urinary bladder weight and lower urinary tract symptoms (LUTS).

Methods: 3D and 2D measurement of parameters necessary to determine bladder weight: Inner and outer radius of the bladder, in 10 male and 10 female patients with LUTS, with urinary bladder filled to at least 200 ml of urine volume.

Results: Average urinary bladder weight in males was 53,8 g and in female patient was 45,2 g. We found no statistically significant difference between male and female patients, all with LUTS. We also found that patients in LUTS have hypertrophied bladder, which means that urinary bladder mass should be larger and results in an increase of blader weight and both inner and outer radius of the urinary bladder, that should be detected ultrasonographically, but not too much over of pre- determined variations of normal bladder weight.

Conclusion: Estimation of urinary bladder weight should be considered as non-invasive approach to patients with LUTS. However, it is more plausibile to measure only urinary bladder wall thickness ultrasonically than to calculate urinary bladder weight without built-in software.

Key words: Urinary bladder weight, ultrasonography

UVOD

Ultrazvukom izmerena težina mokraćne bešike (Ultrasound-estimated bladder weight - UEBW) može da postane značajan indikator u dijagnozi opstrukcije bešičnog izlaza (1). Pojedini autori navode termin ''masa'' jer termin ''težina'' implicira da je organ odstranjen iz tela i nakon toga izmeren, dok ultrazvučno merenje treba da bude neinvazivno po definiciji
(2). Ipak, izraz''masa'' može da se shvati kao ''mase'' što asocira na tumorski proces (tumorske mase), pa je izraz ''težina'' verovatno bolji.
Težina mokraćne bešike ustanovljena ultrazvukom je parametar od značaja u dijagnostici simptoma donjeg urotrakta (LUTS), simptoma opstrukcije bešičnog izlaza (BOO) i u pripremi pacijenata za radikalnu cistektomiju. Takođe, merenje težine mokraćne bešike može biti korisno u pedijatrijskoj urologiji za otkrivanje i lečenje opstrukcije bešičnog izlaza u dece.
Povećanje težine-mase mokraćne bešike znači da je detruzorni mišić u hipertrofiji što je u direktnoj korelaciji sa opstrukcijom bešičnog izlaza ili mogućim tumorskim rastom.
Metode merenja. Težina mokraćne bešike je proizvod sledećih činilaca: Površine bešike, debljine zida bešike i specifične težine mokraćne bešike (1). To je najjednostavniji tačan način, ali je proces najlakši ako ultrazvučni aparat već ima ugrađen softverski algoritam za merenje težine mokraćne bešike. Uglavnom, 3D ultrazvučni aparati imaju to sredstvo. Prema jednoj važnoj studiji ove teme, specifična težina zida mokraćne bešike je 0.957 ± 0.026 što se neminovno zaokružuje na 1 u daljim kalkulacijama (3,4). Tako se jednačina za merenje težine mokraćne bešike dodatno uprošćava da bude proizvod površine i debljine zida. Ako je neophodno, vrednost specifične težine mokraćne bešike može da se nađe iz indeksa telesne mase ili indeksa mase telesnih organa.
U našem radu, koristili smo formulu za izračunavanje zapremine zida mokraćne bešike, pri čemu je vrednost zapremine zida mokraćne bešike jednaka vrednosti njegove težine uzimajući u obzir da je njegova specifična težina 1 (0,957-0,981).
Pacijenti i metode
Selekcija pacijenata: Pregledali smo 10 muškaraca i 10 žena u našoj Urološkoj ambulanti. Najstariji je imao 70, a najmlađi 21 godinu života. Sredstvo selekcije je bilo postojanje barem jednog od simptoma opstrukcije donjeg urotrakta (LUTS) prema uputstvima Evropske Asocijacije urologa (EAU), www.eauguidelines.com. Za muškarce, dodatno smo koristili Internacionalni Prostata Simptom Skor (IPSS).
Ultrazvučni pregledi vršeni su na Chison i3 aparatu, proizvedenom od strane Chison Medical Images Ltd, China, 2013-2014. Ovakav tip aparata ima široku upotebu u ginekologiji, akušerstvu, gastroenterologiji i abdominalnoj hirurgiji, ali ima i zadovoljavajući softver za urologiju (http://medicalstore.hu/en/chison-i3/). Koristili smo konveksnu abdominalnu 3D sondu od 3,5 MHz i 4D Volume sondu od 4 Mhz sa mogućnošću trenutnog prelaza sa 2D na live mod radi obezbeđivanja 4D simulacije, kao i standardnu 3,5 Mhz konveksnu sondu. Svi pregledi i merenja urađeni su od strane istog egzaminatora. Naš aparat nije imao ugrađenu formulu za površinu sfere, tako da su merenja vršena postupno, prema činiocima formule koju prikazujemo, odnosno, nisu vršena automatski.
Svi pacijenti su dali usmenu saglasnost i pristanak za uzimanje podataka. Prethodno smo objasnili način pregleda i naglasili da će zbog toga pregled biti nekoliko minuta duži. Obezbeđena je i saglasnost lokalnog Etičkog komiteta.
Od pacijenata je traženo da ispune mokraćnu bešiku pre pregleda, a u obzir su uzimani volumeni bešike od minimalno 200 ml urina, jer je to donja granica za tačna merenja u ovakvim studijama. U slučajevima sa manje urina u bešici, pacijentima je nalagano da popiju još 2 čaše vode za 20 minuta, i onda bi bili ponovo pregledani.
Metod izračunavanja: Merili smo spoljašnji (ro) i unutrašnji (ri) prečnik mokraćne bešike, u sagitalnom transabdominalnom preseku. Zatim smo izračunavali zapreminu obe sfere-unutrašnje i spoljašnje-koristeći pomenute prečnike, smatrajući da je mokraćna bešika približno sfernog oblika, prema formuli zapremine sfere : . Konačna formula za težinu-masu mokraćne bešike je: UEBW = (Vo−Vi)ρ, gde je ρ specifična težina zida mokraćne bešike, a ranije smo napomenuli da ima vrednost oko 1.
Koristili smo neparametrijski Cochrane Q test koji je ekstenzija hi-kvadrat testa, kao statističko sredstvo.

CILJ

Cilj studije je bio da se ispita odnos ukupne težine, odnosno mase organa i ekspresije simptoma donjeg urotrakta: Učestalo mokrenje, urgentno mokrenje, slabljenje mlaza, nikturija, stres-inkontinencija, deformacija mlaza, bez obzira na primarni uzrok simptoma. Kod simptoma donjeg urotrakta (LUTS) očekuje se zadebljavanje zida mokraćne bešike.

REZULTATI

Tabela 1: Izračunavanje razlike dužina spoljašnjeg i unutrašnjeg prečnika na sagitalnom ultrazvučnom preseku mokraćne bešike. Tehnički, to je vrednost debljine bešičnog zida.

Muškarci (cm bešičnog zida)	Žene (cm bešičnog zida)
9,18-8,70=0,48	9,50-8,87=0,63
9,27-8,57=0,70	9,33-8,50=0,83
8,72-8,0=0,72	8,94-8,11=0,83
9,88-9,21=0,67	8,80-8,01=0,70
8,90-8,35=0.55	9,12-8,77=0,35
9,1-8,56=0,54	9,0-8,52=0.48
9,21-8,67=0,54	8,95-8,23=0,72
8,99-8,31=0,68	9,27-8,69=0,59
8,59-8,11=0,48	9,02-8,37=0,55
9,11-8,60=0,51	8,80-9,02=0,79

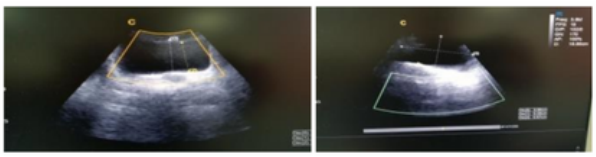
Tabela 2: Razlike između `zapremina unutrašnje i spoljašnje bešične sfere ` u cm3 što je ekvivalentno težini, izraženo u gramima

$V_o = \frac{4}{3}\pi r_o^3$, $UEBW = (V_o - V_i)\rho$

Muškarci (cm^3 ili g bešičnog zida)	Žene (cm^3 ili g bešičnog zida)
309,4-263,4=**46,0**	342,9-279,1=**63,8**
318,6-251,7=**66,9**	324,8-245,6=**79,2**
265,2-204,8=**60,4**	285,8-213,3=**40,2**
385,7-312,4=**73.3**	272,5-205,5=**67,0**
281,9-232,8=**49,1**	303,4-269,8=**33,6**
301,4-250,8=**50,6**	291,6-247,3=**43,7**
312,4-260,6=**51,8**	286,7-222,9=**63,8**
290,6-229,5=**46,2**	318,6-259,7=**58,9**
253,5-213,3=**46,0**	293,5-251,2=**42,3**
302,4-254,4=**48,0**	272,5-206,3=**66,2**

Ustanovljena masa-težina mokraćne bešike u muškaraca bila je 46,0 do 73.3 g, srednja vrednost 53,8 g , a u žena-33,6 do 79,2 g, srednja vrednost 45,2 g.
Nije bilo statistički značajne razlike u težini moraćne bešike između muškaraca i žena. Sve dobijene težine bile su malo iznad ranije ustanovljene prosečne težine mokraćne bešike, bez obzira na pol, što iznosi 35 g ± 18%, a što je ispod statističke značajnosti (p>0,01). Ovakav nalaz objašnjavamo time što su mokraćne bešike svih pacijenata, oba pola, bile hipertofične zbog opstukcije i / ili inflamacije. Mokraćna bešika muškarca je masivnija od mokraćne bešike žene, što je očekivano i u skladu sa tablicama indeksa telesne mase.

