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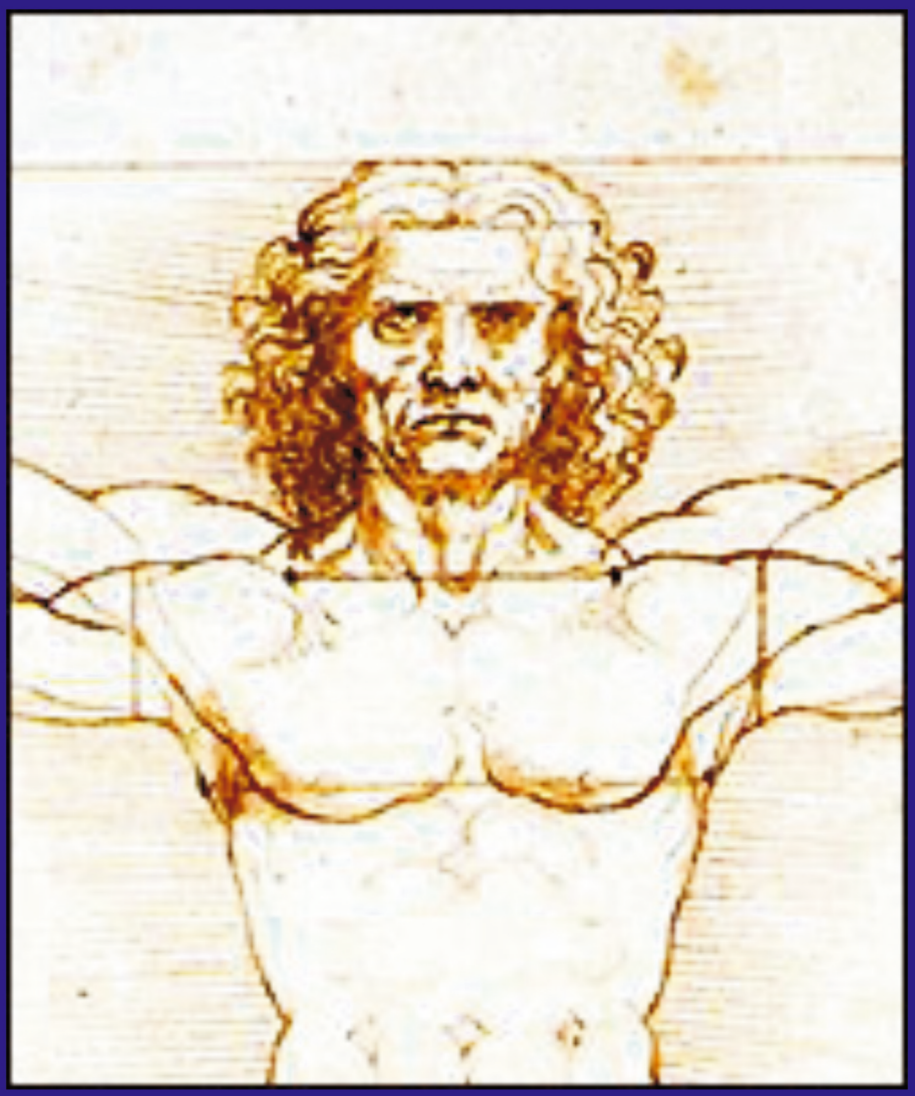

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SANAMED

Riječ urednika

Poštovani i cenjeni profesori saradnici, dragi čitaoci,

Dvanaest punih godina smo zajedno i svi smo tu od kako naš „Sanamed“ izlazi. Neko sa više angažmana, neko sa manje, ali smo na okupu. Sama činjenica da smo u timu i da je naš zajednički rad ovjenčan kvalitetom i uspešnim radom, govori da vredimo. Bilo je u našem radu momenata krize, ali se ona odnosila na finansijski dio. Naporom uredništva uspjeli smo da se održimo i redovno izlazimo.

„Sanamed“ u ovom momentu je najaktivniji i zbog toga imamo i veliki broj radova koje nijesmo u mogućnosti da objavimo odmah po dobijanju istih. Svakako, svaki rad koji prođe sveukupnu proceduru biće objavljen ako ne u ovom, ono u nekom od slijedećih brojeva. Hvala svima koji pišu i koji šalju radove.

Pisanje radova nije puka formalnost. Čitanje onoga što je napisano je još značajnije, a uraditi nešto za nauku u korist čovjeka i društva je od primarne važnosti. U tome je čvor pojedinca, da se dokaže da vrijedi, da se posvjetio nauci i svom napredovanju u njoj. To i jeste razlika i između onih koji vrijede i onih što spavaju. Kako bi ovo društvo u nauci opstalo da nije tih sjajnih ljudi?

Neki dan objaviše svjetske agencije kako je u Kini, prof. He Džankui promenio gene bliznakinjama koje su rodjene pre nekoliko nedelja. On je objasnio da je promenio gene još tokom vještačke oplodnje i na taj način zaštitio embrione od HIV virusa. Iako je genetsko modifikovanje na ljudima zabranjeno u većini zemalja, prof. He je izjavio da je studiju predao jednom naučnom časopisu za objavljivanje, ali nije otkrio ime tog časopisa.

Nije mi namjera da citiram cio tekst u vezi sa ovim naučnim otkrićem, već da se divim onim ljudima koji svojim doprinosom daju mogućnost da se suprotstave najtežim mogućim oboljenjima kod ljudi bez obzira da li je to područje malignih bolesti, infektivnih ili bilo koji problem u vezi sa ljudskim zdravljem. Nauka i Etički komitet, kao i Svjetska zdravstvena organizacija će dati odgovor na opravdanost modifikacije genetske strukture i do kojih granica je moguće ići. Medjutim, taj i svaki, pa čak i onaj najmanji osvrt na bilo kakvo istraživanje u nauci, iako mali korak za čovječanstvo, veliki je za čovjeka da bi ostao zdrav i produžio zdravu populaciju.

Nema ništa svjetlije i vrednije od zdravlja. Bez dobrog zdravlja ukočene su sve poluge ka napredovanju društva u svim sveopštim segmentima. Snaga jedne zemlje proističe iz zdrave populacije koja je osnovni motor za sva dešavanja. Tačno je da se u mnogim zemljama malo ulaže u nauku, barem kada je medicinska nauka u pitanju, ali entuzijazam pojedinaca nas ohrabruje da se taj korak održi i svaki ulog u zdravlje daje višestruki odgovor društvu.

Poštovani prijetelji, moja malenkost i lekari koji rade na ovom časopisu uspješno nastavljamo sa radom i jako se radujem što nas sve okuplja isti cilj - očuvanje i unapređenje zdravlja. Naš časopis će se truditi i dalje da napreduje u postizanju još kvalitetnijeg nivoa.

Na kraju želim da svima čestitam nastupajuću Novu 2019. godinu, uz želje da u nju zakoračite sa dobrim zdravljem, uspjesima i blagoslovima.

Avdo Ćeranić

A word from the editor

Dear esteemed professors associates, dear readers,

We are together for full twelve years since our "Sanamed" started coming out. Some with more engagement, some with less, but we are together. The very fact that we are a team and that our joint work is marked with quality and success says it is worth it. There were moments of crisis within our work, but it referred to financial part only. With the efforts of editors we managed to maintain regular publications.

"Sanamed" is most active at this moment and this is why we have large number of papers we are not able to publish immediately after receiving them. Of course, every paper we receive will be reviewed, processed and published in this or some of our future publications. Big thanks to all of you who write and send their work.

Paper writing is not a mere formality. Reading what is written is even more significant, and to do something for the science in favor of man and society is primary. This is the knot of an individual, to prove its worthiness, to dedicate itself to science and its advancement in it. This is the difference amongst those that are worthwhile and those that are sleeping. How would this society survive within science if there were not for these amazing people?

Some days ago it has been published how in China prof. He Jiankui changed genes to twin girls born only a few weeks ago. He explained that he changed genes even during artificial insemination and in this way protected embryos from HIV virus. Although genetic modification in humans is forbidden in most countries, prof. He stated that he gave the study to one scientific journal for publications, but he never revealed the name of the journal.

It is not my intent to quote the text in connection to this scientific discovery, but only to admire those people who by their contribution give the opportunity for confrontation to hardest possible diseases whether this is the area of malignant, infective diseases or any other problem related to health. Science and ethical board, as well as World Health Organization will give their response on justification

of gene structure modification and to what borders it is possible to go. However, this and every even the smallest review of to any research in science, although a small step for humanity it is big for man to remain healthy and prolong a healthy population.

There is nothing brighter and more valuable than health. Without good health, every lever towards the advancement of society in all segments is numb. The strength of one country stems from a healthy population that is main engine for all events. It is true that many countries are poor investors in science, at least when it comes to medical science, but enthusiasm of individuals encourages us to keep the pace and every contribution to health gives larger response to society.

Respected friends, myself and doctors that work on this journal continue successful work and I am glad that we are gathered around the same goal – preservation and promotion of health. Our journal will continue its effort in achieving even higher quality level.

In the end, I want to congratulate everyone upcoming New Year, with wishes to step into 2019. with good health, success and blessings.

Avdo Ceranic

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COMPARATIVE STUDY ON THE EVALUATION OF TEMPOROMANDIBULAR JOINT AND NECK STRUCTURES IN HEALTHY VOLUNTEERS AND IDIOPATHIC SCOLIOSIS PATIENTS

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Abstract: **Objective:** The aim of this study was to investigate the correlation of temporomandibular joint disorders (TMD) and neck structure changes in adolescents with idiopathic scoliosis (IS) by clinical examination. **Material and Methods:** The study included 51 patients affected by IS (24 males, 27 females; mean age: 13.5 ± 2.1 years) selected using simple random sampling, and a healthy control group of 50 subjects (23 males, 27 females; mean age: 14.5 ± 2.3 years). The Diagnostic Criteria for Temporomandibular Disorders: Clinical Protocol and Assessment Instruments (DC/TMD) form was utilized to assess the signs and symptoms of TMD in the subjects. For the evaluation of neck structures, masseter and temporalis muscles, pressure pain threshold (PPT) values were measured with a hand-held pressure algometer. Obtained data were analyzed statistically applying Mann-Whitney U test, Wilcoxon, and chi-squared tests with a significance level of 0.05. **Results:** According to the DC/TMD form, the following parameters showed statistically significant differences between the groups ($p \leq 0.001$): presence of TMD, temporal headache, midline deviation, and right and left lateral movements. The PPT values were higher in the control group compared with the study group ($p < 0.001$). Additionally, the type of pain-related TMD identified in the subjects was myalgia. The myalgia was significantly ($p < 0.001$) higher in the study group (68.6%) than in the control group (22%). **Conclusion:** This study concluded that spinal diseases which cause postural changes, like IS, in the head and shoulder region are associated with muscle adaptation and alterations in the temporomandibular joint area.

Key words: Temporomandibular disorders, scoliosis, headache, pain, myalgia.

INTRODUCTION

The influence of spinal deformities on temporomandibular joint disorders (TMD) is a current topic with no consensus as of yet. Temporomandibular disorders (TMD) have a multifactorial etiology, and the guidelines of the American Academy of Orofacial Pain have proposed a link between cervical spine disorders and TMD. Recent literature investigates the etiologic factors of TMD and the link between different postural anomalies and spinal diseases. Since idiopathic scoliosis (IS) is a common cervical spinal disease, the possible association between disease-induced postural changes and TMD poses a question in the minds of researchers.

The symptoms of TMD are headache, joint sounds, pain, alterations in functional dynamics, limitation of mandibular movements and other changes in muscle tonus (1). Although pain and restriction of the mandibular opening are the main complaints of TMD, these may be accompanied by muscle tiredness, deviation in the spine axis and consequently, postural problems (2). Postural problems contributing to the development of dentofacial anomalies may lead to a chronic influence on head posture over the long term (3, 4). A study by Kondo et al. demonstrated that changes in head posture can cause structural deformities in TMJ or TMD (5). These findings, which are also present in scoliosis, raise the question of whether this disease is related to TMD or not. However, there is not sufficient data in the literature.

The most well-known type of IS is right convex dorsal scoliosis, which belongs to the non-balanced types and causes a left-inclined head position with postural changes. The literature notes that bad posture influ-

ences the muscles and tendons and affects mandibular position, concluding that alterations in the TMJ region may be associated with joint dysfunction. Some studies in the literature have indicated that postural alterations of the head and cervical spine function over burden the TMJ and are treated as a causal agent of TMD, while others did not demonstrate any relevance, therefore highlighting the need for further studies on this issue (6-9).

AIM

In the above-mentioned contradictory situations, it seems that current studies in the literature has not evaluated the possible relationship between IS and TMD. Therefore, the present study aims to answer this question and collect data for further studies related to this topic. The null hypothesis is that IS is associated with the presence of TMD and changes in neighboring structures.