Slike 1,2: Ultrazvučno merenje unutrašnjeg i spoljašnjeg prečnika mokraćne bešike.



DISKUSIJA

Kojima et al.(3) je izvestio da prosečna težina prazne mokraćne bešike u zdravih subjekata iznosi 35 grama, ali postoji velika verovatnoća da je ta vrednost za 18% veća i da iznosi preko 40 grama, što važi za merenje ultrazvukom. Ova razlika se objašnjava time, prvo, da mokraćna bešika nema idealno sferni oblik dok ultrazvučni aparat vrši kalkulaciju kao da se radi o idealnoj, geometrijskoj sferi. Drugo, rezultati variraju zavisno od odabrane formule-da li je to algorutam sa merenjem površine ili algoritam sa merenjem radijusa (kojeg smo mi koristili).Treće, ako aparat nema ugrađen program za izračunavanje zapremine sfere, kalkulacija nije automatska, treba da se odloži posle merenja i posledično je subjektivna, odnosno, egzaminator-zavisna.

Svi naši ispitanici su imali zadebljali zid mokraćne bešike, što je ranije objašnjeno u radu, i kao što je očekivano, to je koreliralo sa povećanjem mase-težine mokraćne bešike.

U svakodnevnoj urološkoj praksi mnogo je ergonomičnije da se meri samo debljina zida mokraćne bešike, umesto da se izračunava njena težina.

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STANDARD AND ADVANCED METHODS FOR DIAGNOSIS OF METABOLIC SYNDROME AND ITS COMORBIDITIES IN CHILDREN

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SUMMARY

The metabolic syndrome (MS) is a clinical entity of substantial heterogeneity, represented by the combination of obesity (especially central obesity), insulin resistance, impaired glucose tolerance, atherogenic dyslipidemia (high triglyceride levels and low levels of HDL-cholesterol (HDL-C)), and hypertension. Childhood obesity has become more common as a result of urbanization, bad diets, and more sedentary lifestyles
The incidence of metabolic syndrome is ten times higher in children with obesity, and a special risk factor is the presence of obesity in the pediatric population, the classification of metabolic syndrome is based on standards set by the International Diabetes Federation (IDF).
Our goal is to summarize the diagnostic procedure of metabolic syndrome as well as comorbidity based on conventional methods and modern imaging procedures by analyzing the published papers.

Keywords: obesity, children, visceral fat tissue, Metabolic syndrome, Body Mass Index, diagnosis, comorbidities, insulin resistance

SRPSKI

STANDARDNE I NAPREDNE METODE ZA DIJAGNOSTIKU METABOLIČKOG SINDROMA I NJEGOVIH KOMORBIDITETA U DECE

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SAŽETAK

Metabolički sindrom (MS) je klinički entitet nastao kombinacijom razliciitih patofizioloških poremećaja: gojaznosti (posebno centralne gojaznosti), insulinske rezistencije, poremećene tolerancije glukoze, aterogene dislipidemije (visoki nivoi triglicerida i niski nivoi HDL- holesterola (HDL-C)) i hipertenzije.
Incidenca metaboličkog sindroma je deset puta veća kod dece sa gojaznošću, a poseban faktor rizika je prisustvo gojaznosti u detinjstvu. Klasifikacija metaboličkog sindroma zasniva se na standardima koje je postavila Međunarodna federacija za dijabetes (IDF).
Naš cilj je da analizom objavljenih radova sumiramo dijagnostičku proceduru metaboličkog sindroma kao i komorbiditeta na osnovu konvencionalnih metoda i savremenih imidžing tehnika.

Ključne reči: gojaznost, deca, visceralno masno tkivo, metabolički sindrom, Indeks Telesne Mase, komorbiditeti, insulinska rezistencija

INTRODUCTION

The International Diabetes Society (1,2) has defined Metabolic syndrome (MS) as "a cluster of the cardiovascular risk factors" - diabetes or elevated fasting plasma glucose, abdominal obesity, high cholesterol and high blood pressure."
As the proportion of the population with obesity continues to rise, the prevalence of metabolic syndrome is increasing in both children and adolescents. Elevated triglycerides (TG), altered glucose metabolism, reduced high-density lipoprotein cholesterol (HDL-C), and elevated blood pressure and adiposity are the main risk factors (3,4). They are primarily caused by insulin resistance, leading to diabetes mellitus, hepatic steatosis, polycystic ovary syndrome, and obstructive sleep apnea.

The definition of MS in children and adolescents remains unclear due to the absence of gold standard diagnostic criteria of MS for the pediatric population.
Some of the diagnostic criteria used by studies include the International Diabetes Federation (IDF) criteria, the World Health Organization criteria, the National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III) criteria modified for age, the de Ferranti et al. the Weiss et al., and the Cruz and Goran criteria (3,4,5).
Prevalence of MS among the children (6,7) ranges from 0.2% to 38.9%, according to different studies. The prevalence was considerably higher in the overweight (11.9%) and obese (29.2%) population.
In a systematic review of 85 studies in children (8), the median prevalence of metabolic syndrome in whole populations was 3.3% (range 0–19.2%), and in overweight children it was Dyslipidemia linked to metabolic syndrome can also accelerate the atherosclerotic process (16,17, 18).
Dyslipidemia is defined as increased free fatty acid flow, elevated triglyceride levels, decreased high density lipoprotein (HDL) cholesterol values, increased low-density lipoprotein (LDL) cholesterol, and increased apolipoprotein (apo) B. Overproduction of very low-density lipoprotein (VLDL) / apo B-100, reduced catabolism of apo B-containing particles, and increased catabolism of HDL-apo / A-I particles may all contribute to dyslipidemia in MS patients (18,19). The major problem in the genesis of MS is related to the adipose tissue's failure to convert free fatty acids to triglycerides (inadequate esterification).
Under conditions of insulin resistance, the antilipolytic effect of insulin on adipose tissue is weak (20), increasing plasma free fatty acid levels. Insulin resistance lowers LDL receptor expression and raises hepatic cholesterol production and VLDL secretion.
The increased hepatic cholesterol production in people with MS results in non-decrease in the breakdown of triglyceride leftovers in the postprandial state. Abnormal postprandial lipemia has been detected in individuals with coronary heart disease and other disorders linked to an increased cardiovascular risk. (9,21)
Increased plasma uric acid has been thought to possess antioxidant properties (22). However, uric acid's harmful effects include an inhibitory influence on nitric oxide (NO) generation, platelet aggregation, and pro-inflammatory action. It has been claimed that hyperuricemia may predict the onset of metabolic syndrome, diabetes, hypertension, renal disease, and cardiovascular disease.

PURPOSE

In the last decade and a half, several novel methods and biochemical parameters have emerged in the diagnosis of obesity and metabolic syndrome: ultrasonography (US), bioelectrical impedance analyzer, computed tomography (CT), magnetic resonance (MRI), magnetic resonance spectroscopy (MRS), positron emission tomography (PET), 8F-fluorodeoxyglucose (FDG) PET, Dual-Energy x-ray Absorptiometry (D However, traditional markers such as BMI, WC, fasting glucose, arterial blood pressure, and hyperlipidemia are still used to define metabolic syndrome. In this study, we evaluated at whether innovative approaches outperformed established ones in predicting metabolic syndrome and associated comorbidities.