MATERIAL AND METHODS

Study sample

The Ethics Committee of the Istanbul University Faculty of Dentistry approved this research under protocol number 2017/49 and the research was conducted in accordance with the Helsinki Declaration of 1975. Subjects attending the study received detailed formal information about the procedures, and their caregivers provided written informed consent for participation. Based on a preliminary pilot study, a power analysis was performed using G*Power (v3.1.7) to determine the essential sample size required to achieve a minimum 80% power with an alpha error probability of 5%; this generated a sample size of at least 26 participants. Authors decided to increase the number of participants as it was not difficult to reach a large number of patients and healthy controls in the institution where the study was conducted. Accordingly, initial sample size was increased to 50 per group so the authenticity and results of the study could be improved. Final calculations were performed based on the new sample size. A simple random sampling from a list which included more subjects was used to recruit participants for the study.

Protocol

The present study was conducted in the Department of Prosthodontics, Faculty of Dentistry, Istanbul University, Istanbul. The total sample size consisted of 101 subjects between the age of 10–17 years. Included in the study were 51 patients affected by IS (24 males, 27 females; mean age: 13.5 ± 2.1 years) and a healthy control group of 50 subjects (23 males, 27 females; mean age: 14.5 ± 2.3 years).

All the subjects had to meet the following inclusion criteria: diagnosis of IS (for the experimental group), under 18 years of age, absence of pregnancy, absence of spontaneous pain (myogenous pain at rest or without preciseconditions), good general health based on medical history, absence of trauma which could affect postural position, absence of distinct postural problems, absence of dentofacial deformity, absence of ongoing orthodontic treatment or former orthodontic treatment in the past 3 years, and the absence of neurological disorders. Subjects with congenital or acquired skeletal abnormalities, earache or headache, mental disorders, were undertaking any physical therapy for postural alteration or had back surgery were excluded from the study due to possible impact on the results.

In the study group, 58 patients with diagnosed IS were referred by the Department of Orthopaedics and Traumatology, Istanbul Faculty of Medicine, Istanbul University. Seven of these patients were excluded from the study, as two of them had ongoing orthodontic treatment and five had backsurgery for scoliosis treatment. The remaining 51 patients (mean age: 13.5 ± 2.1 years) and the control group underwent a TMD clinical diagnosis according to the Diagnostic Criteria for Temporomandibular Disorders: Clinical Protocol and Assessment Instruments (DC/TMD) with a focus on the criteria of axis I. For the evaluation of muscles, upper trapezius muscle and SCM (sternocleidomastoid muscle) were added to the category during examination as ažsupplemental muscle group' upon complaints of the subjects. Using these criteria, individual records of each subject examined were created and data records obtained to investigate the effect of clinical status on the possible relationship of IS and TMD.

In addition to the DC/TMD protocols, pain of the head and neck muscles during clinical examination was assessed by obtaining pressure pain threshold (PPT) measurements taken from the points listed in Table 1 with a hand-held algometer (Force Dial model FDK 40 Push Pull Force Gage; Wagner Instruments, Riverside, CT, USA). The PPT was bilaterally assessed by applying pressure to the lateral pole and around the lateral pole of TMJ and the following four muscles for three consecutive series in a random sequence: masseter, temporalis,

Table 1. *Anatomical sites of PPT (pressure pain threshold) assessment of evaluated muscles*

Evaluated muscle	Segments
Masseter	Origin, body, and insertion
Temporalis	Anterior, middle, and posterior
SCM†	Upper, middle, and lower
Upper trapezius	Midpoint between C7 and acromion

SCM†: sternocleidomastoid muscle

SCM, and upper trapezius. During muscle evaluation, the most sensitive points in those areas were measured and average values were used for analysis. The blinded examiner was trained to apply a steady pressure of 1 kg/cm^2/s with optimal positioning of the algometer vertically to the evaluated surfaces. A 90.8% specificity value was used to determine the appropriate PPT cut off values for all muscles studied. The examination of the above mentioned muscles was applied extraorally by the same examiner and the interval rate between the examination of the right and left sides was five seconds (10). A digital metronome was used in all evaluations to supply an audio feedback and standardize testing speed for the examination. Participants were informed that the aim of the study was to define the pain threshold and they were asked to report when they first felt pain. All participants were trained formally on the the nar area of the right hand with a first assessment at the beginning of the study.

All the data obtained from the tests were collected and separate files were prepared for each subject.

Statistical tests

The IBM SPSS V23 software package (IBM Corp., Armonk, NY, USA) was used for data analysis. Data normality was confirmed by the Shapiro-Wilk test. The Mann-Whitney U test and Wilcoxon tests were used for comparison of data with non-normal distributions. To evaluate the qualitative variables, the chi-squared test was performed. Quantitative data that do not correspond to normal distribution are presented as median (min-max) and qualitative data are shown as frequency (percent). Significancelevels were set at $p < 0.05$.

RESULTS

Resulting PPT values were higher in the control group compared with the study group, as verified by the statistically significant difference between the two groups ($p < 0.001$).When the right and left mean values of the groups were analyzed for intragroup evaluation, a statistically significant difference was noted for temporalis muscle (right-left: 3.6 kg/f/cm^2 [2.1 kg/f/cm^2– 4.1 kg/f/cm^2] - 3.1 kg/f/cm^2 [2.9 kg/f/cm^2 – 3.6 kg/f/cm^2] and TMJ (right-left: 3.7 kg/f/cm^2 [2.9 kg/f/cm^2 – 4.2 kg/f/cm^2] - 2.9 kg/f/cm^2 [2.1 kg/f/cm^2– 3.3 kg/f/cm^2]) in the control group ($p < 0.001$) (Table 2).

Protrusive movement, pain-free opening, maximum unassisted opening, and incisal overjet and overbite showed no statistically significant difference between the study and control groups ($p > 0.05$). However, midline deviation was slightly higher in subjects with IS (2 mm [1 mm – 3 mm]), and the IS group had lower right-left lateral movement values (5 mm [2 mm

Table 2. *PPT (pressure pain threshold) values of anatomical structures assessedwithan algometer*

	Control Median (Minimum-Maximum) (kg/f/cm^2)	**Study** Median (Minimum-Maximum) (kg/f/cm^2)	p*
Right temporalis	3.6 (2.1–4.1)	1.2 (1–1.3)	< 0.001
Left temporalis	3.1 (2.9–3.6)	1.2 (1–1.3)	< 0.001
p**	< 0.001	0.083	
Right masseter	3.2 (0.7–4)	1.2 (1–1.3)	< 0.001
Left masseter	3.3 (2.3–4)	1.2 (0.6–1.5)	< 0.001
p**	0.051	0.797	
Right TMJ‡	3.7 (2.9–4.2)	1.2 (0.7–1.5)	< 0.001
Left TMJ‡	2.9 (2.1–3.3)	1.2 (0.8–1.2)	< 0.001
p**	< 0.001	0.476	
Right upper trapezius	3.7 (2.5–4.1)	1.2 (0.6–1.5)	< 0.001
Left upper trapezius	3.7 (2.8–4.1)	1.1 (0.8–1.3)	< 0.001
p**	0.730	0.960	
Right SCM†	3.1 (2.5–3.9)	1.1 (0.5–1.3)	< 0.001
Left SCM†	3.1 (2.–3.9)	1.1 (0.5–1.3)	< 0.001
p**	0.355	0.959	

SCM†: sternocleidomastoid muscle
TMJ‡: Lateral pole and around lateral pole of temporomandibular joint
* Mann-Whitney U test
**Wilcoxon test

Table 3. *Descriptive statistics of study measurement values*

	Control Median (Minimum-Maximum) (mm)	**Study** Median (Minimum-Maximum) (mm)	p*
Incisal overjet	2 (1–10)	2 (1–5)	0.716
Incisal overbite	2 (0–4)	3 (0–5)	0.590
Midline deviation	0 (0–3)	2 (1–3)	< 0.001
Right lateral movement	7 (4–8)	5 (2–8)	0.001
Left lateral movement	7 (2–8)	5 (3–8)	< 0.001
Protrusive movement	5 (2–6)	4 (3–7)	0.087
Pain-free opening	45 (40–58)	45 (32–55)	0.911
Maximum unassisted opening	45 (40–58)	45 (34–55)	0.563

* Mann-Whitney U test

Table 4. *Comparison of t qualitative data (Frequency-%)*

	Control	**Study**	p*
Pain disorders			
None	39 (78)	16 (31.4)	< 0.001
Myalgia	11 (22)	35 (68.6)	
Location of headache			
None	41 (82)	32 (62.8)	< 0.001
Temporal	9 (18)	19 (37.2)	

* Chi-squared test

– 8 mm], 5 mm [3 mm – 8 mm]) than the healthy control group (7 mm [4 mm – 8 mm], 7 mm [2 mm – 8 mm]) by a significant difference ($p \leq 0.001$) (Table 3).

The type of pain-related TMD identified in the groups was myalgia. The myalgia was significantly higher in the IS group (68.6%) than in the control group (22%) ($p < 0.001$) (Table 4).

Temporal headache results were higher in the IS group (37.2%) compared with the control group (18%), as conWrmed by the signiWcant diference between the two groups ($p < 0.001$) (Table 4).

DISCUSSION

This study was performed to gain a deeper insight into the effect of characteristic features of IS on TMD, and to contribute to the scarce amount of data about this topic. The findings obtained in the current study are original,as no specific study has been conducted on patients with idiopathic scoliosis regarding TMD.

According to the DC/TMD examination form of axis I assessment, statistically significant differences were found between the values of the study and control groups for the following parameters: presence of TMD (pain disorders), PPT values, temporal headache, midline deviation, and right/left lateral movements. Findings show these changes in idiopathic scoliosis patients may play a predisposing role in TMD and in changes to incorporated structures, thus, the null hypothesis can beaccepted. Other measurements of incisal overjet and overbite, protrusive movements, mandibular opening pattern, and right and left TMJ disorders were approximately equal, and there were no statistically significant differences. When examining the values of midline deviation, lateral movements, incisal overjet and overbite, it was discovered that the obtained numerical values in the study group were in accordance with a previous study in literature (11). Pain-free opening 45mm (32 mm – 55 mm) and maximum unassisted opening 45 mm (34 mm – 55 mm) values were in the normal range for the study group and showed no signiWcant differences between groups (12). These parameters, investigated in the current study, can be used during routine TMJ examination in clinics and are practical in terms of early diagnosis and the need for early treatment options for TMD.

In the literature, a variety of results have been reported regarding body posture-TMD correlation. Some studies found a correlation between body posture and TMD, while others did not state any kind of relationship (9, 13-17). In this respect, some researchers support the theory that the forward-inclined head position and the dislocated center of gravity could be a risk factor in TMD development; others report that a laterally inclined head position loads the joint area asymmetrically and this situation leads to mandibular deviation (4, 5). The same variational situation is also described in reports of pediatric patients and postural changes (18). This group of patients with IS were chosen to perform this study because they have precise postural changes on the frontal plane. According to the present study, the obtained values of midline deviation, asymmetrical characterization of lateral movement ranges, PPT values, and temporal headache

parameters seem to support the null hypothesis regarding the relationship between IS and the presence of TMD and changes in neighboring structures. This data suggests the possibility of development of unilateral dentofacial deformities or TMD in this patient group.

The data obtained in the study indicates patients with IS are more likely to have muscular disorders than any other TMD type. While 68.6% of the subjects in the study group had pain-related TMD, this was 22% in the control group ($p < 0.001$) (Table 4). PPT values for the examined muscles showed a statistically significant difference between groups ($p < 0.001$) (Table 2). The results of the present study show lower PPT values for the study group; this suggests that the patient group is more prone to have pain in the evaluated muscles than the control group. Another supporting finding is that 37.2% of the IS group had temporal headaches, as opposed to 18% of the control group ($p < 0.001$) (Table 4). These can be attributed to idiopathic scoliosis-related postural changes or resulting reactions from the adaptation of the surrounding tissues. Thus, the involvement of muscles in IS isan important factor in terms of TMD and postural changes and indicates the importance of muscle examination for both orthopedists and dentists during clinical examinations in daily practice.

The findings of the present study can be supported by the recent study from Nota et al.,demonstrating the role of muscles in the appearance of TMD (19). Other literature in agreement with the present studyis Vegh et al.,which includes the evaluation of scoliosis patients and shows 21.42% of the scoliosis group had pathological symptoms of TMJ, in comparison to another study group with Scheuermann's disease. But that research did not mention the type of TMD or any symptoms (11). Furthermore, the results of the present study support the hypothesis of Deriu et al.that the presence of oligosynaptic and polysynaptic pathways between the vestibular labyrinth and the masticatory muscles (named vestibulo-masseteric reflex) can be considered a potential relationship between myogenous and postural disorders, though arthrogenous ones (20). However, this hypothesis is thought to be speculative and could not be proven due to the limited findings.

Based on previous studies, opinions differ in terms of correlation between postural alterations and TMD. If this correlation exists, the relationship between postural alterations and TMD is still not clearly explained. This theory is inconsistent with the study by Rocha et al., as they found no significant differences in posture-TMD correlation between subjects with and without unilateral disc displacement of joints by explaining these findings as habitual daily postures or functional adaptations like compensatory cervical extensions (9). However, they admit that the uncoordinated actions of forces can contribute to a change in the center of mass and cause imbalance in the musculoskeletal system. IS leads to changes in the center of mass on the frontal plane by the characteristic right/left tilted head position and resulting postural balance problems, which may also take place in TMJ, as this change occurs in the whole body. From this point of view, the findings of the present study are in accordance with the literature and indicate postural changes caused by idiopathic scoliosis (IS) may play a role in increasing the risk of TMD by affecting TMJ and incorporated structures (9, 19). However, available information is insufficient to achieve a clear conclusion in this regard, and this topic needs further clinical long-term study.

Limitations of the study

As a suggestion for future researchers, we recommend taking into consideration the type of TMD in evaluating possible postural effects due to the multifactorial etiology and variety of clinical conditions. For this purpose, MRI assessment which is one of the limitations of the present study can be utilized to detect the status of TMJ and the type of TMD. This type of assessment would also be helpful in excluding false positives that may occuras clinically asymptomatic TMD during the workflow. Another limitation of this study is that only the superior body quadrant was considered in the evaluation of posture-TMD correlation. Appraising global body posture is recommended to reveal all possible effects of postural stability on the musculoskeletal system and TMD. Such an approach may be beneficial for both improving knowledge of the physiology of the postural change-TMD relationship and carrying out robust comparisons among studies in the literature, providing standardization in the methodology.

CONCLUSION

Within the limitations of the study, it may be concluded that a relationship can be found between craniocervical posture in the frontal plane and the presence of muscular TMD in IS patients. An original finding of the current study was that the spinal alterations may be a risk factor for pain disorders of TMJ. Therefore, patients with IS should be routinely monitored in terms of TMD and neck structure changes, and early measures should be taken to reduce the need for further treatment. In this regard, it becomes essential to improve rehabilitation and orientation programs for this group of adolescents with the aim of hindering possible future complications of TMD, improving quality of lifeand providing psychosocial and financial advantages. There is a need for further studies with a larger sample in order to reveal the relevance of this important factor in TMD diagnosis and to develop relevant scientific knowledge on this topic.

DECLARATION OF INTEREST

The authors declare that there are no conflicts of interest.

ABBREVIATIONS

DC/TMD — Diagnostic Criteria for Temporomandibular Disorders: Clinical Protocol and Assessment Instruments
IS — Idiopathic scoliosis
PTT — Pressure pain threshold
SCM — sternocleidomastoid muscle
TMD — Temporomandibular joint disorders
TMJ — Temporomandibular joint

Sažetak

KOMPARATIVNA STUDIJA PROCENE TEMPOROMANDIBULARNOG ZGLOBA I STRUKTURA U VRATU KOD ZDRAVIH VOLONTERA I KOD PACIJENATA KOJI BOLUJU OD IDIOPATSKE SKOLIOZE

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Cilj: Cilj ove studije bio je da se ispita povezanost poremećaja temporomandibularnog zgloba (TMD) i promena struktura u vratu kod adolescenata sa idiopatskom skoliozom (IS) kliničkim ispitivanjima. **Materijal i metode:** U studiju je uključen 51 pacijent oboleo od IS (24 muškarca i 27 žena; prosečne starosti: 13,5 ± 2,1 godina) koji su selektovani primenom jednostavne nasumične metode i zdrave osobe, koje su činile kontrolnu grupu, koja se brojala 50 članova (23 muškarca; 27 žena, prosečne starosti: 14,5 ± 2,3 godine). Dijagnostički kriterijumi za oboljenja temporomandibularnog zgloba: klinički protokoli procena instrumenata (DC/TMD) bili su korišćeni radi procene znakova i simptoma TMD kod ispitanika. Za procenu struktura vrata, masseter i temporalni mišić su bili korišćeni. Meren je bolni prag draži na pritisak (PPT) korišćenjem ručnog algometra. Dobijeni rezultati analizirani su korišćenjem statističkog Mann-Whitney U testa, Wilkoksoni Hi kvadrat testa sa nivoom značajnosti p = 0,05. **Rezultati:** Prema DC/TMD formularu, prikazani parametri su pokazali statističku značajnu razliku između grupa ($p \leq 0,001$): prisustvo TMD, temporalne glavobolje, devijacije u odnosu na središnju liniju, levi i desni pokreti u stranu. PPT vrednosti su bile više u kontrolnoj grupi u poređenju sa grupom obolelih ($p < 0,001$). Štaviše, vrsta bolno-zavisnog TMD utvrđena je u pacijenata sa mijalgijom. Mijalgija je bila statistički značajno viša u grupi obolelih (68,6%) nego u kontrolnoj grupi (22%). **Zaključak:** U ovoj studiji je zaključeno da spinalni poremećaji koji uzrokuju posturalne promene, kao što su idiopatska skleroza, u regionu vrata i ramena su povezani sa mišićnom adaptacijom i promenama u regiji temporomandibularnog zgloba.

Ključne reči: temporomandibularni poremećaji, skolioza, glavobolja, bol, mijalgija.

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PLACING A THREADED PLUG IN THE HOLE OF A LOCKING PLATE AT THE FRACTURE LEVEL CAN INCREASE THE RESISTANCE OF THE PLATE: A BIOMECHANICAL STUDY

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Abstract: **Objectives:** This study aimed to evaluate whether placing a threaded plug in the hole of a locking plate at the fracture level is beneficial for increasing the resistance of the plate.

Methods: This experimental study analyzed load and compression forces in sheep tibia bone models. The following groups were assessed: Group 1 ($n = 4$), control bone samples; Group 2 ($n = 4$), samples of screw plate fixation without threaded plug in the hole at the fracture level; and Group 3 ($n = 4$), samples of screw plate fixation with a threaded plug in the hole at the fracture level. Elastic force, bending moment, elastic compression, and rigidity were evaluated using a three-point bending test.

Results: Group 1 showed the greatest elastic force and the least amount of compression. The rigidity and elastic force were better in Group 3 than in Group 2. The mean elastic force in Group 3 was 22.4% of that in Group 1, whereas the mean elastic force in Group 2 was 19% of that in Group 1. Rigidity in Group 3 was 24.7% of that in Group 1, whereas rigidity in Group 2 was 18.3% of that in Group 1. Improved results were obtained in Group 3 when compared with Group 2.

Conclusions: Our results suggest that placing a threaded plug in the hole of the plate at the fracture level provides additional rigidity and stability by improving resistance to loading forces, but the differences were not statistically significant.

Key words: locking plate; elasticity; rigidity, threaded; plug.

INTRODUCTION

The locking compression plate allows the combination of standard plate technology and locking screws having angular stability along with inter-fragmentary compression, and it is contemporarily being used for fracture fixation (1, 2, 3).

Further understanding of fracture biology and biomechanics has allowed surgeons to use better-designed implants. To restore anatomy and mechanical stability, adequate plate fixation is necessary; thus, uneventful fracture healing can be achieved (4). A plate screw system maintains functionality if the forces applied to the system do not impair stability (5). However, failure can still occur. Distribution and appropriate positioning of screws are important to avoid insufficiency of the plate. Mechanical forces may lead to disruption of the implant after reduction and fixation of the fracture (6, 7, 8). Screws may break, and plate breakage or plastic deformation may occur. When fatigue failure occurs, it is likely to be at the level of the open hole over the fracture site (9, 10). Various factors, such as the quality of bone, surgical technique, and materials used, may influence the mechanical environment of the implant.

However, there is limited research in the literature, particularly on the distribution of tension and deformation associated with forces applied after fixation of a fracture with implants and on whether placement of a threaded plug in the hole of the implant at the fracture level is useful.

The aim of the present study was to evaluate if the rigidity, elastic force, bending moment, and elastic deformation are improved by placing an additional threaded plug at the fracture level. We hypothesize that all these parameters will be improved by filling the empty hole at the fracture level.

MATERIAL AND METHODS

Study Design

This trial was carried out after receiving approval from the local ethics committee for experimental studies. The study included a total of 12 sheep tibia bones. For all the bones, soft tissue was removed, and all bones, except for control bones, were cut at the midshaft level with an electric saw. We used a standard 3.5 mm titanium 10-hole locking compression plate. The plate was placed and held with reduction forceps after obtaining adequate axial compression according to AO principles, and then, the plate was fixed with locking screws. The bones were randomly allocated into three groups. Group 1 ($n = 4$) included intact bones with no fracture or surgical intervention. In Group 2 ($n = 4$), tibial fractures were fixed with implants, but there was no threaded plug in the hole at the fracture level. In Group 3 ($n = 4$), screw fixation of the implant was performed, and a threaded plug was placed in the hole at the fracture level. The plate was on the side of force application in the three-point bending test. Figure 1 demonstrates the fixation of tibial fractures in Groups 2 and 3.

Figure 1. *Tibial bone fracture after fixation with an implant devoid of a threaded plug and additional threaded plug in the hole at the level of fracture in group 2 and group 3 respectively*

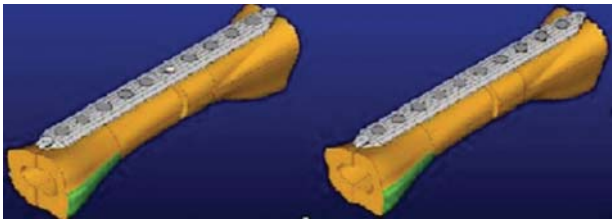

Figure 2. *Three dimensional models of implant fixation in groups 2 and 3*

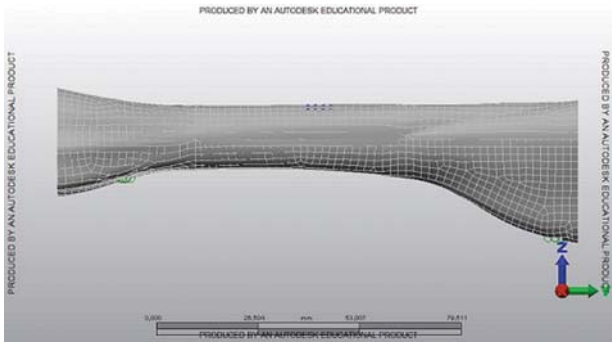

Figure 3. *Finite element analysis of intact bone*

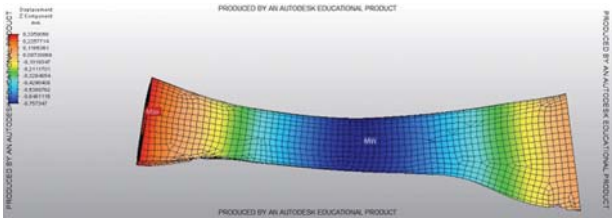

Figure 4. *Evaluation of the deformation and tension of the intact bone*

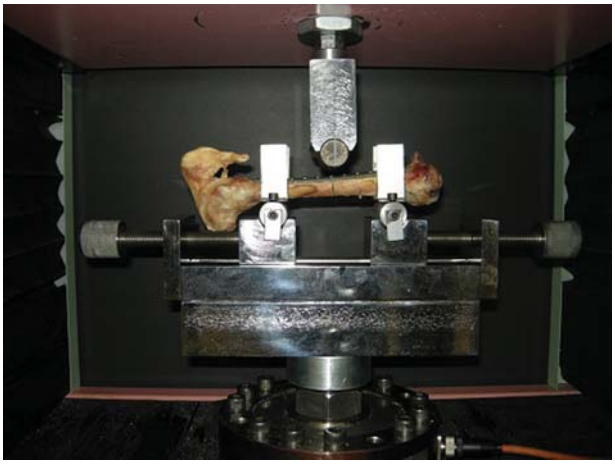

Figure 5. *The three-point bending test*

Finite element analysis (FEA) is a computerized method for predicting how a product would react to certain conditions in the real world, and it might indicate whether a product will break or work the way it was designed. The models were analyzed using Autodesk FEA software. Three-dimensional models of bones were obtained by using two-dimensional computed tomography (CT) images. Figure 2 demonstrates three-dimensional models of implant fixation in Groups 2 and 3. During analysis of the intact bone model, a force of 1224 N was applied, and the distance between two support points was 105 mm. As the load employed in the experimental model for the limit of elasticity was 1224 N, this value was selected in FEA as well. Figure 3 exhibits the FEA of a bone model in which 20,996 finite elements and 12,511 knots were used. Evaluation of the deformation and tension of the intact bone after application of 1224 N of force indicated compression of 0.757 mm (Figure 4).

Tension in the vertical axis of the bone and total equivalent tension were calculated. In the middle part of the bone, pulling tension at the lower portion and compression tension at the upper portion were 61.2 and 68.6 MPa, respectively. These values were within the elasticity limits of the bone.

Analysis of the bone fracture model was performed after fixation involving an implant and eight

screws. The use of an additional threaded plug at the fracture level of the implant was considered to increase the resistance of the system to bending. The bone FEA model involved 79.444 finite elements (largest diameter of 1.5 mm) and 36.960 knots. The implant involved 20.632 finite elements (largest diameter of 1 mm) and 10,467 knots. The eight screws fixed on the implant and bone involved 5674 finite elements (largest diameter of 1 mm) and 4453 knots. The threaded plug used to fix the hole involved 418 finite elements (largest diameter of 1 mm) and 274 knots.