RESULT

Obesity is diagnosed based on body mass index (BMI). Children with a BMI ≥95th percentile for gender and age are considered obese, and those with BMI ≥85th percentile and <95th percentile - overweight. Additionally, visceral fat accumulation (23), independent of the degree of obesity, is strongly associated with both childhood metabolic syndrome and cardiovascular diseases later in life.

Waist circumference (WC) is used to define central obesity. The World Health Organization and the International Diabetes Federation (24) suggest measuring WC in the horizontal plane midway between the lowest ribs and the iliac crest (Table 2).(25)
Our research (26) on a sample of 60 obese children aged 2 to 17 years revealed that waist circumference is a criterion that exhibits a strong relation with BMI, LDL-cholesterol and insulin levels, as well as with subcutaneous fat thickness (measured in the subscapular area).
In the pediatric population, emphasis should be given to history on the course of pregnancy, with a focus on the child's birth weight (SGA, children with birth weight defined as small for gestational age). Many studies (27,28) have examined the increased risk of obesity and metabolic syndrome in SGA children later in life; however, neither the proportion of SGA in childhood obesity nor the prevalence of obesity in SGA is known. In a Belarusian (29) birth cohort study, 8.9 percent of participants were born SGA and made up a minor proportion of those who were overweight or obese when compared to those born big for gestational age.

Body weight, (BW). Body Mass Index - as well as arterial blood pressure should be obtained during physical examination. While waist circumference is considered indicative of visceral adiposity (30), the lack of pediatric reference range data precludes its use in the routine evaluation for childhood obesity.
Visceral adiposity can also be estimated using waist to hip ratio and magnetic resonance imaging. Alternatively, waist to height ratio is used in children. A ratio of 0.6 or more is indicative of increased risk for metabolic syndrome (31) and cardiovascular diseases.
Signs of MS comorbidities, such as acanthosis nigricans (indicative of insulin resistance) and genu valga should be registered during the examination. Polycystic ovaries (with hypertrichosis, menstrual cycle irregularities, acne, and so on) in girls may be the first symptom of insulin resistance and MS complications.
Biochemical parameters including liver function indexes and a fasting lipid profile should be obtained. Lipids and HDL lipid profile should be measured in overweight children between the ages of 2–8 and repeated between 12 - 16. The presence (32) of high triglycerides – low HDL cholesterol profile is highly suggestive of insulin resistance.
Non-HDL-C represents the total of highly atherogenic lipoprotein particles, computed as TC minus HDL-C. Recent guidelines advocate universal lipid screening with nonfasting non-HDL-C testing in all youth aged 9–11 and 17–21.
Hypertriglyceridemia can be diagnosed if TG level is ≥100 mg/dL (1.69 mmol/L) in children (<10 year) or ≥130 mg/dL (1.47mmol/l) in adolescents (10–19 year) based on an average of two fasting measurements (33)
The American Diabetes Association (ADA), has advised an oral glucose tolerance test as screening for type 2 diabetes, every 3 years from the age of 10 or from the start of puberty in the context of the presence of any two of the following features: a family history of T2D, high risk ethnicity, signs of insulin resistance, or associated diseases (hypertension, dyslipidemia, polycystic ovarian disease, or being born small for gestational age) or maternal history of diabetes or gestational diabetes affecting the overweight child.
According to guidelines of the ADA, prediabetes can be diagnosed by one of three laboratory values: (1) elevated fasting glucose of 100 to 125 mg/dL (5.6–6.9 mmol/L) or (2) elevated glucose at 2 hours during an oral glucose tolerance test, 140 to 199 mg/dL (7.8–11.0 mmol/L) or (3) hemoglobin A1C (HbA1C) level between 5.7% and 6.4% (39–46 mmol/mol. Puberty, which is linked to a considerable rise in insulin resistance and may play a role in the development of T2DM, is one factor that exacerbates prediabetes in adolescence (34).
The link between BMI/WC, hyperinsulinemia and blood pressure was discovered in children as young as four years old.

Obesity is commonly associated with non-alcoholic fatty liver disease, elevated alanine transaminase (ALT) levels as well as other liver function abnormalities (35). Features of metabolic syndrome are not only highly prevalent in patients with Nonalcoholic Fatty Liver Disease (NAFLD) but components of MS also increase the risk of developing NAFLD. In the majority of patients, NAFLD is commonly associated with metabolic comorbidities such as obesity, diabetes mellitus, and dyslipidemia. The most prevalent and well-established risk factor for NAFLD is obesity (excessive body mass index and visceral obesity). In actuality, NAFLD is linked to the full spectrum of obesity, from overweight to obese to very obese (36). The majority (>95%) of patients with severe obesity undergoing bariatric surgery will have NAFLD.

NASPGHAN (North American Society For Pediatric Gastroenterology, Hepatology & Nutrition) guidelines recommend ALT as the best screening test for NAFLD in children. These guidelines propose an ALT ≥ 80 U/L on initial screening or ALT greater than or equal to twice the upper limit of normal (ALT ≥ 44 U/L for females and ALT ≥ 52 U/L for males) on repeated screening as an indication for further evaluation. As demonstrated in the SAFETY study, for the general population including children with obesity, the 95th percentile for ALT was 26.0 U/L in females and 37.2 U/L in males. However, the diagnosis of NAFLD should not be made solely based on ALT (37), despite the fact that it may be an important screening tool.

ALT and MS components (visceral fat, body mass index, waist circumference, percentage body fat, blood pressure, elevated blood glucose, and lipid profiles) were significantly correlated, according to a study by Elizondo-Montemayor et al (38). The best indicator of a high ALT was waist circumference.

Liver function tests (serum alanine and aspartate aminotransferases) is advised biannually starting from 10 years of age in obese children or those overweight with risk factors.

The metabolic syndrome is characterized by low-grade inflammation. C-reactive protein (CRP), an inflammatory biomarker often increased in children with MS, is also an independent predictor of future cardiovascular events. Tumor necrosis factor (TNF), interleukin 6 (IL-6), interleukin 8 (IL-8), and resistin are other important actors in inflammation linked to diabetes and insulin resistance (39). Concentrations of anti-inflammatory cytokines (IL-10), ghrelin, adiponectin, and antioxidant factors (PON-1) are decreased in MS, and the decreases correlated with specific disorders within the cluster. Recent studies point to causal relationship between uric acid and insulin resistance (40).

Metabolic syndrome is associated with an increased risk of cardiovascular disease (CDC) and type 2 diabetes mellitus. Carotid intima–media thickness and lumen diameters were increased in children with MS as compared to children without MS. The correlation between Carotid Intima-Media Thickness (CIMT) and waist circumference (WC) in adolescents has been proven, and the association between BMI and CIMT is supported by Iannuzzi et al (41) and White et al who observed that obese children had a larger CIMT than children with a healthy BMI.

Imaging studies

Ultrasonography (US), computed tomography (CT), and magnetic resonance (MR) imaging may assess the subcutaneous adipose and visceral abdominal tissue (VAT).

Ultrasonography have been used to measure VAT, intra-abdominal fat thickness and abdominal fat index (ratio of the thicknesses of the pre-peritoneal and subcutaneous abdominal fat). Computed tomography can even more accurately assess VAT. Subcutaneous fat thickness was defined as the measurement from the skin-fat interface to the linea alba, and visceral fat thickness (VFT) was defined as the thickness from the linea alba to the aorta. Computed tomography (CT) and dual X-ray absorptiometry (DXA) are well-established techniques used in clinical and scientific research to evaluate abdominal adipose tissue compartments.

Several studies (42) utilized positron emission tomography (PET) for assessing insulin resistance. 8F-fluorodeoxyglucose (FDG) PET imaging revealed insulin-stimulated FDG uptake in skeletal muscle as well as glucose absorption throughout the body.

Dual-energy x-ray absorptiometry is the imaging modality used to quantify adipose tissue (DXA). DXA detects fat, lean mass, and bone mineral content by measuring the attenuation of two X-ray photon energies with minimal radiation exposure (1mSv/scan16), short scanning time (5–13 minutes), high precision, and cheap cost. 17 A bioelectrical impedance analyzer can be applied to measure fat mass, muscle mass and fat-to-muscle ratio. DEXA body composition analysis is quick and easy, and the patient experiences little discomfort or radiation exposure. These characteristics promoted the use of DEXA in clinical settings and studies to accurately measure body fat.

Although hepatic biopsy represents golden standard in fatty liver diagnosis, it is rarely used comparing to ultrasound and aminotransferase levels.