The three-point bending test (Figure 5) is a mechanical experiment used to measure Young's modulus of a material in the shape of a beam. The amount of deformation (δ) is calculated using the following formula:

$$\delta = \frac{PL^3}{48EI}$$

where P indicates the amount of force employed, L indicates the distance between two support points, and EI indicates the rigidity of the sample. Substances with high rigidity have small δ values, whereas those with low rigidity have large δ values. As P and δ values can be measured during testing, EI can be calculated using the following formula:

$$EI = \frac{PL^3}{48\delta}$$

The EI value is important for evaluating the mechanical and physical behaviors of materials.

Results obtained after the experiments are presented in Table 1.

Statistical Analysis

All statistical analyses were performed using commercially available software (Statistical Package for Social Sciences, version 23, (IBM Corp., Armonk, NY, USA.) with 95% confidence intervals. One-way analysis of variance (ANOVA) and Tukey tests were used to compare differences among groups.

RESULTS

We found that the greatest rigidity and elastic force in conjunction with the lowest amount of deformation were in Group 1 (control group). Elasticity and rigidity were better in Group 3 than in Group 2, and deformation was less obvious in Group 3. The mean elastic force in Group 3 was 22.4% of that in Group 1, whereas the mean elastic force in Group 2 was 19% of that in Group 1. Similarly, the rigidity in Group 3 was 24.7% of that in Group 1, whereas the rigidity in Group 2 was 18.3% of that in Group 1. In other words, placement of an additional threaded plug at the fracture level appeared to improve stabilization; however, the difference between Groups 2 and 3 was not statistically significant.

Analysis of the situation without a threaded plug placed in the hole at the fracture level revealed a defor-

Table 1. *Results of elastic force, bending moment, elastic deformation and rigidity in 3 experimental groups*

Group	Sample #	Elastic force (N)	Bending moment (Nmm)	Elastic deformation (mm)	Rigidity (Nmm^2)
1	I	1236.06	32446.58	4.245	7.15E + 06
	II	1245.87	32704.09	2.989	1.04E + 07
	III	1265.49	33219.11	6.244	6.03E + 06
	IV	1147.77	30128.96	3.933	7.52E + 06
	Average	1223.80	32124.68	4.353	7.78E + 06
2	I	215.82	5665.28	5.670	8,65E + 05
	II	235.44	6180.30	4.690	1.67E + 06
	III	245.25	6437.81	8.066	8.49E + 05
	IV	235.44	6180.30	3.407	2.33E + 06
	Average	232.99	6115.92	5.458	1.43E + 06
3	I	264.87	6952.84	4.873	2.47E + 06
	II	294.3	7725.38	5.141	1.64E + 06
	III	294.3	7725.38	4.040	2.43E + 06
	IV	245.25	6437.81	4.802	1.15E + 06
	Average	274.68	7210.35	4.714	1.92E + 06

N: Newton, **Nmm**: Newton millimeter, **mm**: millimeter, $\mathbf{Nmm^2}$: Newton millimetersquare

mation of 1.65 mm in the vertical axis. Moreover, tension values detected in the pulling and compression axes were 888 and 1106 MPa, respectively. Tension was most prominent at the fracture level where the hole of the implant was empty.

In the bone implant model with a threaded plug placed in the hole of the implant at the fracture level, a force of 724 N was administered at the plug with a distance of 105 mm between support points. The greatest deformation in the vertical plane was 1.163 mm, and the greatest amount of tension measured at the implant for pulling and compression were 599 and 795 MPa, respectively.

The intact bone in Group 1 showed the highest resistance. Although the force applied in this group was higher than the forces applied in Groups 2 and 3, deformation and tension were lower. The same amount of force (724 N) was applied in Groups 2 and 3. Deformation in the vertical axis was less obvious, and tension at the upper and lower surfaces of the implant was reduced in Group 3.

With regard to elastic force, ANOVA showed a significant difference between the tested groups ($p < 0.05$). The mean elastic force was 1223.80 in Group 1, 232.99 in Group 2, and 274.68 in Group 3. The Tukey test showed significant differences between Group 1 and Groups 2 and 3 ($p < 0.05$). However, the difference between Groups 2 and 3 was not significant (Table 2).

The mean bending moment was 32,124.68 in Group 1, 6115.92 in Group 2, and 7210 in Group 3. ANOVA showed significant differences between the groups ($p < 0.05$). The Tukey test showed significant differences between Group 1 and Groups 2 and 3 ($p < 0.05$). However, the difference between Groups 2 and 3 was not significant (Table 3).

Although Group 1 showed the greatest rigidity and lowest deformation, there were no statistically significant differences according to ANOVA and Tukey tests ($p > 0.05$).

DISCUSSION

The present experimental study attempted to determine whether placement of an additional threaded plug at the fracture level could alter the biomechanics and resistance of the system in a sheep tibia model. We found that placement of a threaded plug in the hole at the fracture level improved the rigidity of the system and increased resistance to external impacts. Results obtained in Group 3 were better than those obtained in Group 2; however, the differences were not statistically significant. The data were confirmed in a finite element model of the tibia where generated and mechanical effects of loading forces were evaluated.

Following placement of the implant, the process of healing, which leads to osteogenesis in the surrounding region of the implant surface, starts. After installation of the implant, implant stability depends only on mechanical contact between the surrounding bone tissue and the implant. During successful healing, new bone formation facilitates implant stability over time, and the degree of initial implant stability (resistance to micromotion) is influenced by the implant design and its relation to the preparation for osteotomy. Micromo-

Table 2. *Comparison of the groups according to Tukey test with regard to elastic force*

			Average difference	**p**
Elastic Force (N)	Group 1	Group 2	990,81000*	**0,000**
		Group 3	949,11800*	**0,000**
	Group 2	Group 1	-990,81000*	**0,000**
		Group 3	-41,69200	**0,103**
	Group 3	Group 1	-949,11800*	**0,000**
		Group 2	41,69200	**0,103**

Table 3. *Comparison of the groups according to Tukey test with regard to bending moment*

			Average difference	**p**
Bending Moment (Nmm)	Grup 1	Grup 2	26008,76200*	**0,000**
		Grup 3	24914,33200*	**0,000**
	Grup 2	Grup 1	-26008,76200*	**0,000**
		Grup 3	-1094,43000	**0,103**
	Grup 3	Grup 1	-24914,33200*	**0,000**
		Grup 2	1094,43000	**0,103**

tion of the implant may cause interfacial deformation of tissue, which can subsequently affect the type of tissue formed. Therefore, it is important to achieve sufficient implant stability for osteointegration (11).

The mechanical loading of bone may positively influence bone mass by facilitating bone formation over bone resorption. It may increase bone mineral density and improve trabecular and cortical microarchitecture that contribute to bone strength (12). The interaction of various factors plays a role in the stabilization of the fracture and maintenance of appropriate physical and mechanical conditions after fixation (13).

The presence of an open hole in the load-bearing region of the plate results in stress concentration. To evaluate the effects of placing a threaded plug in the empty hole of a locking one-third tubular plate, Bellapianta et al. conducted FEA and then tested four different plate configurations at physiologically relevant loads experimentally using synthetic bone models. In their study, they found that the stress concentration factor reduced to 1.0, with reduction in stress to a level comparable to that with a solid plate (no hole) (14).

In another study, 20 five-hole tubular locking plates were mounted on an oak dowel with a 1 cm gap, and it was found that addition of screw-hole inserts did not change the biomechanical properties of the plate in a meaningful way (15). However, this was a simple study, and plate bending was not tested.

In a segmental defect model, Tompkins et al. tested the fatigue life of four constructs using an eight-hole locking plate. In their study, locking screws did not improve fatigue life; however, a locking button increased the fatigue life of the locking plate (16).

In this current study, we used fresh sheep tibia bones, which were randomly allocated into three groups, and created a transverse fracture without a gap. The same implant design was used in this trial, but two different fixation methods and a control group were utilized. In our opinion, the weakness is evaluation of the effect of the threaded plug in distraction. Further research is necessary to demonstrate the effects of this approach in different applications.

The present study provides new insights on the biomechanics and interaction of forces in a sheep tibia model. Realistic representation of deformation and tension on exposure to forces with different implant fixation techniques provides useful data for circumstances in physiological conditions. We found that placement of an additional threaded plug at the fracture level can be beneficial for stabilization and resistance.

The present study had some limitations, including a small sample size and experimental design. On the other hand, one of the major strengths was the use of FEA that allowed assessment of whether a threaded plug could alter the mechanical resistance of an implant. However, during interpretation of our results, it should be noted that in orthopedic biomechanics, FEA is considered a comparative tool rather than a predictive measure.

CONCLUSION

The results of the present study suggest that placement of a threaded plug in the hole of an implant at the fracture level might provide additional rigidity and stability by improving resistance to loading forces. However, the benefit might not be significant. Further controlled trials with a larger series are required to further assess the present results.

Abbreviations

FEA — Finite Element Analaysis
CT — Computed tomography

Declarations

Ethics approval and consent to participate

Not applicable

Availability of data and material

The datasets used and/or analysed during this study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests

Authors' contributions

GRU: Conception of the study, Collecting the data, Writing the manuscript, Editing the manuscript.

AB: Collecting the data, Editing the manuscript

YA: Collecting the data, Reviewing the manuscript

MA: Conception of the study, Supervising the study, Editing the manuscript

ŞE: Collecting the data, Editing the manuscript

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Sažetak

UGRAĐIVANJE NAVOJNOG ŠRAFA U OTVOR ZAKLJUČAVAJUĆE PLOČE NA MESTU PRELOMA MOŽE POVEĆATI ČVRSTINU PLOČE NA OPTEREĆENJA: BIOMEHANIČKA STUDIJA

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Cilj: Cilj ove studije bio je da se proceni kolika je korisnost ugradnje navojnog šrafa u otvor zaključavajuće na mestu preloma kod povećanog otpora istog.

Metode: Ova ekperimentalna studija analizirala je teret i kompresionu silu tibijalne kosti kod ove. Sledeće grupe su posmatrane: Grupa 1 (n = 4), kontrolni uzorci kosti; Grupa 2 (n = 4), uzorci prelomljene kosti bez uvijenog šrafa u otvoru na mestu preloma; i Grupa 3 (n = 4) činili su uzorci prelomljene kosti u koji je bio ugrađen navijeni šraf u otvor na mestu preloma. Elastična sila, mogućnost savijanja, elastična kompresija i rigidnost bili su procenjivani koristeći *three-point bending* test.

Rezultati: Grupa 1 pokazala je najveći stepen elastične sile i najmanji stepen kompresije. Rigidnost i sila elastičnosti bile su bolje u Grupi 3 u odnosu na grupu 2. Srednja vrednost elastične sile u Grupi 3 iznosila je 22,4% one procenjene u Grupi 1, dok je srednja vrednost elastične sile u Grupi 2 bila 19% od one procenje u Grupi 1. Rigidnost u Grupi 3 iznosila je 24,7% od one vrednosti procenjene u Grupi 1, dok je rigidnost u Grupi 2 bila 18,3% od one u Grupi 1. Bolji rezultati nađeni su u Grupi 3 kada smo ih uporedili saGrupom 2.

Zaključak: Naši rezultati sugerišu da ugradnja navijenog šrafa u otvor na mestu preloma omogućava dodatnu rigidnost i stabilnost, time što pojačava otpor na mestu sile, ali razlike nisu pokazale statističku značajnost.

Ključne reči: locking plate, elastičnost, rigidnost, navoj, šraf.

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THE INFLUENCE OF NUTRITION ON MUSCLE WASTING IN CRITICALLY ILL PATIENTS – A PILOT STUDY

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Abstract: **Introduction:** Adequate nutrition is necessary to prevent muscle wasting in critically ill patients. Decision about enteral or parenteral nutrition is always questionable. **Objective:** The aim of our study was to assess the impact of nutrition on muscle wasting in critically ill patients with trauma injury. **Material and methods:** The study was conducted in the period from January to December 2017 and included 30 critically ill patients with trauma injury hospitalized on the Intensive care unit (ICU) of the University clinic for anesthesiology and intensive care in Skopje. Included patients were divided into two groups: **group E** - patients where enteral nutrition was conducted after the third day of their admission in ICU and **group P** - patients where total parenteral nutrition was implemented in the first 24 hours of their admission.

The study monitored the impact of two different types of nutrition on muscle wasting evaluated by ultrasound measurements of m.quadriceps femoris thickness and biochemical measurements of the serum creatinine level. **Results:** In group E there was statistically significant muscle wasting evaluated by ultrasound between the1st and the 3rd and the1st and the 7th day. Difference in measured muscle thickness was 1.90 ± 1.49 mm between the 1st and the 3rd (p = 0.015) and 4.46 ± 2.81 mm between the 1st and the 7th day (p = 0.006). In group P muscle wasting in the same period was without statistical significance. Both groups showed statistically significant decrease in serum creatinine levels between the 1st and the 3rd (p = 0.003, p = 0.03) and the 1st and 7th (p = 0.003) day. The values of differences between the 1st and the 3rd and the 1st and the 7th day were 7.57 ± 4.12 mg/dl and 10.71 ± 5.79 mg/dl in group E and 11.43 ± 10.66 mg/dl and 15.28 ± 8.28 mg/dl in group P.

Conclusion: In our study we determined a significant decrease of muscle mass evaluated by ultrasound measurements of m.quadriceps femoris thickness in patients with enteral nutrition after the third day.

Key words: Critically ill patients, Enteral or parenteral nutrition, Muscle wasting, Ultrasonography, Serum creatinine concentration.

INTRODUCTION

In critically ill patients there is often muscle mass wasting and impaired muscle function. This leads to prolonged treatment, delayed rehabilitation, and reduced quality of life even up to five years after the acute suffering (1, 2). Muscle wasting as a complex problem beside from malnutrition it can be is also caused by immobilization, inflammation, and hyperglycemia. In order to prevent muscle-protein depletion and to provide nitrogen balance over the years, numerous strategies have been proposed. One of these strategies is adequate nutrition, which plays an important role in the general therapy of critically ill patients. Enteral nutrition has been always the primary alternative for nutrition in critically ill patients, and it is a superior nutritional type. The importance of the intestines as a part of the systemic response to injury and trauma is well known (3, 4). The non-use of the gastrointestinal tract leads to changes in intestinal microflora, impaired mucosal and immunological barrier leading to septic complications and organic failure (5). Unfortunately even in patients without contraindications for enteral nutrition, efforts to ensure proper nutrition through this pathway in the early stages of the disease are often hampered by the symptoms of gastrointestinal intolerance. In that case, the next option is parenteral nutrition. The parenteral nutrition is often called hyperalimentation, although it does not provide excessive caloric value. However, the parenteral nutrition sometimes is associated with seve-

ral complications and harmful effects on the immune system to the extent that it is often called a "total poisonous diet". The recent studies and obtained data do not agree with previously mentioned conclusions (6, 7).

Despite the advances in nutritional therapy, its main goal to prevent further protein loss often cannot be achieved. Patients in intensive care units (ICU) are continuously nourished and they do not starve, but catabolism and muscle reduction continues for a longer period of time. The muscle wasting in patients can be masked by the excess fat in sarcopenic obesity or fluid retention that can account for 10 to 20% of the body weight of critically ill patients (8, 9).

There are several methods for assessing muscle mass and muscle wasting. Ultrasonography is a new non-invasive technique that allows identification of changes in the muscular structure and morphology (10). Campbell et al. showed that ultrasonography allows identification and quantification of muscle wasting in edematous patients with multiple organic weaknesses (11). Also, the measures obtained by ultrasonography correlate with the measures obtained with CT diagnostics (12).

Creatinine is an endogenous substance with muscle origin generated by non-enzyme conversion of creatine and creatine phosphate (13). It is filtered through the kidneys without tubular reabsorption. So, the serum creatinine concentration is used to estimate glomerular filtration and renal function. It is also a powerful predictive indicator for mortality and outcome for hospital patients (14). As a consequence of the confirmed correlation between the serum creatinine and muscle mass, the serum creatinine concentration is used as a surrogate measure of muscle mass wasting (15).

The aim of the study was to assess the impact of two different types of nutrition on muscle wasting primary evaluated with ultrasound measurements of of m. quadriceps femoris muscle thickness and secondary evaluated by serum creatinine level determination in critically ill patients with trauma injury.

MATERIAL AND METHODS

The study was conducted in the period from January to December 2017., and included 30 critically ill patients with trauma injury hospitalized on the ICU of the University clinic for anesthesiology and intensive care. The included patients had mean age of 34 years (range from 16 to 50 years) and were equally divided into two groups: **group E** – with 15 patients where enteral nutrition was conducted after the third day of their admission and **group P** –with 15 patients where total parenteral nutrition was implemented in the first 24 hours of their admission. The aim of both types of nutrition was to obtain energy requirements with 20-25 kal/kg/day for each patient.

The study included patients older than 18 years of age where there was a need for intubation and mechanical ventilation, the need for treatment in ICU for more than seven days, patients with relative contraindications for enteral nutrition and indication for hospitalization due to polytrauma graded with medium to heavy Injury severity scores (ISS) (16). The study excluded the patients who did not meet the before mentioned criteria, pregnant women, patients with lower limb amputation and those with primary neuromuscular disease, disseminated carcinoma, renal disease, acute shock with systolic blood pressure less than 90 mm Hg or median arterial pressure below 70 mmHg, nutritional allergy, and absolute contraindication for enteral nutrition.

Absolute contraindication for enteral nutrition was:

- Massive intestines resection, with or without colon resection
- Proximal fistula with high output
- Perforation of the small intestines

The study evaluated the effect of two types of nutrition on patients muscle wasting which was measured by ultrasonography on the 1st, 3rd, and 7th day of their admission in ICU. The measurements were carried out by a single operator with a portable ultrasonograph Siemens Acuson X 300 and transducer VF13-5 (Figure 1). To determine muscle wasting, the thickness of m. quadriceps femoris (m. vastus intermedius and m. rectus femoris) - was measured at a two precisely determined points: the point between the lower third and the upper two-thirds of m. quadriceps femoris and the median point between the spina illiaca anterior superior and the upper pole of the patella, with the patientin the supinated position and the leg relaxed in extension (Figure 2).The mean value of the measurements at both points was calculated finally.

Biochemical analysis of serum creatinine concentration was performed on the 1st, 3rd, and 7th day of the admission in ICU.

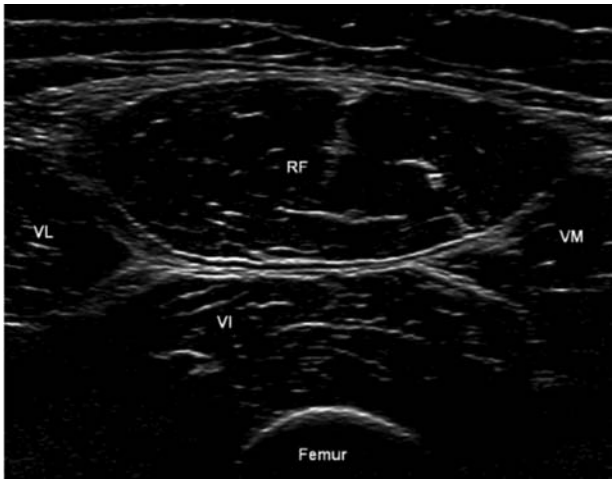

Figure 1. *Ultrasound image of m. quadriceps femoris*

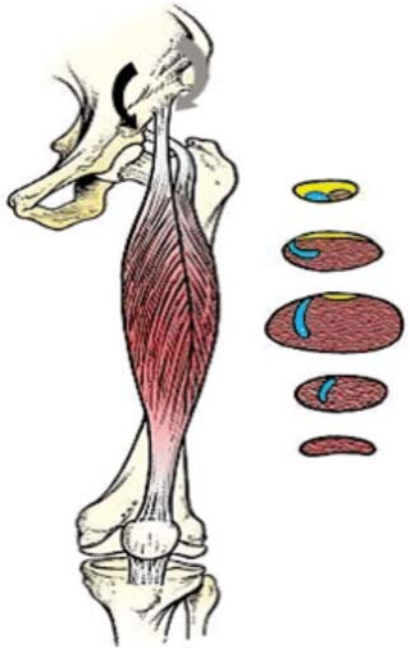

Figure 2. *Picture with anatomic presentation of m. vastus intermedius and m. rectus femoris*

Randomization was performed with closed envelopes, with number 1 for E group and number 2 for P group. The relatives of the patients were familiar with this research and they voluntarily signed a document for informational consent and took part in randomization.The research was prospective and randomized.

Statistical analysis

All data were presented as a mean value ± standard deviation and analyzed with SPSS 12.0 software. The comparison between the groups was made with t test and the difference of $p < 0.05$ was considered statistically significant.

RESULTS

Ultrasound analysis

Analysis between the 1st and the 3rd, the 1st and the 7th, as well as the 3rd and the 7th day (Table 1) showed that in group E with enteral nutrition there is a statistically significant decrease in muscle mass between the 1st and the 3rd day ($p = 0.015$) and between the 1st and the 7th day ($p = 0.006$). The difference between the 3rd and the 7th day was near the border of statistical significance ($p = 0.065$).

Analysis between the 1st and the 3rd, the 1st and the 7th, as well as the 3rd and the 7th day in the group P with early parenteral nutrition in all cases showed a decreased muscle mass but without statistical significance (Table 2). The greatest reduction in muscle mass was seen between the 1st and the 7th day ($p = 0.070$).

Serum creatinine analysis

Analysis of serum creatinine level measured in group E showed that there is a decreasing in the measu-

Table 1*. Differences in muscle mass loss (mm) at different time intervals in group E with enteral nutrition measured by ultrasonography*

Time intervals for Ultrasound measurements	Differences in Ultrasound measured muscle thickness (mm)		
	MV± SD	Min - Max	p value
1-3 day	1,90 ± 1,49	0,51 – 3,29	0,015
1-7 day	4,46 ± 2,81	1,86 – 7,06	0,006
3-7 day	2,56 ± 3,00	0,22 – 5,34	0,065

Table 2. *Differences in muscle mass loss (mm) at different time intervals in group P with early parenteral nutrition measured by ultrasonography*

Time intervals for Ultrasound measurements	Differences in Ultrasound measured muscle thickness (mm)		
	MV± SD	Min - Max	p value
1-3 day	1,81 ± 3,25	1,19 – 4,82	0,190
1-7 day	2,44 ± 2,94	0,27 – 5,16	0,070
3-7 day	0,63 ± 2,67	1,84 – 3,09	0,556

Table 3. *Differences in serum creatinine concentration (mg/dl)at different time intervals in Group E with enteral nutrition*

Time intervals for serum creatinine measurements	Differences in serum creatinine measurements (mg/dl)		
	MV± SD	Min - Max	p value
1-3 day	7,57 ± 4,12	3,76 – 11,38	0,003
1-7 day	10,71 ± 5,79	5,35 – 16,07	0,003
3-7 day	3,14 ± 5,30	1,76 – 8,05	0,168

Table 4. *Differences in serum creatinine concentration (mg/dl) at different time intervals in group P with early parenteral nutrition*

Time intervals for serum creatinine measurements	Differences in serum creatinine measurements (mg/dl)		
	MV± SD	Min - Max	p value
1-3 day	11,43 ± 10,66	1,57 – 21,29	0,030
1-7 day	15,28 ± 8,28	7,63 – 22,94	0,003
3-7 day	3,86 ± 6,59	2,24 – 9,95	0,173

red values of serum creatinine concentration with statistical significant difference between the 1st andthe 3rd (p = 0.003) andthe 1st and the 7th (p = 0.003) day (Table 3).

The analysis of serum creatinine level measured in group P showed that there is a decreasing in the measured values of serum creatinine concentration with statistical significant difference between the 1st and the 3rd (p = 0.03) and the 1st and the 7th (p = 0.003) day (Table 4).

DISCUSSION

In healthy persons, skeletal muscles are maintained as a balance between protein synthesis and protein digestion. Any prolonged change in balance will result in increased or decreased muscle mass (17).

Negative nitrogen balance and loss of muscle mass in correlation with trauma was described for the first time in 1932. Trauma is a cascade of inflammatory, immune, endocrine, and metabolic changes and it causes catabolism characterized by loss of body weight, muscle mass and strength reduction, as a consequence of the dominant proteolysis in terms of protein synthesis. Critically ill patients in the catabolic phase excreted 15 grams of nitrogen in urine versus normal losses of 0.7 to 1.4 grams per day, which is 94 grams of muscle protein or daily loss of 0.47 kg muscle mass. It's extremely severe muscle reduction (18). That is why critically ill patients need nutrients either in the form of enteral or parenteral nutrition, in order to avoid the energy deficiency which can lead to protein utilization and muscle tissue wasting (19). It is estimated that most patients in intensive care units receive only 49% to 70% of estimated caloric needs (20, 21). Although there is general agreement that excessive hypo-caloric or hyper-caloric nutrition should be avoided, there is still no consensus on how much the daily needs should be (22). Except the right caloric intake nutrition must also obtain the right protein intake in order to prevent muscle mass wasting (23, 24, 25, 26). Although there are some investigations, the pathophysiology of muscle wasting and the influence of nutrition on muscle wasting is still not well known. Different studies present different results according to this pathology.

Puthucheary et al. (27) showed that the catabolic condition and rapid muscle wasting in the first week of the critical illness may be independent of enteral nutrition. Using ultrasonography they determined 17% muscle mass wasting of rectus femoris muscle in the first 7 days of hospitalization. Contrary to expectations, in their study, high delivery of proteins through a nasogastric probe in the first week of a critical illness was associated with greater muscle wasting, thus challenging the idea that the beginning of enteral nutrition is beneficial. The criteria and timing of parenteral nutrition are also debatable. The study from Ferrie et al. (28) showed that the patients who took parenteral nutrition with 1.2 g/kg/day proteins had less muscle wasting of rectus femoris muscle than those who took 0.8 g/kg/day. Opposite to this study the EPaNIC study did not find any benefit of early parenteral nutrition on muscle wasting in the first days of hospitalization. According to the study from Casaer et al. (29) the early parenteral nutrition is associated with inhibited autophagy and impaired muscle integrity. Tolerating the macronutrient deficiency in the first week reduces the risk of muscle wasting. Hermans et al.considering the EPANIC study, concluded that the muscle wasting in patients with late parenteral nutrition group is slightly lower than in patients with early parenteral nutrition (30). Opposite to him Doig et al. (31) found lower muscle wasting in the early parenteral nutrition group. In another large multicentre study in patients with relative contraindication for enteral nutrition, the early application of parenteral nutrition reduced the duration of mechanical ventilation and potentially reduced the risk of muscle wasting (32, 33).