Several MR methods can also be used for imaging abdominal obesity. Magnetic Resonance offers the advantage of no radiation exposure but has been used less frequently due to higher cost. Magnetic resonance spectroscopy (MRS) using carbon (13C) is ideally suited for the research purposes, e.g., studies of metabolism due to the extensive range of compounds that can be detected and the ability to attribute signals to the different carbon atoms within individual molecules (43).

An ECG, ECG-stress test, stress echocardiography, stress single-photon emission computed tomography, or myocardial perfusion imaging should be performed to evaluate any symptoms of myocardial ischemia, arrhythmias, and hypertension associated with structural heart disease (Table 3) (44).

Comorbidity in the Metabolic syndrome

Obesity / metabolic syndrome leads to numerous early complications (45,46) such as persistent low-level inflammation (47,39), hypertension (48) and left ventricular hypertrophy.

The Framingham Heart Study states that the risk of heart failure was doubled with obesity (49). The central risk factor concerning the MS in adolescence is juvenile obesity. Numerous studies (50,51) have demonstrated that vascular alterations associated with this syndrome result in much more prevalent strokes, dementia, and Alzheimer's disease.

The connection between asthma and obesity has long been noticed, (52) as well as immune system dysregulation. Non-alcoholic liver disease, cholecystitis (53,54), as well as pancreatitis, gastroesophageal reflux, and esophageal adenocarcinomas are many times more common in overweight individuals.

Obesity is one of the leading causes of osteoarthritis. It affects the knee and hand joints (55).

The risk of polycystic ovary syndrome (PCOS) is increased with obesity (56) with more serious PCO phenotype. Obese children are frequently subjected to societal condemnation and stigma (57) resulting in social isolation and depression, with girls facing more prejudice.

Conclusion

Metabolic syndrome is common in this child population, particularly among children who are overweight or obese. Preventing this disorder requires lifestyle changes, eating habits correction, and consistent physical activity.

New biomarkers, in addition to standard clinical and biochemical measurements, allow for the rapid and accurate diagnosis of pediatric metabolic syndrome.

Table 1: International Diabetes Federation (IDF) criteria for Metabolic syndrome in children (13)

Variables	IDF definition age <10 years	IDF definition ages 10–16 years	Cook *et al.*
Defining criteria	Cannot be diagnosed in the age group	Central obesity plus at least 2 out of 4 criteria	≥3 criteria
Central obesity		WC ≥90th percentile or adult cut-off if lower	WC ≥90th percentile
Hypertension		SBP ≥130 mmHg or DBP ≥85 mmHg or treatment with anti-hypertensive medication	BP ≥90th percentile
Hypertriglyceridemia		TG ≥150 mg/dL	TG ≥110 mg/dL
Low HDL		HDL <40 mg/dL	HDL ≤40 mg/dL
Impaired glucose		FPG ≥100 mg/dL or known T2DM	FPG ≥110 mg/dL

Table 2: Waist circumference reference values in boys and girls presented by percentile classification (27)

Age (years)	BOY (cm)		GIRL (cm)	
	50th Percentile	90th percentile	50th Percentile	90th percentile
10	63.7	77.7	62.5	75.5
11	65.8	81.1	64.4	78.3
12	67.9	84.5	66.3	81.2
13	70.0	87.9	68.2	84.1
14	72.1	91.3	70.1	86.9
15	74.1	94.7	74.1	89.8
16	76.2	98.1	73.9	92.7
17	78.3	101.5	75.8	95.5
18	80.4	104.9	77.7	98.4

Table 3: Diagnostic parameters of metabolic syndrome in children

PROCEDURE	PARAMETERS	RISK FACTORS
History	- gestational age - birth weight - eating habits - parental weight	SGA (small for gestational age) obesity or overweight parents
Anthropometric measurements	- Body weight - Body height - Waist circumference (WC) - BMI (kg/m²) - BMI/WC	Overweight or obesity abdominal obesity
Clinical examination	- Acanthosis nigricans - Signs of hyperandrogenism - Musculoskeletal deformities - blood pressure	- systolic blood pressure of ≥130 mmHg or a diastolic blood pressure of ≥ 85 mmHg;
Biochemical test	- Glycemia - OGTT and insulinemia, HbA1c - lipid profile (HDL, triglyceride, LDL) - Alanine aminotransferase (ALT)	impaired fasting glucose -triglycerides ≥ 1.47 mmol/L, and low values of high-density lipoprotein < 1.03 mmol/L The 95th percentile for ALT was 26.0 U/L in females and 37.2 U/L in males
Biomarkers	- CRP, IL-6, TNF-α markers of pro-oxidant status (OxLDL, uric acid) prothrombic factors (PAI-1)	

Table 4. Radiological diagnostic procedures of metabolic syndrome in children

Imaging studies	Ultrasonography (US)
	Bioelectrical impedance analyzer
	Computed Tomography (CT), Magnetic Resonance (MRI)
	Magnetic Resonance Spectroscopy (MRS)
	Positron Emission Tomography (PET)
	8F-fluorodeoxyglucose (FDG) PET
	Dual-Energy x-ray Absorptiometry (DXA)

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THE IMPORTANCE OF EARLY DETECTION OF DIABETES INSIPIDUS IN CHILDHOOD - CASE REPORT

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SUMMARY

Introduction: Diabetes insipidus (DI) is a disease that occurs due to inappropriate secretion of anti-diuretic hormone from the pituitary, or as a result of disorder in which the level of the kidneys cannot adequately respond to the secretion of this hormone. Also, it is known as central diabetes insipidus. The most common causes are head traumas, tumors of the hypothalamus and pituitary glands, inflammatory processes, histiocytosis, anomalies in the development of brain. It can appear in the form of familial diabetes insipidus or in certain syndromes (Wolfram syndrome). It is characterized by hypotonic polyuria higher than 3l/24h (which persists if even taking liquids stops), then by nocturia and compensatory polydipsia. Enuresis often occurs among children. Case report: A boy, aged 11, lives with his mother and brothers. Mother noticed that the boy was urinating frequently in last few months (diuresis 4.6 l/24h, and 3.25 l/24h). After two months, the boy developed double images and severe headaches, vomiting, inability to see, squinting in the right eye and headache in the back of the head. MNR of the endocranium indicates the presence of a tumor formation. The tumor was surgically removed, and the boy started with chemotherapy and radiotherapy. Due to persistent diabetes insipidus, the boy started using desmopressin-acetate - in tablet form. Active substance desmopressin - acts in the same way as the natural hormone vasopressin and regulates the kidney's ability to concentrate urine. The positive effect of taking the drug appeared after three weeks from the start of taking the therapy. Conclusion: Central (neurogenic) DI occurs as a result of a relative or absolute deficiency of antidiuretic hormone, which is responsible for the osmolality of body fluids. Based on this case, we want to show the importance of early diagnosis of the disease in order to improve the prognosis and the necessity of careful monitoring of these patients.

Key words: diabetes insipidus; antidiuretic hormone; dieresis; tumor; desmopressin-acetate.

SRPSKI

ZNAČAJ RANOG OTKRIVANJA DIJABETESA INSIPIDUSA U DETINJSTVU - PRIKAZ SLUČAJA

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SAŽETAK

Uvod: Insipidni dijabetes (DI) je bolest koja nastaje usled neodgovarajuće sekrecije antidiuretskog hormona iz hipofize ili poremećaja na nivou bubrega koji ne mogu adekvatno da odgovore na sekreciju ovog homona. Naziva se jos i centralni. Najčešći uzročnici su trauma glave, tumori hipotalamusa i hipofize, zapaljenski procesi, histiocitoza, anomalije u razvoju mozga. Moze se javiti i kao familijarni dijabetes insipidus ili u sklopu nekih sindroma (Volframov sindrom). Karakteriše se hipotoničnom poliurijom većom od 3l/24h, koja istrajava čak i nakon prestajanja uzimanja tečnosti, zatim nokturijom i kompezantornom polidipsijom. Enureza se često javlja kod dece. Prikaz slučaja: Dečak, uzrasta 11 godina, živi sa majkom i braćom. Unazad nekoliko dana majka je primetila da dečak učestalo mokri (diureza 4.6 l/24h, i 3.25 l/24h) . Nakon dva meseca, dečaku se javljaju duple slike i jake glavobolje, povraćanje, nemogućnost gledanja, žmiranje na desnom oku i glavoblje u potiljačnom delu glave. MNR endokranijuma ukazuje na prisustvo tumorske formacije. Tumor je operativnim putem odstranjen, a dečaku je određena hemo- i radioterapija. Zbog perzistentnog insipidnog dijabetesa dečak je počeo da koristi desmopressin-acetat - u tabletiranom obliku. Aktivna supstanaca dezmopresin - deluje na isti način kao i prirodni hormon vazopresin i reguliše sposobnost bubrega da koncentriše urin. Pozitivan efekat uzimanja leka javio se nakon tri nedelje od početka uzimanja terapije. Zaključak: Centralni (neurogeni) DI, nastaje kao posledica relativnog ili apsolutnog deficita antidiuretskog hormona, koji je odgovoran za osmolalanost telesnih tečnosti. Na osnovu ovog slučaja, želimo da prikažemo značaj rane dijagnoze bolesti u cilju poboljšanja prognoze i neophodnost pažljivog praćenja ovih bolesnika.