In our study, it was found that in Group E with patients who received enteral nutrition after the third day, there was a progressive muscle mass wasting with a statistical significance between the first and the third (p = 0.015) and the first and the seventh (p = 0.006) day. In group P patients who began to receive parenteral nutrition in the first 24 hours, did not show significant muscle mass wasting. Our results correlate with the results of the Doig et al. who reported lower muscle wasting in the group with early parenteral nutrition versus the group with standard nutrition (31). In our study to determine muscle wasting, the thickness of m. quadriceps femoris (m. vastus intermedius and m. rectus femoris) was measured by ultrasonography. Measure-

ment of muscle wasting by ultrasonography in patients in intensive care units is selected as a very practical one and at the same time the only possible solution compared to other techniques such as computed tomography, magnetic resonance, densitometry and others (34, 35, 36, 37). So far, different muscle measurements have been described to determine muscle mass wasting (38, 39, 40, 41). As in other studies, m. quadriceps femoris was used in our evaluation study as a muscle that is well described and easily visualized in conditions of impaired muscular architecture (36, 37).

To determine muscle wasting we also measured the concentration of serum creatinine. The leading cause of low serum creatinine concentration is low muscle mass (Table 5). The correlation between muscle mass and serum creatinine in one of the studies is r = 0.734 [95% CI 0.656 to 0.797] and r = 0.706 [95% CI 0.620; 0.774]; with a significance (p = 0.0001). In other words, malnourished people with lower muscle mass have lower levels of serum creatinine (42). In our study, the values of serum creatinine in group E significantly decreased between the first and third day and between the first and the seventh day p = 0.003. The same decrease in serum creatinine values occurred in the group P with statistical significance of (p = 0.03) between the first and the third day, and between the first and the seventh day (p = 0.003).

Table 5. *Factors affecting low serum creatinine levels*

Small muscle mass
Malnutrition
Hepatic lesion
Water shift
Increased renal clearance

CONCLUSION

From a brief review through the literature, it can be concluded that controversies about providing optimum energy, form of nutrition, and timing of initiation exist continuously, especially in the early phase of the critical illness. The nutritional strategy and goal should be personalized for individual patients. Muscles wasting measured with ultrasonography and serum creatinine analysis, are indicators of malnutrition, but also conditions subjected to other influences. In our pilot study, we determined a significant reduction in muscle mass in patients with relative contraindication of enteral nutrition and beginning of enteral nutrition after the third day, versus patients with early beginning of parenteral nutrition where we came to the conclusion that there is a decrease in muscle mass, but without statistical significance. Regarding the values of serum creatinine in both groups, there was a significant decrease in values in the both groups. The series of patients included in the study was small, and the reliability of the results required an extension of the study.

DECLARATION OF INTEREST

The authors declare that there are no conflicts of interest.

Ethical approval

This study is the part of a doctoral study. The local institutional review board approved this study.

Abbreviations

ICU — Intensive care units
CT — Computer tomography
ISS — Injury Severity Score

Licensing

Sažetak

UTICAJ ISHRANE NA GUBITAK MIŠIĆA KOD KRITIČNO OBOLELIH PACIJENATA - PILOT STUDIJA

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Uvod: Adekvatna ishrana je neophodna kako bi se sprečio gubitak mišića kod kritično obolelih pacijenata. Odluka o enteralnoj ili parenteralnoj ishrani uvek je dovedena u pitanje.

Cilj: Cilj naše studije bio je utvrditi uticaj ishrane na gubitak mišića kod kritično obolelih pacijenata sa traumatskim povredama. **Materijali i metode:** Istraživanje je sprovedeno od januara do decembra 2017. godine i uključilo je 30 kritično obolelih pacijenata sa traumatskim povredama, hospitalizovanih u jedinici intenzivne nege (JIN) na Univerzitetskoj klinici za anesteziologiju i intenzivnu negu u Skoplju. Pacijenti, koji

su bili uključeni u studiju, bili su podeljeni u dve grupe: grupu E - sa pacijentima kod kojih je enteralna ishrana sprovedena trećeg dana nakon njihovog prijema u JIN i grupu P - sa pacijentima kod kojih je kompletna parenteralna ishrana sprovedena u prva 24 sata od prijema u JIN.

Studija je pratila uticaj dva različita tipa ishrane na gubitak mišićne mase evaluirane ultrazvučnim merenjem debljine m. quadriceps femorisa i biohemijskim merenjem nivoa kreatinina u serumu. **Rezultati:** U grupi E je postojao statistički značajan gubitak mišićne mase procenjen ultrazvukom između 1. i 3. i 1. i 7. dana. Razlika u debljini mišića iznosila je 1,90 ± 1,49 mm između 1. i 3. (p = 0,015) i 4,46 ± 2,81 mm između 1. i 7. dana (p = 0,006). U grupi P gubitak mišićne mase u istom periodu nije bio statistički značajan. Obe grupe pokazale su statistički značajno smanjenje nivoa kreatinina u serumu od 1. do 3. (p = 0,003, p = 0,03) i 1. i 7. (p = 0,003) dana. Vrednosti razlika između 1. i 3. i 1. i 7. dana bile su 7,57 ± 4,12 mg/dl i 10,71 ± 5,79 mg/dl u grupi E i 11,43 ± 10,66 mg/dl i 15,28 ± 8,28 mg/dl u grupi P. **Zaključak:** U našoj studiji utvrdili smo značajno smanjenje mišićne mase procenjene ultrazvučnim merenjem m.quadriceps femoris - a kod pacijenata na enteralnoj ishrani nakon trećeg dana.

Ključne reči: kritično oboleli pacijenti, enteralna ili parenteralna ishrana, gubitak mišićne mase, ultrasonografija, koncentracija kreatinina u serumu.

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Original article

THE EFFICIENCY OF SUCTION DRAIN USAGE IN ARTHROSCOPIC KNEE SURGERY

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Abstract: **Aim:** The study was designed to investigate the efficiency of suction drain after arthroscopic knee surgery. It is hypothesized that suction drain decreases postoperative hemarthrosis after arthroscopic knee surgery.

Methods: Patients were randomized into two groups. Suction drain was used in Group I and no drain was used in Group II. The groups were compared in terms of rest and activity pain, range of motion, Lysholm and International Knee Documentation Committee (IKDC) scores, patellar shock, need for postoperative knee puncture, amount of drainage, time of hospitalization, and loss of labor. Arthroscopic interventions like meniscectomy, synovectomy, meniscus repair and microfracture were also compared for the amount of patellar shock, need for postoperative knee puncture and amount of drainage.

Results: The difference for activity pain and range of motion between the two groups was statistically nonsignificant. Rest pain improved faster in control group. Lysholm and IKDC scores were improved in both groups but the amount of increase was statistically nonsignificant. The amount of patellar shock was also statistically nonsignificant between the two groups. The amount of patellar shock, need for postoperative knee puncture and amount of drainage were also statistically nonsignifiant for arthroscopic interventions like meniscectomy and synovectomy.

Conclusions: Suction drain application was unnecessary in many situations after arthroscopic knee surgery in this study. Although suction drain usage delayed the recovery from postoperative pain in this study, other parameters of pain were not affected from suction drain usage. Routine usage of a suction drain after arthroscopic knee surgery was not recommended.

Key words: Suction drain, knee arthroscopy, hemarthrosis, postoperative pain, patellar shock.

INTRODUCTION

Suction drains are widely used after knee surgery in orthopaedic practice to decrease the amount of postoperative hematoma however benefits of suction drain usage is still controversial (1, 2). Suction drain usage is not a routine procedure after arthroscopic knee surgery, and it is a controversial subject (2, 3).

It was thought that the postoperative hematoma after arthroscopic knee surgery may irritate the synovium causing postoperative effusion and capsular distension and eventual patient discomfort (3, 4). Postoperative complaints, mobilization capacity, hospitalization time and time of occupation loss can change according to amount of hematoma and rehabilitation can be delayed. There is no study in the literature which proves the effect of suction drain usage on postoperative hemarhrosis and effusion after knee arthroscopy. Most of the studies about this subject was performed after anterior cruciate ligament (ACL) reconstruction. There are a few case series about this subject however they are away from explaining the problem (1, 3). Therefore we aimed to clarify suction drain usage after arthroscopic knee surgery.

According to our hypothesis suction drain usage after arthroscopic knee surgery decreases postoperative hemarthrosis and subsequent knee effusion and increases postoperative comfort.

MATERIAL AND METHODS

In this randomized double blind study 113 patients who underwent arthroscopic knee surgery were evaluated. Arthrotomy was needed in three patients du-

ring operation, therefore these three patients were removed from the study. The patients who were treated for ACL reconstruction were not included to the study. The patients with systemic disorder, bleeding diathesis, history of acute major knee trauma or synovial disorder were also excluded from the study. Institutional review board approval and patient informed consent were obtained for all patients.

The patients were randomly divided into two groups by a computer program. Group 1 (mean age 41.42, 33 male (60%) and 22 female (40%)) included 55 patients with a suction drain and Group 2 (mean age 41.62, 32 male (58%) and 23 female (42%)) included 55 patients without a suction drain. The study was designed double blind, meaning that the surgeon and the follow-up physicians were not informed about the drain status of the patients. All patients were operated by the samesurgeon under spinal or general anesthesia. Arthroscopic pump was not used in any of the patients. Standart tourniquet which was inflated to 300 mmHg was used in all operations. Asuction drain (Bıcakcilar, Turkey, B-VAK 400 Wound Drainage System 12CH) with an external diameter of 4mm was inserted at the end of operation in Group 1. After a compressive dressing was applied from tigh to ankle, the clamp of the drain was opened.

Suction drains were removed 24h after the operation and the amount of drainage was noted. The same rehabilitation programme was applied to all patients including active quadriceps strengthening and range of motion increasing exercises, and they were allowed to bear weight as soon as they tolerated.

The patients were controlled four times postoperatively (first day, second and sixth week, and third month). Pain during daily routine activities (climbing upstairs, walking, squatting etc.) of the patients were recorded before and after the surgery and called as routine activity pain. Rest pain of the patients were also recorded before and after the operation and called as rest pain. Preoperative knee range of motion of the patients were measured and compared with postoperative measurements. Severity of pain was evaluated with Visual Analogue Scale (VAS). VAS is a horizontal line divided into ten equal intervals in which zero represents no pain and ten represents the worst pain ever felt. Operative findings and surgical interventions were noted for each patient. The most common surgical interventions were meniscectomy, synovectomy, meniscal repair and subchondral microfracture.

Preoperative and postoperative sixth week and third Lysholm scores (5) and International Knee Documentation (IKDC) 2000 knee evaluation scores (6) of the patients were measured and noted.

Postoperative knee effusion was determined by patellar shock. Patellar shock was graded in four scales: Grade 1, some notable fluid, Grade 2, minimally elevated patella, Grade 3, patellar ballottement, and Grade 4, tense knee capsule, unable to compress patella (7). Knee puncture was applied to all Grade 4 and symptomatic Grade 3 patients. The patients who needed postoperative knee puncture and the amount of the fluid (puncture fluid) were noted.

A power analysis was conducted to minimize error and bias. According to post hoc power analysis enrolling 55 subjects in each group would provide an adequate sample size to achieve a power of > 80% at a $p < 0.05$ significance level to detect a difference of ten points in the knee score (Lysholm) improvement and a difference of ten degrees in the knee motion improvement.

The Statistical Package for the Social Sciences for Windows (Version 20, serial 10240642) was used for statistical analysis. Suitability of quantitative data to normal distribution was determined by one sample Kolmogorov Smirnov test.

For normally distributed data variance analysis was used to make comparisons between the groups, and to describe changes in repeated measurements in each group. T-test was used in comparisons of independent groups. For the data that was not normally distributed, Mann Whitney-U test was used to compare groups, Friedman and Wilcoxon two sample tests were used in intra-group comparisons. Yates corrected X^2, Fisher's exact X^2 and KolmogorovSmirnov two sample tests were used in qualitative data. Median (minimum – maximum) and mean value ± standart deviations were given as descriptive statistics. The level of significance was set at $p < 0.05$.

RESULTS

The groups were comperable in terms of age and gender ($p = 0.912$ for age (t-test for independent groups) and $p = 1.000$ for gender (Fisher's exact Chi-Square test). Arthroscopic interventions were summarized in Table 1, and also there was no statistically significant difference between the groups in terms of arthroscopic interventions.

The decrease in rest and routine activity pain during follow-up was statistically siginificant for both groups. Rest and routine activity pain was summarized in Table 2.

Postoperative first day rest pain was increased when compared with preoperative rest pain, and this increase was statistically significant for both groups ($p = 0.003$ for Group 1 and $p < 0.001$ for Group 2, Wilcoxon signed rank test). In Group 1 this increase in rest pain was statistically significant for males ($p < 0.001$, Wilcoxon signed rank test), however in females, rest pain also increased but this increase was not statisti-

Table 1. *Arthroscopic interventions and distribution between two groups*

	Group-1	Group-2	P value
Synovectomy applied/not applied (%)	87.3% / 12.7%	78.2% / 21.8%	0.313*
Meniscectomy applied/not applied (%)	67.3% / 32.7%	78.2% / 21.8%	0.284*
Meniscus repair applied/not applied (%)	10.9% / 89.1%	5.5% / 94.5%	0.489**
Microfracture applied/not applied (%)	14.5% / 85.5%	12.7% / 87.3%	1.000**

*Chi-Square Continuity Correction.
**Fisher's exact Chi-Square test.

Table 2. *Postoperative rest and routine activity pain in follow-up controls*

Pain	Follow-up control number	Grup-1 mean (min-max)	Grup-1 mean (min-max)
Rest pain	1	3.55 (0-8)	3.05 (0-8)
	2	2.69 (0-6)	1.85 (0-5)
	3	2.07 (0-6)	1.27 (0-5)
	4	1.78 (0-6)	1.09 (0-4)
	P value	< 0.001*	< 0.001*
Activity pain	1	5.47 (2-8)	5.31 (1-8)
	2	4.40 (1-7)	3.64 (0-7)
	3	3.55 (0-7)	2.76 (0-7)
	4	3.04 (0-8)	2.35 (0-6)
	P value	< 0.001*	< 0.001*

min: minimum value, max: maximum value
*Friedman test

cally significant ($p = 0.873$, Wilcoxon signed rank test). In Group 2 rest pain increased for males and females significantly ($p = 0.025$ for males, $p = 0.002$ for females, Wilcoxon signed rank test).

Postoperative 15th day rest pain was compared with preoperative rest pain. In Group 1 no statistically significant difference was found ($p = 0.086$, Wilcoxon Signed Rank test), however in Group 2 postoperative 15th day rest pain was a statistically lower than preoperative pain ($p = 0.005$, Wilcoxon Signed Rank test).

Preoperative flexion values were compared with postoperative first and 15th day flexion values in both groups. The first postoperative and 15th day flexion values were decreased when compared with preoperative values and this decrease was statistically significant for both groups ($p < 0.001$ for both groups for all measurements, Wilkinson signed ranks test). However no statistically significant differrence was observed between the groups for flexion decrease ($p = 0.474$ and $p = 0.395$ for first and 15th day follow-up respectively). On the other hand flexion was increased gradually from first postoperative control till last one for both groups ($p < 0.001$ for both groups, Friedman test) final flexion values were reached in last control (3 months) in both groups.

Extension lost was also compared by the same manner between the two groups. Extension lost was seen in postoperative first and 15th day follow-up controls and it was statistically significant for both groups groups ($p < 0.001$ for both groups for all measurements, Wilkinson signed ranks test). Extension loss was not statistically different between the two groups in first and 15th postoperative days ($p = 0.397$ and $p = 0.160$ for first and 15th day follow-up respectively). Extension values were also improved gradually during follow-up period and this increase was statistically sig-

Table 3. *Preoperative (Lysholm-1), postoperative 6th week (Lysholm-2) and postoperative 3rd month (Lysholm-3) Lysholm scores, and preoperative (IKDC-1), postoperative 6th week (IKDC-2) and postoperative 3rd month (IKDC-3) IKDC scores*

	Lysholm-1 (mean ± std. dev.)	Lysholm-2 (mean ± std. dev.)	Lysholm-3 (mean ± std. dev.)
Group-1 (n = 55)	57.80 ± 18.35	67.71 ± 17.378	75.56 ± 15.33
Group-2 (n = 55)	58.18 ± 17.598	69.60 ± 16.186	76.35 ± 16.463

	IKDC-1 (mean ± std. dev.)	IKDC -2 (mean ± std. dev.)	IKDC -3 (mean ± std. dev.)
Group-1 (n = 55)	54.87 ± 17.313	63.87 ± 16.488	71.16 ± 15.561
Group-2 (n = 55)	55.40 ± 16.346	65.22 ± 16.582	72.44 ± 17.427

std. dev. = Standart deviation

Table 4. *Need of puncture for each arthroscopic intervention and comparisons between the two groups*

	Group-1 (n = 55)	Group-2 (n = 55)	P value (for puncture)
Synovectomy (% of total) / Puncture (% in synovectomy)	87.3% / 25%	78.2% / 20.9%	1.000
Meniscectomy (% of total) / Puncture (% in meniscectomy)	67.3% / 27%	78.2% / 23%	0.341
Meniscus repair (% of total) / Puncture (% in meniscus repair)	10.9% / 16.7%	5.5% / 0%	1.000
Microfracture (% of total) / Puncture (% in microfracture)	14.5% / 37.5%	12.7% / 14.2%	0.604

nificant for both groups ($p < 0.001$ for both groups, Friedman test). The patients in Group 1 reached their preopertative extension values in third control (6 weeks), however the patients in Group 2 reached it in second control (second week). Recovery of extension was faster in Group 2.

Preoperative Lysholm and IKDC scores were improved significantly in both groups after operation ($p < 0.001$ for both groups and scores). The amount of increase was not statistically different between the two groups ($p = 0,735$ for Lysholm and $p = 0.729$ for IKDC-repeated measures of ANOVA). Lysholm and IKDC scores were given in Table 3.

Knee puncture was applied to 14 patients in Group 1 and 11 patients in Group 2. Need of puncture was not statistically different between the two groups ($p = 0.649$, continuity to correction). The mean amount of aspirated fluid was 45cc (20cc-110cc) in Group 1 and 60cc (30cc-145cc) in Group 2. The amount of fluid which was aspirated from the knee was not also statistically different between the two groups ($p = 0.151$, Mann-Whitney U test).

The relationship between the arthroscopic interventions and need of puncture was compared between the two groups. Need of puncture was not statistically different between the groups for synovectomy, meniscectomy, meniscus repair and microfracture ($p = 1.000$, 0.341, 1.000 and 0.604 respectively, Fisher's Exact Chi-Square) (Table 4).

The grade of patellar shock was not statistically different between the two groups in all four postoperative follow-up controls ($p = 0.606$ and 1.000 for control one and two respectively, Two Sample Kolmogorov Smirnov test, $p = 0.740$ for control three, Continuity to Correction, $p = 1.000$ for control four, Fisher's Exact Chi-square).

The patients with and without synovectomy were compared in first and second postoperative controls for patellar shock in Group 1, and no statistically significant difference was found ($p = 1.000$ and $p = 0.860$ for controls one and two respectively, Two Sample Kolmogorov Smirnov test). It was no also statistically different in Group 2 ($p = 0.095$ and $p = 0.819$ for controls one and two respectively, Two Sample Kolmogorov Smirnov test).

Table 5. *Amount of drainage in Group-1 and its distribution for each arthroscopic intervention*

	(+) amount of drainage (ml) median (min-max)	(-) amount of drainage (ml) median (min-max)	P*
Synovectomy	45 (15-250)	40 (25-325)	0.970*
Meniscectomy	45 (15-250)	42.5 (20-325)	0.633*
Meniscus repair	37.5 (30-325)	45 (15-250)	0.588*
Microfracture	45 (25-110)	45 (15-325)0.755*	

(+) represents the patients with the corresponding intervention
(-) represents the patients without corresponding intervention
min-max: minimum – maximum
* Mann Whitney U

The same comparisons were also done for patients with meniscectomy and without meniscectomy. No statistical difference was found for both groups in first and second controls (p = 0.184 and p = 0.856 for Group-1 in first and second controls respectively; p = 0.994 and p = 0.972 for Group 2 in first and second controls respectively, Two Sample Kolmogorov Smirnov test).

The comparison of patellar shock was not done for microfracture and meniscal repair due to small number of patient population.

The patients with synovectomy and without synovectomy in Group-1 were compared for the amount of drainage. The same comparison was also done for meniscectomy, meniscal repair and microfracture. The amount of fluid was not statistically different for all arthroscopic interventions in Group 1 (Table 5).

The patients with synovectomy were compared for patellar shock between the two groups. No statistically significant difference was found between the two groups in all four follow-up controls (p = 0.765 and p = 0.999 for controls one and two, Two Sample Kolmogorov Smirnov test, p = 0.717 and p = 1.000 for control three and four, Fisher's Exact Chi-square). Need for knee puncture (p = 0.833, Continuity to Correction) and amount of fluid from knee puncture (p = 0.114, Mann Whitney U test) were not also statistically different between the two groups in patients with synovectomy.

The patients with meniscectomy were compared for patellar shock between the two groups. No statistically significant difference was found between the two groups in all four follow-up controls (p = 0.990 and p = 1.000 for controls one and two, Two Sample Kolmogorov Smirnov test, 1.000 and p = 0.462 for control three and four, Fisher's Exact Chi-square). Need for knee puncture (p = 0.987, Continuity to Correction) and amount of fluid from knee puncture (p = 0.149, Mann Whitney U test) were not also statistically different between the two groups in patients with meniscectomy.

Type of anesthesia (spinal block or general anesthesia) and the amount of drainage fluid were compared and no statistically significant difference was found (p = 0.867, Mann Whitney U).

Time of hospitalization was not statistically different between Group 1 (4.02 ± 2.649 days) and Group 2 (3.18 ± 1.906 days) (p = 0.132 Mann Whitney U test).

Time to return occupation was 20.36 ± 13.012 days for Group 1 and 18.15 ± 11.715 days fro Group 2. There was not a statistically significant difference between the two groups (p = 0.310, Mann Whitney U test).

DISCUSSION

According to our hypothesis suction drain usage after arthroscopic knee surgery decreases postoperative hemarthrosis and subsequent knee effusion and increases postoperative comfort. This hypothesis was refused after this investigation.

Suction drains are useful in drainage of hematoma or fluid from cavitary regions (4). During knee arthroscopy some surgical interventions like synovectomy or meniscectomy may lead to bleeding and hemarthrosis (2, 8, 9). Hemarthrosis may irritate synovium and may stretch joint capsule causing to postoperative pain (1). Postoperative pain is one of the most important parameters decreasing patient complience to postoperative rehabilitation, therefore may alter recovery (4). In theory suction drains can decrease the formation of hemarthrosis and indirectly may affect recovery. This study was designed to investigate the benefits of suction drain application after arthroscopic knee surgery.

Rest pain and routine activity pain were both decreased statistically after the operation in both groups. This result was an indicator of patient recovery after the operation.

Postoperative first day rest pain was statistically increased in both groups when compared with preoperative rest pain. Increased rest pain was observed in both groups, therefore it was thought that increase in pain was not related with suction drain usage. This pain increase was interpreted as postoperative surgical pain.

In control group post operative rest pain increase did not differ between the two sex. However, in suction drain group postoperative first day rest pain increase was observed in males but it was not observed in females. It can be thought that females might be more tolerable for drain usage.

Postoperative 15th day rest pain was compared with preoperative rest pain to evaluate the relief of surgical pain. In suction drain group no statistical difference was found between the preoperative and postoperative 15th day rest pain. However, in control group, postoperative 15th day rest pain was statistically lower than preoperative rest pain. Therefore it was thought that, suction drain usage after knee arthroscopy may delay the recovery of postoperative pain.

Some amount of flexion - extension loss is expected after arthroscopic knee surgery during the early postoperative period due to hemarthrosis, edema and postoperative pain (10). Flexion and extension values of both groups were compared to evaluate the effect of suction drain inpostoperative loss of range of motion.

When postoperative 1st and 15th day flexion degrees were compared with preoperative flexion values, a statistically significant decrease was observed in both groups. This loss in flexion values was an expected finding. Postoperative loss of flexion was not statistically different for both groups, therefore it was thought that, loss of flexion during the early postoperative period was not related with suction drain usage. Flexion values were increased gradually during the follow-up period and preoperative flexion values were reached in the last control (postoperative 3rd month) in both groups. It was thought that recovery of flexion values during the postoperative period was not affected by suction drain usage in this study.

Extension loss was also observed in both groups postoperatively, however it was not statistically different between the two groups. Therefore it was thought that, loss of extension in the early postoperative period was due to postoperative changes. Extension values were also improved gradually during the postoperative period, and this improvement was not statistically different between the two groups. Preoperative extention values were obtained in second week control in control group, and in 6th week in suction drain group. Preoperative extension values were reached in both groups, however this recovery of extension was faster in control group. Therefore it can be thought that, suction drain usage may delay recovery of extension after arthroscopic knee surgery.

When the scoring systems were evaluated it was observed that both IKDC and Lysholm scores were improved statistically in both groups. Improvement in IKDC and Lysholm scores were not statistically different between the two groups. According to these results, it was observed that, the pain of the patients was decreased, and quality of life was increased after arthroscopic knee surgery, however suction drain usage did not affect these results.

Knee hemarthrosis is one of the most commonly seen complications after knee arthroscopy (11). Occasionally hemarthrosis stretches the joint capsule leading to pain and tenderness and it decreases patient compliance to postoperative rehabilitation (1). When hemarthrosis is observed in the postoperative period a knee puncture may be needed to drain the knee. In this study 25 patients needed knee puncture. Need of knee puncture was not statistically different between the two groups, therefore using suction drains did not decrease the need of knee puncture in this study. The amount of aspirated fluid was also measured and compared between the two groups. The amount of aspirate was not also statistically different between the two groups. Therefore, usage of suction drains after knee arthroscopy did not improve the need of knee puncture and did not decrease the amount of aspirate material in this study.