Ključne reči: dijabetes insipidus; antidiuretski hormon; diureza; tumor; desmopresin-acetat

INTRODUCTION

Central diabetes insipidus is a disorder induced by an aberrant release of anti-diuretic hormone from the pituitary gland, or by an issue in which the kidneys' function does not respond adequately to this hormone's output. Because the kidneys are unable to prevent water excretion, frequent urination occurs. The patient grew extremely thirsty and drank copious amounts of fluids. This cycle may persist when sleeping, resulting in nicturia. Peripheral or nephrogenic diabetes is another kind of diabetes insipidus. The arginine vasopressin receptors on tubular cells are absent in this illness. Despite the fact that both types of diabetes produce increased thirst and urine production, the conditions are vastly different (1).

A reduction in antidiuretic hormone synthesis causes central diabetes insipidus. Antidiuretic hormone (ADH) is a hypothalamic hormone that is stored in the posterior pituitary gland and subsequently released. ADH maintains the body's water balance by controlling how much water the kidneys reabsorb. More ADH is generated or released in response to dehydration or hypotension. In the majority of instances of diabetes insipidus, either the hypothalamus or the pituitary gland fails to produce adequate ADH. This causes frequent and significant urine loss (2).

When pathological lesions affect any part of the neurosecretory system, including the hypothalamic supraoptic and paraventricular nuclei, pituitary-hypothalamic tract, and pituitary gland's posterior lobe, ADH secretion and synthesis are diminished. Permanent diabetes insipidus occurs when a disease condition impacts the hypothalamic structures, resulting in the loss of secretory neurons. The loss of the posterior pituitary gland which stores ADH(3) may cause a transitory DI. The renal distal and collecting tubules do not absorb water in the absence of the hormone, leading to polyuria.

Vasopressin (AVP) increases water reabsorption in renal tubular cells by binding to V2 receptors and activating adenyl cyclase. This raises the concentration of cyclic adenosine monophosphate, which activates protein kinase A and phosphorylates protein aquaporin 2. This component subsequently fuses with the apical cell membrane, generating microtubules that allow water to diffuse.

People with central DI had lower aquaporin 2 expression as well as lower aquaporin 3 activity. It is thought that these deficiencies are the primary cause of polyuria in DI patients (4).

The most common causes of DI include head injuries, hypothalamic and pituitary tumors, inflammatory disorders, histiocytosis, and brain development anomalies. It might present as a genetic solitary condition or with specific symptoms (Wolfram syndrome). Because the etiology is uncertain in 30-40% of instances, it is classified as idiopathic diabetic insipidus with a probable autoimmune origin. Central DI with a rapid onset should be suspected of craniopharyngioma or germinoma if it develops before the age of 30, and of metastases if it appears beyond the age of 50 (5).

It is distinguished by nocturia and compensatory polydipsia, as well as hypotonic polyuria of more than 3l/24h (which persists even when liquid intake is halted). Children frequently have enuresis. DI is defined as serum osmolality greater than 300 mOsm/kg and urine osmolality less than 300 mOsm/kg.

Arginine vasopressin medication is used to treat diabetes insipidus. Desmopressin, a synthetic AVP equivalent, is more strong, has a longer half-life, and is easier to use. It is administered intravenously, subcutaneously, or as an intranasal spray. As a palliative therapy, the vasopressor actions of arginine vasopressin have been employed to minimize acute gastrointestinal bleeding. Hyponatremia and water intoxication are rare adverse effects that should be addressed when using these medication (6). The medication's therapeutic impact usually became obvious after three weeks of treatment.

AIM

Our study's goal is to provide a case with both standard and unusual symptoms of diabetes insipidus, as well as to explain the etiology of this condition.

CASE REPORT

A 11 years old lives with his mother and brothers. The boy's mother had noticed him urinating excessively for several months (2-3 times in one hour). He also needs to urinate multiple times during the night. Urination does not cause discomfort, however a tingling feeling may occur.

The patient is awake, oriented, afebrile, eupnoic, and developed normally upon admission to the Regional Hospital. The skull is slightly distorted, but the ocular bulbules and pupils are normal. Overall, the clinical results are normal. Diuresis was 4.6 l on the day of delivery and 3.25 l the next day, corresponding to 0.124 l/kg/BW. RBC: 3.21 x 109/L, HGB: 110 g/L, SE: 8/20 mm/h, serum lucose: 2.9 mmol/l, blood urea: 3.75 mmol/l, creatinine: 56 mmol/l, AST: 21 U/L, ALT: 26 U/L, RF: 10 IU/ml. Urinary tract ultrasonography revealed normal findings. The patient is taken to a tertiary health care facility for verification of the diagnosis and, if necessary, the commencement of therapy.

During the first hospitalization at Institute for Mother and Child (IMC) in New Belgrade, the diagnosis diabetes insipidus (DI) is confirmed. The oral therapy starts with Desmopressin (Minirin) 6,2mg at 1 + 0 + 1/2 per day.

The baseline cortisol level (550mmol) and TSH level (0.97) do not suggest a reduction in pituitary gland output.

The child experiences diplopia and severe headaches particularly in the nape of the neck, occur often throughout the night. He was also unable to blink his right eye. Vomiting occurs three to four times a day.

The MDCT (multi-dector computed tomography) of the endocranium (native and with IV contrast) detected tumor during the repeat hospitalization (AP 2.5 mm, a 19mm, 20mm LL). The tumor obstructs cerebral aqueducts between the third and fourth ventricles, causing hydrocephalus and a rise in both the lateral and third ventricles while leaving the fourth ventricle normal. As a result of fluid transudation via the ependyma, there is visible and early periventricular white matter edema. The condition required surgical treatment in the Institute of Neurosurgery in Belgrade.

At the time of admission to the neurosurgical hospital, the kid is conscious, oriented, active, with normal mental status, with no evidence of pyramidal lateralization. The oftalmology examination revealed exophthalmos and stretched conjunctival blood vessel. The other ocular tests results were normal.

MRI indicated a developing oval tumor in the pineal region (lamina kvadrigemina), dimension 2 x 1.5 x 2 mm, partially solid, partially cystic. The patient underwent single voxel proton MR spectroscopy with short duration (30ms) sequences, which identified the tumor in the pineal gland. The tumor was constituted of lipid / lactoid and lipid tisssue. The presented profile suggests cell proliferation and lymphocyte infiltration, and it corresponds to the emergence of the early germinoma.

Following the surgery preparation, an endoscopic ventriculocisteroskopia and tumor biopsy are performed. Pathohistological studies confirmed the presence of germinoma. Malignant cells were not detected in the cerebrospinal fluid, and beta HCG and alpha-feto protein levels in the serum and cerebrospinal fluid were normal. The membranous area of the floor of the third ventricle was fenestrated during the surgery, and contact was achieved between the interpendicular tanks and the ventricular system.

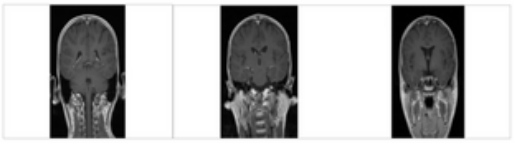

Fig. 1 - 3. Clear withdrawal of chamber system, without acute exacerbation of hydrocephalus with moderate collapse of the chamber

The post-operative course is adequate. A clean retraction of the chamber system, with slight constriction of the chamber and no substantial exacerbation of hydrocephalus, was detected by postoperative MRI, showing that the stoma was operating properly (Figure 1-3). Because of the boy's persistent diabetic insipidus, Minirin Spray therapy was combined with radiation treatment.
The child underwent chemotherapy and radiation therapy for the following five months, with satisfactory subjective and hematological tolerance.
An examination of growth hormone secretion is performed one year following surgery (table 1).

Table 1: Clonidine test results

Time	-30	0	30	60	90	120	150
Growth hormone	1.1	0.6	0.7	4.1	4.4	3.9	2.2

The lack of growth hormone, which had been suspected based on the patient's low growth rate during the previous 18 months, was verified on this occasion. Low growth hormone readings during the glucagon test (GH 1.1,1.2,1.4, 1.7, and 1.8mU/l) and IGF 1 (117 ng/ml) levels at the lower limit indicated growth hormone defficiency.
Following the consultation with the child and his mother, growth hormone substitution treatment was initiated in order to improve muscular and skeletal system development. A control MRI of the endocranium and spine should be performed within 6 months of starting growth hormone prescription. All of the possible risks of this treatment, including the likelihood of tumor recurrence, were reviewed. Hydrocortizone and thyroxine replacement were evaluated during the follow-up since therapy worsened hypocorticism and hypothyroidism.
Somatropin (Genotropin) was received for 26 months at a dosage of 0.03 mg/kg/24h. Check-ups were carried out on a regular basis by neuro-oncologists, neurosurgeons, and endocrinologists. The MRI of the endocranium was performed once a year to ensure that the primary disease has not recurred.
The child is now in good overall health, with no subjective discomfort, no substantial changes in body weight, and no headaches.

DISCUSSION

The most prevalent cause of DI in children and people under the age of 30 is germinoma or craniopharyngeoma, trauma and inflammatory processes, as well as tumor metastases.
Determining the pathophysiology of the vasopressin system has several major clinical consequences. The cerebral vasopressin cells are dispersed throughout the hypothalamus, tumors that induce diabetes insipidus must be either large and/or infiltrative, or positioned in the infundibulum - at the region of confluence of the hypothalamo-neurohypophyseal neuronal tract.
The germinomas causing diabetes iinsipidus can be relatively minor and undetectable by imaging for years after the development of polyuria. As a result, in infants with idiopathic or unexplained diabetes insipidus, assessment of the beta-subunit of human chorionic gonadotropin and MRI scans should be undertaken on a regular basis (7). This unit is frequently released by germinomas and pinealomas.
As a result, the DI may only be the tip of the iceberg, the first and only sign of tumors, possibly malignant ones (8). Early detection of these tumors (e.g., thyroid cancer, lymphoma), may affect survival (8).
In individuals with full central diabetes insipidus, the maximum urine-concentrating capacity is roughly 100mOsm/kg. Patients with untreated diabetic insipidus may survive well for a long time if their thirst and ability to take fluids is retained. If this capacity is compromised for any reason, dehydration occurs quickly, with potential hypotension, collapse, and death.
Vasopressin treatment can be used to treat central diabetic insipidus in children following neurosurgery in the early postoperative period (9, 10). Furthermore, vasopressin and its analogues treatment improves patients' quality of life.
Nocturia should be the trigger that causes the physician to investigate diabetes insipidus as a possible cause. Despite a substantial diuresis (more than 3l/24), our patient was not subjected to fluid restriction or a DDAVP (desmopresin) test. A positive family history (three years older brother had the same complaints and diagnosis) suggests that all patients be subjected to comprehensive genetic testing. The precise cause of this problem was discovered only after an MRI, and the potentially devastating consequences were avoided in this occasion.

CONCLUSIONS

A variety of conditions and diseases can lead to central diabetes insipidus. Clinical examination can provide critical information in the diagnosis of such illnesses. The age of the patient, as well as fluid consumption, vomiting, irritability, sleep problems, and mental impairment, all contribute to the diagnosis.
Based on this case, we want to emphasize the need of early detection in order to enhance patient prognosis and survival, as well as the importance of closely checking the treated persons for symptoms and signs of relapse.

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IMPACTED MAXILLARY CENTRAL INCISORS WITH SUPERNUMERARY TOOTH - CASE REPORT

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SUMMARY

Introduction: Presence mesiodens is not uncommon in clinic practice. It is cause of impacted permanent maxillary central incisors. Diagnosis of the delayed tooth is usually made on the basis of clinical and radiographic findings. The treatment include surgical exposure of the impacted maxillary central incisors and extraction of supernumerary tooth, because it is a direct obstruction for the eruption of maxillary central incisors. Impacted maxillary central incisors is moved into it's proper position with orthodontic traction. The aim is presented surgical-orthodontic treatment of impacted teeth, which is necessary to achieve stability esthetic and functional results.

Case report: This case report describes a surgical-orthodontic treatment of 9.5-old boy with both impacted permanent maxillary central incisors with supernumerary tooth which disturbs their normal eruption.

Conclusion: The gnathometric evaluation of spaces in dental arch, the assessment of dental age and radiographic analysis are preconditions of successful therapy. The impacted maxillary central incisors were successfully positioned in the maxillary arch, with an adequate width of attached gingiva. The careful and persuasive treatment planning of an orthodontist, oral surgeon and periodontist are the key to success in resolving such cases.
Keywords: impaction;maxillary incisors, mesiodens, treatment

SRPSKI

IMPAKTIRANI MAKSILARNI CENTRALNI SEKUTIĆI SA PREKOBROJNIM ZUBOM- PRIKAZ SLUČAJA

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SAŽETAK

Uvod: Prisustvo prekobrojnog zuba mesio-densa nije retka pojava u praksi. Njegovo prisustvo je vrlo često uzrok impakciji maksilarnih sekutića. Njihova dijagnostika je isključivo radiografska. Neophodno je ukloniti hirurški prekobrojni zub koji predstavljaju prepreku na putu nicanja maksilarnim sekutićima, a najčešće je ortodontska terapija nastavak terapije. Cilj je predstaviti da je ortodontsko-hirurška terapija impaktiranih zuba složena kako bi se došli do stabilnih fukcionalnih i estetskih rezultata.

Prikaz slučaja: Opisan je ortodontsko-hirurški tretman dečaka uzrasta 9.5 godina sa impakcijama oba centralna maksilarna sekutića uz prisustvo prekobrojnog zuba koji je ometao njihovo nicanje.

Zaključak: Analiza prostora u zubnom luku, tačna procena dentalnog doba i detaljna radiološka analiza su preduslovi za dobar plan terapije. Maksilarni centralni sekutići su uspešno postavljeni u zubnom luku sa zadovoljavajućom širinom pripojne gingive.Ujedno i hirurško-ortodontsko-parodontološka saradnja su ključ uspeha u rešavanju ovakvih slučajeva.

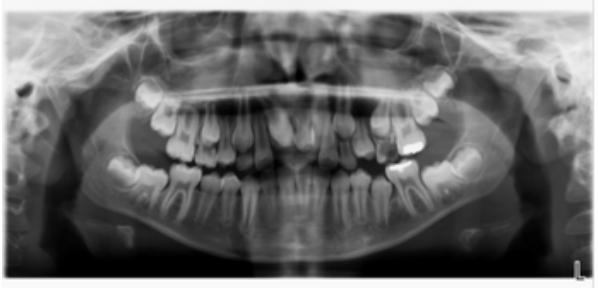
Ključne reči: impakcija; maksilarni sekutići, mesiodens, therapija

INTRODUCTION

It is often stated that the maxillary central incisor is the third-most commonly impacted tooth after third permanent molars and maxillary canines.[1] Impaction of permanent maxillary incisors occurs in 0,2-1% of the population [2-4], early referral of patients in the mixed dentition is common due to concern of parents and general dentists regarding delayed eruption of the permanent maxillary central incisors. The causes of impaction of maxillary central incisors can be obstructive (supernumerary teeth, odontome, ectopic position of the tooth) and traumatic (obstruction due to soft tissue repair, dilacerations, acute traumatic intrusion, arrested root development). [5] The most common etiological factor is the presence one or more supernumerary teeth or trauma to primary dentition. Mesiodens is supernumerary tooth which is situated between the central incisors. The majority of the mesiodens were unilateral located in the premaxillary region, were conical shaped, and remained unerupted. Supernumerary teeth are commonly observed as an isolated developmental anomaly. While the familial tendency of supernumerary teeth has been documented, its genetic causality has not yet been determined.[6] 56-60% of supernumerary teeth-mesiodens is cause impaction of permanent incisors due to a direct obstruction for the eruption.[7]
In case, when supernumerary tooth is in midline of maxilla, between permanent central incisors, it don't disturb their eruption. Then, both central incisors and mesiodens can eruption. But, when the supernumerary tooth crosses the midline, it may provide the physical obstacle to the normal eruption of central incisors. Alternatively other physical obstacles, such as above supernumerary teeth, may be the more likely reason for a secondary displacement of these teeth. It may be found one or both impacted maxillary permanent incisors.[8]
An increase in the patient's age or abnormalities in the shape and direction of eruption of supernumerary teeth is associated with complications. These parameters should be considered while formulating the treatment plan.[9] As the majority of unerupted incisors presented with complications, a systematic and organized method of history taking as well as clinical and radiographic examinations is mandatory in the diagnosis.[10] Clinical inspection and palpation of the alveolar process is recommended.[5,11] The choice of surgical method depends of the position of the impacted tooth. The correct choice of the surgical method with orthodontics forced eruption of teeth means more successful aesthetics result.[12-15]

CASE REPORT

This case report describes a surgical-orthodontic treatment of a patient with a both impacted permanent maxillary central incisors with supernumerary tooth which disturbs their normal eruption.
Patient was a 9.5 year-old boy in early mixed dentition. The child was physically healthy and had no history of medical and dental trauma. There was 9 months after the extraction of the deciduous maxillary incisors. Intraoral clinical examination revealed a missing maxillary permanent central incisors and erupted permanent lateral maxillary incisors. There was crowding in lower jaw and an Angle's class ½ II molar relationship. Oral hygiene was compromised.
Panoramic imaging revealed the bilaterally impaction of permanent maxillary incisors and supernumerary tooth. It was superimposed on unerupted left central incisor. The incisors were in the level of the apical third of the roots of the erupted maxillary lateral incisors.

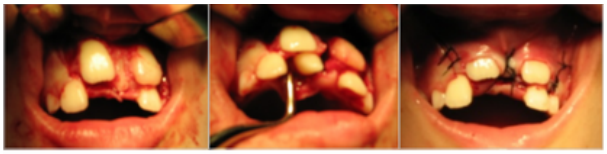


[Figure 1] 9.5years old boy. Ortopanthomograph

Gnatometric evaluation showed the following results: the sum of upper incisors was 36mm (macrodontia), the heritage crowding and less width of upper and lower dental arches, the total tooth width of the side segment (CP2) in the upper and lower jaw obtained from Moyers's analysis was less than average.[16]
The dental age of the patients lags behind the chronological age, as witnessed radiographic by less root formation than is to be expected at a given age. Result from Demerjian table for dental age was same as radiographic-a late developing dentition.[17]
For this case was developed 2-stage treatment plan. The first stage included surgical exposure of the impacted central incisors and extraction of supernumerary tooth; in the second stage -orthodontic treatment for alignment maxillary incisors with a fixed orthodontic appliance 4x2.

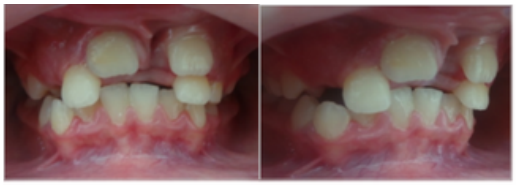
1. Surgical exposure of impacted central incisors and extraction of supernumerary tooth

At surgery, after careful elevation of the flap, the supernumerary tooth were identified on the palatal side, behind right incisor and extracted to leave empty sockets. A minimal area of the labial surface of the incisors was exposed, without removing surrounding bone. Removal of bone inferior to the incisors would have left a deep defect, by including the socket of the extracted supernumerary tooth.



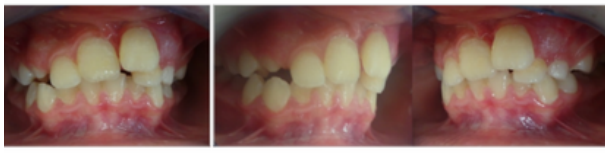
[Figure 2] 9.5years old boy. Surgical exposure of impacted maxillary central incisors and extraction of supernumerary teeth (mesiodens)

Apically repositioned flap was sutured back. The distance between the maxillary incisors was 8mm, after extraction of mesiodens.



[Figure 3] 9.5years old boy. Two weeks after surgical exposure of impacted maxillary central incisors

We followed up eruption of central maxillary incisors, when they were approaching to occlusal plan the distance was reduced. This distance was 1mm after six month. The left lateral incisor was behind central incisor and middle of upper dental arch was moved on left side.

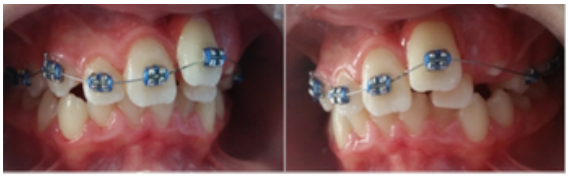


[Figure 4] 10years old boy.Eruption of maxillary incisors 6 month after surgical exposure and frenectomy, diastema mediana closed

There was inadequate space distribution of the maxillary incisors causing midline deviation. In this case, there was indication for frenectomy. It was done before the orthodontic treatment.[18]

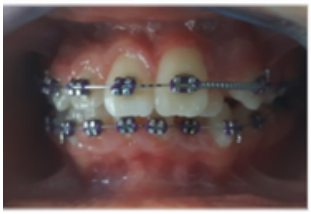
2. Orthodontic treatment

Then orthodontic therapy started with a fixed orthodontic appliance 4x2 in upper and lower jaw and it should be retained until full eruption of the permanent tooth has occurred.



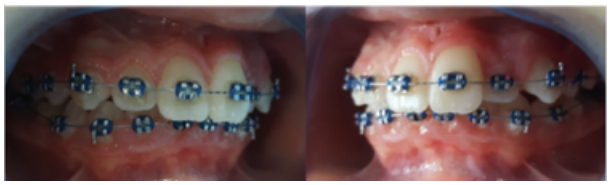
[Figure 5] 10 years old boy. Orthodontic treatment with fixed appliance 4x2

A mixed dentition treatment can effectively be provided using fixed appliances over traditionally used removable appliances.[19]
The fixed orthodontic treatment consisting of brackets on the incisors and bands on the first permanent molars in the upper arch. Direction of force was adjusted occlusally to guide the movement of the central incisors into the correct position. At the end of six months of treatment, the central incisors were in right position in dental arch and midline is corrected. After six month full fixed orthodontic treatment was started, because the maxillary and mandibular arch were not aligned. We distalized the maxillary posterior teeth and correcting the dental Class II relationship. During the therapy, we used a nickel-titanium open-spring for space for left lateral incisor. The therapy continues that will remain leveling for teeth #22 #35 #45.



[Figure 6] 10.4 years old boy. Orthodontic treatment with nickel-titanium open spring for left lateral incisor

No tooth was extracted for getting additional space in arhes. The dental age of the patients lags behind the chronological age, and conclusion is that have enough time for developing of jaws and getting space to accommodate all the teeth.[5]
Results: The impacted maxillary central incisors were successfully positioned by getting additional space in the arch. The both central maxillary incisors reached the occlusal plane, stable occlusion was achieved. Although, there was some vertical discrepancy in the gingival height between the right and left central incisors. This fact could be explained that the position of unerupted left incisor was higher than the right incisor. Gingivoplasty is our plan, but now the patient and his parents don't want any further surgery.



[Figure 7] 10.8 years old boy. After 9 months orthodontic therapy, relationship Class I

DISCUCSION

Most impactions are symptomless and aside from maxillary central incisors, do not usually an obviously abnormal appearance. An impacted central incisor is usually diagnosed accurately when there is delay in the eruption of tooth. Because impaction occurs only in the young patients, the orthodontic-surgical solution was chosen. The aim of therapy is traction of the impacted central incisor into proper position.[20]
The prognosis of the result depends on several factors: root length, surgical exposure, type and height of periodontal attachment, oral hygiene and treatment duration.[21,22] Chaushu et al[23] treated 64 impacted incisors with the orthodontic-surgical modality and reported that overall success rate was 90%.

Impacted teeth are often associated with a lack of space in the immediate area. This is frequently due to the drifting of adjacent teeth, although crowding of the dentition in general may be the prime cause. For this facts, it is very important measurement of side segment (CP2) in dental arches from Moyers's analysis.[5,16] The eruptive events may be guided and directed, so that teeth may occupy the space prepared to receive them in the dental arch. Regardless of the position of an unerupted tooth, it may be biologically directed to its place in the dental arch.[24] Treatment initiation with operation in the absence of the required eruption space is not recommended. Space creation followed by surgical removal of any obstruction together with orthodontic traction initiation produces excellent results, while waiting for spontaneous eruption is indicated only in cases of favourable patient's age and tooth location [25].
An incorrectly indicated surgical method can cause some undesirable consequences, as gingival recession, reintrusion of tooth. Surgical management of an impacted tooth is considered the key to achieving desirable esthetic results.
As suggested by Becker A.[26] surgical exposure can be performed in 3 accepted ways: 1.circular excision of the oral mucosa, 2. apically repositioning of the raised flap and 3.closed eruption technique in which the raised flap that incorporates attached gingiva is fully replaced back in it's former position after an attachment has been bonded to the impacted tooth.
It has been suggested and shown that the "window" approach causes statistically significant loss of attachment, recession and gingival inflammation occur on maxillary teeth after surgical exposure. Therefore, a part of keratinized gingiva must be preserved or an apical flap should be used. This approach aims at obtaining keratinized gingiva around the entire erupting tooth. It is important for a tooth to erupt through attached gingival, and not through alveolar mucosa.[1,27,28] In our case, apically repositioning flap was carried out.
Accordingly, motivation for treatment in these cases is minimal and much time has to be spent with the patient before child agrees to treatment.[1,5] The story does not end there, since these patients may often and require periodic talking to maintain their cooperation and the resolve to complete the treatment. That story was same in our case. Patient did not maintain the required standard of oral hygiene and while it is so difficult to justify continuing treatment in this circumstances. His request in the middle of treatment was to remove appliances. Missing motivation of patient and his parents and rare visiting to orthodontist are reasons way this orthodontic treatment isn't finished. Therefore, while ambitious and innovative treatment plans may be suggested, it is essential to take motivation into account before advising lengthy and complicated treatment, since the risk of non-completion may be high. Ideally, examination and treatment planning should be undertaken within a multidisciplinary clinic.
The impacted maxillary central incisors were successfully positioned by getting additional space in the maxillary arch, with an adequate width of attached gingiva. The careful and persuasive treatment planning of an orthodontist, oral surgeon and periodontist, are the key to success in resolving such cases.

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Conflict of interest statement: The authors state that there is no conflict of interest regarding the publication of this article.

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Treba se pridržavati jezičkog standarda BritishEnglish. Radovi koji se u celini dostave na engleskom jeziku imaju prioritet u objavljivanju.

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Skraćenice. Koristiti samo kada je neophodno, i to za veoma dugačke nazive hemijskih jedinjenja, odnosno nazive koji su kao skraćenice već prepoznatljivi (standardne skraćenice, kao npr. DNK, sida, HIV, ATP). Za svaku skraćenicu pun termin treba navesti pri prvom navođenju u tekstu, sem ako nije standardna jedinica mere. Ne koristiti skraćenice u naslovu. Izbegavati korišćenje skraćenica u kratkom sadržaju, ali ako su neophodne, svaku skraćenicu ponovo objasniti pri prvom navođenju u tekstu.

Decimalni brojevi. U tekstu rada na srpskom decimalne brojeve pisati sa zarezom, a u tekstu na engleskom, u tabelama, na grafikonima i drugim prilozima, budući da se i u njima navodi i prevod na engleskom jeziku, decimalne brojeve pisati sa tačkom (npr. u tekstu će biti 12,5±3,8, a u tabeli 12.5±3.8). Kad god je to moguće, broj zaokružiti na jednu decimalu.

Jedinice mera. Dužinu, visinu, težinu i zapreminu izražavati u metričkim jedinicama (metar m, kilogram – kg, litar – l) ili njihovim delovima. Temperaturu izražavati u stepenima Celzijusa (°C), količinu supstance u molima (mol), a pritisak krvi u milimetrima živinog stuba (mm Hg). Sve rezultate hematoloških, kliničkih i biohemijskih merenja navoditi u metričkom sistemu prema Međunarodnom sistemu jedinica (SI).

Obim rukopisa. Celokupni rukopis rada – koji čine naslovna strana, kratak sadržaj, tekst rada, spisak literature, svi prilozi, odnosno potpisi za njih i legenda (tabele, slike, grafikoni, sheme, crteži), naslovna strana i sažetak na engleskom jeziku – mora iznositi za originalni rad, saopštenje, rad iz istorije medicine i pregled literature do 5.000 reči, a za prikaz bolesnika, rad za praksu, edukativni članak i rad za "Jezik medicine" do 3.000 reči; radovi za ostale rubrike moraju imati do 1.500 reči.

Provera broja reči u dokumentu može se izvršiti u programu Word kroz podmeniTools–Word Count ili File–Properties–Statistics.

Tabele. Svaka tabela treba da bude sama po sebi jasno razumljiva. Naslov treba otkucati iznad tabele, a objašnjenja ispod nje. Tabele se označavaju arapskim brojevima po redosledu navođenja u tekstu, sa nazivom na srpskom i engleskom jeziku (Table). Tabele raditi isključivo u programu Word, kroz meni Table–Insert–Table, uz definisanje tačnog broja kolona i redova koji će činiti mrežu tabele. Desnim klikom na mišu – pomoću opcija Merge Cells i Split Cells – spajati, odnosno deliti ćelije. U jednu tabelu, u okviru iste ćelije, uneti i tekst na srpskom i tekst na engleskom jeziku – nikako ne praviti dve tabele sa dva jezika! Kucati fontom Times New Roman, veličinom slova 12 pt, sa jednostrukim proredom i bez uvlačenja teksta. Korišćene skraćenice u tabeli treba objasniti u legendi ispod tabele na srpskom i engleskom jeziku. Svaku tabelu odštampati na posebnom listu papira i dostaviti po jedan primerak uz svaku kopiju rada (ukupno tri primerka tabele za rad koji se predaje).

Slike. Slike se označavaju arapskim brojevima po redosledu navođenja u tekstu, sa nazivom na srpskom i engleskom jeziku (Figure). Za svaku sliku dostaviti tri primerka ili tri seta u odvojenim kovertama. Primaju se isključivo originalne fotografije (crno-bele ili u boji), na sjajnom (glatkom, a ne mat) papiru, po mogućstvu formata 9×13 cm ili 10×15 cm. Na poleđini svake slike staviti nalepnicu sa rednim brojem slike i strelicom koja označava gornji deo slike. Voditi računa da se fotografije ne oštete na bilo koji način. Slike snimljene digitalnim fotoaparatom dostaviti na CD i odštampane na papiru, vodeći računa o kvalitetu (oštrini) i veličini digitalnog zapisa. Rezolucija treba da bude 300dpi, format slike 10×15 cm, a format zapisa .JPG ili .TIFF. Ukoliko autori nisu u mogućnosti da dostave originalne fotografije, treba ih skenirati kao Grayscaleu rezoluciji 300 dpi i u originalnoj veličini i snimiti na CD.
Slike se mogu objaviti u boji, ali dodatne troškove štampe snosi autor.

Grafikoni. Grafikoni treba da budu urađeni i dostavljeni u programu Excel, da bi se videle prateće vrednosti raspoređene po ćelijama. Iste grafikone linkovati i u Word-ov dokument, gde se grafikoni označavaju arapskim brojevima po redosledu navođenja u tekstu, sa nazivom na srpskom i engleskom jeziku (Graph). Svi podaci na grafikonu kucaju se u fontu Times New Roman, na srpskom i engleskom jeziku. Korišćene skraćenice na grafikonu treba objasniti u legendi ispod grafikona na srpskom i engleskom jeziku. Svaki grafikon odštampati na posebnom listu papira i dostaviti po jedan primerak uz svaku kopiju rada (ukupno tri primerka za rad koji se predaje).

Sheme (crteži). Sheme raditi u programu Corel Drawili Adobe Illustrator(programi za rad sa vektorima, krivama). Svi podaci na shemi kucaju se u fontu Times New Roman, na srpskom i engleskom jeziku (Scheme, Drawing), veličina slova 10 pt.Korišćene skraćenice na shemi treba objasniti u legendi ispod sheme na srpskom i engleskom jeziku. Svaku shemu odštampati na posebnom listu papira i dostaviti po jedan primerak uz svaku kopiju rada (ukupno tri primerka za rad koji se predaje).

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pridržavati sepomenutog standarda, jer je to jedan od tri najbitinija faktora za indeksiranje prilikom klasifikacije naučnih časopisa. Pravilnim navođenjem literature Praxis medica bi dobio na kvalitetu i bolje bi se kotirao na listi svetskih naučnih časopisa.

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