Some interventions during arthroscopic knee surgery may cause more bleeding than the others like synovectomy and microfracture (11). In these synovectomy and microfracture patients, more bleeding is expected after the operation, which increases the need of knee puncture due to hemarthrosis. Need of knee puncture and the effect of suction drain usage were investigated for each arthroscopic procedure in the study. The relationship between the arthroscopic interventions and need of puncture was compared between the two groups. Need of puncture was not statistically different between the groups for synovectomy, meniscectomy, meniscus repair and microfracture. It was observed that, suction drain usage did not decrease the need of postoperative knee puncture even in synovectomy and microfracture patients where much bleeding is expected.

Patellar shock is a valuable finding in the follow-up of postoperative knee effusion. Both groups were investigated for the development of patellar shock during the follow-up periods. Patellar shock was not statistically different between the two groups in all four postoperative follow-up controls. Using postoperative suction drain did not affect the development of patellar shock in this study.

Patellar shock is an important finding of early postoperative hemarthrosis after arthroscopic knee surgery (7). Synovial tissue is a vascular tissue, therefore after synovectomy postoperative patellar shock is expected due to increased bleeding (1, 11). Using a suction drain after synovectomy may decrease the amount of patellar shock theoretically. The patients with and without synovectomy in Group 1 were compared for

patellar shock in first and second postoperative controls to investigate the benefits of suction drain usage in synovectomy patients. However no statistically significant difference was observed for patellar shock in first and second controls between the patients with synovectomy and without synovectomy. The same comparisons were also done for Group 2 and no statistically significant difference was observed. According to these results it was thought that, synovectomy did not increase the risk of hemarthrosis and patellar shock development alone. It was thought that, causes of knee hemarthrosis after synovectomy must be investigated with further studies. It was also observed that suction drain usage did not decrease the hemarthrosis after arthroscopic synovectomy. As a result it was concluded that, using suction drain after arthroscopic synovectomy to decrease the amount of hemarthrosis is an invaluable procedure.

The same comparisons about patellar shock were also done for patients with meniscectomy and without meniscectomy. No statistical difference was found between the patients with meniscectomy and without meniscectomy for both groups in first and second controls. It was also concluded that using suction drain after arthroscopic meniscectomy to decrease the amount of hemarthrosis is an invaluable procedure.

The amount of drainage fluid in the suction drain was measured in the patient Group 1. This drainage was composed of blood in all cases, therefore it is used as a measurement of early postoperative bleeding. The patients with synovectomy and without synovectomy in Group 1 were compared for the amount of drainage. The same comparison was also done for meniscectomy, meniscal repair and microfracture. The amount of fluid was not statistically different for all arthroscopic interventions in Group 1. It was thought that, the amount of drainage was not directly related with arthroscopic intervention. However such a result may not be correct since, more than one interventions were applied to all patients during arthroscopy. This is one of the weak points of this study.

The patients with synovectomy in two groups were compared for patellar shock. No statistically significant difference was found between the two groups in all four follow-up controls. The same comparisons were also done for need of knee puncture and amount of fluid which was aspirated during knee puncture. Need for knee puncture and the amount of fluid from knee puncture were not also statistically different between the two groups in patients with synovectomy. Therefore it was thought that using suction drain after arthroscopic knee surgery did not affect patellar shock development, need of knee puncture and the amount of fluid from knee puncture after arthroscopic synovectomy.

The patients with meniscectomy in two groups were also compared for the parameters above. No statistically significant difference was found between the two groups in all four follow-up controls for the development of patellar shock. Need for knee puncture and amount of fluid from knee puncture were not also statistically different between the two groups in patients with meniscectomy. Therefore it was thought that using suction drain after arthroscopic knee surgery did not affect patellar shock development, need of knee puncture and the amount of fluid from knee puncture after arthroscopic meniscectomy.

As a result, it was thought that, development of postoperative knee effusion (hemarthrosis) after arthroscopic meniscectomy and synovectomy was independent of suction drain usage.

There are three meta analysis in the literature about the comparison of general and regional anesthesia in knee and hip surgery (12, 13, 14). Although there is a marked heterogenity about peroperative blood loss and need of blood transfusion, there is a tendency of increased blood loss in general anesthesia. The effect of anesthesia on bleeding after arthroscopic knee surgery was also investigated in this study. The amount of drainage fluid from suction drain was compared between the patients who had spinal or general anesthesia. There was no statistically significant difference between the two anesthesia types for the amount of drainage. Therefore it can be suggested that early postoperative hemorrhage after arthroscopic knee surgery is not related with the type of anesthesia in this study.

Hospitalization time was not statistically different between the two groups. The patients with suction drain did not discharge early from the hospital. The time from the operation till return to occupation was also compared between the two groups and again no statistical difference was observed. Loss of labor did not decrease after the usage of suction drains.

Limitations

Statistical comparisons cannot be done for meniscal repair and microfracture subgroups due to small sample size to evaluate the risk of hemarthrosis. Further studies with much larger series are needed development after arthroscopic meniscal repair and microfracture.

More than one arthroscopic intervention was applied to all patints, therefore generalizing the results for a single intervention might cause bias. For more precise results the observations must be performed after a single arthroscopic intervention, but randomization of these patients is not possible, since decision making is done during the operation in arthroscopy. The preoperative diagnosis may change during arthro-

scopy, additional pathologies can be observed, and preoperative plan can be changed according to these new findings.

CONCLUSION

We do not suggest routine usage of a suction drain after arthroscopic knee surgery. Although recovery of extension loss was faster in the control group, preoperative flexion and extension values were obtained in both groups in the last follow up. Although suction drain usage delayed the recovery of postoperative pain in this study other parameters of pain were not affected from suction drain usage. It can be used selectively in patients with high risk of bleeding like total arthroscopic synovectomy.

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This subject was graduation thesis of Dr. Cüneyt Öncel (one of our residents in Trakya University, Edirne, Turkey) and preliminary results were reported as graduation thesis (about a total of 70 patients). The study was finished by us and a manuscript was prepared. These preliminary results were also reported in the XXIIth National Turkish Orthopedics and Traumatology Congress in 2011 Antalya, TURKEY as an oral presentation. Dr Nurhak Yavuz was also helped in data collection for this research. We confirm that, this manuscript is original and has not been submitted elsewhere for publication or has been published elsewhere.

DECLARATION OF INTEREST

The autors declare that there are no conflicts of interests.

Sažetak

EFIKASNOST PRIMENE DRENAŽE U ARTROSKOPSKOJ OPERACIJI KOLENA

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Cilj: Cilj ove studije bio je da se ispita efikasnost sukcionog drena nakon artoskopske operacije kolena. Hipotetički govoreći, pošli smo od pretpostavke da sukcioni dren smanjuje postoperativnu hemartrozu nakon artroskopske operacije kolena.

Metode: Pacijenti su nasumično podeljeni u dve grupe. U Grupi I korišćen je sukcioni dren, a u Grupi II nije korišćena sukciona drenaža postoperativno. Grupe su poređene u pogledu oporavka, bolova pri pokretima, opsega pokreta, prema tablicama Lisholma i internacionalnog saveta za dokumetaciju o operacijama kolena (IKDC), patelarnog stresa, potrebe za postoperativnom punkcijom kolena, količine dreniranog sadržaja, vremena provedenog u hospitalizaciji i gubitka radne snage obolelog kolena. Artroskopske intervencije koje su bile korišćene uključivale su meniscektomiju, sinoviektomiju, popravku meniskusa i mikrofrakture. Ove intervencije su takođe bile upoređivane u pogledu ukupnog stresa po patelu, potrebe za postoperativnom drenažom i količine dreniranog sadržaja.

Rezultati: Nije nađena statistički značajna razlika u pogledu postoperativnog bola i opsega pokreta u zglobu kolena između grupa. Parametar – bol u mirovanju je značajno brže zaceljivao u kontrolnoj grupi. Lisholm vrednosti skorova I IKDS skor su značajno bili bolji u obe grupe, ali brzina porasta nije bila od statističke značajnosti. Statistička značajnost u pogledu parametra – količina patelarnog stresa takođe nije bila od statističke značajnosti među grupama. Stepen patelarnog stresa, potreba za postoperativnom punkcijom kolena i količina dreniranog sadržaja nisu bili statistički značajni za artroskopske intervencije kao što su meniscektomija i sinoviektomija.

Zaključak: Primena sukcionog drena bila je nepotrebna u mnogim slučajevima nakon artoskopske operacije kolena u ovoj studiji. Iako je primena sukcione drenaže imala za posledicu duži period oporavka od postoperativnog bola, drugi parametri bola nisu bili uzrokovani primenom sukcionog drena. Prema rezultatima ove studije, rutinsko korišćenje sukcionog drena nakon artroskopske operacije kolena se ne preporučuje.

Ključne reči: sukciona drenaža, artroskopija kolena, hemartroza, postoperativni bol, patelarni stres.

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SCREENING FOR HEPATITIS B AND C SEROPREVALENCE AND PREVALENCE OF HIV INFECTION AMONG AFGHAN REFUGEES NEWLY ARRIVED IN COASTAL REGION TURKEY IN 2018: A SYSTEMATIC SINGLE-CENTRE ANALYSIS

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Abstract: **Introduction:** Previous studies showed that refugee status have been associated with various deteriorated effects on human health including higher prevalence of hepatitis B, C and HIV infections. In this study we aim to bridge the gap between Afghan immigrants and naive Turkish population by identifying HBV, HCV and HIV profiles. In addition, a large number of laboratory parameters was collected for all participants, including hematologic and biochemical test results.

Materials and Methods: We performed a retrospective review of laboratory records at a tertiary center in Northern Turkey from January 1, 2018, to April 15, 2018. Our population based study comprising hospital data of 403 Afghan refugees and 400 naive Turkish citizens. **Results:** Afghan refugees had higher anti-HIV seropositivity than Turkish citizens ($p < 0.05$). There were no difference between the two groups according to HbsAg and anti-HCV seropositivity. Also Afghan refugees had statistically lower ALT levels, higher hemoglobin levels and higher mean TSH level ($p < 0.05$). Mean T4 level did not show significant difference between the two groups.

Conclusion: We need further investigations to find out the risk of infections that originated from immigration.

Key words: Immigrants, Infectious diseases, Viral Hepatitis, AIDS.

INTRODUCTION

Hepatitis B virus (HBV) infection, hepatitis C virus (HCV) infection and Human immune deficiency virus (HIV) infection are among the top ten causes of infectious disease-related mortality globally (1).

On the other hand, infection with HBV, HCV and HIV continue to be significant causes of morbidity and mortality all over the world and are endemic in South East Asia including Afghanistan (2). Recent reports showed that these increasing trends on that viruses have been attributed to increased traditional opioid use, civil war, and the displaced Afghans into another countries where refugee camps are overcrowded (3).

HBV infection has a high (≥ 8%) or intermediate (2–7%) prevalence in approximately many parts of Asia (4). In Afghanistan, the prevalence of HBV infection has been estimated as high as 8.3 % (5).

Low prevalence of HIV (0.063%) and HCV (0.82%) has been detected among Afghan National Army (ANA) recruits (6). However it has been also reported that there was a huge increase for both HCV and HIV infections (3.8% and 4.6% respectively) among male injecting drug users in Kabul, Afghanistan (7). However, limited data exist to indicate health parameters involving hepatotrophic viruses for Afghans. To address this data gap, we conducted a study among Afghan refugees newly entering the Turkey. We also compared Afghans to naive Turkish citizens.

MATHERIALS AND METHODS

Giresun Hospital, University of Medical Sciences, TR, Turkey

Giresun Hospital is a 500 bed tertiary care hospital, affiliated with Giresun University of Medical Sciences, Giresun, Turkey, which also serves as an urban general hospital in Giresun. It serves as a referral hospital in the area with about 1 million inhabitants in coastal region of Northern Turkey.

Study design

We performed a cross sectional sociodemographic and laboratory survey among Afghan refugees living in Giresun city (near the coast of eastern Black sea) in Turkey. All Afghan refugees between 2017 and 2018 in the Giresun city were identified using the hospital data system.

Study population

Refugees (403 subjects) that met the following inclusion criteria were eligible to participate in the study: (i) aged above than 18 years, (ii) originating from Afghanistan, and (iii) living in a reception center in the Turkey. A total of 400 healthy Turkish controls were also enrolled in the final analysis.

Serological analysis

Hepatitis B (markers: HBsAg and antiHBs) serology was performed using chemoluminescence assays performed on the ADVIA Centaur XP assay system (Siemens HBsAg II assay, HBcT, aHBs2, AHAVT). Anti-HBc positivity with presence of HBsAg indicates a chronic infection.

HCV positivity was defined as having newly reactive HCV antibody (HCV Ab) by a rapid diagnostic test (RDT) confirmed by either detectable HCV viremia or HCV Ab. HIV positivity was defined as confirmed HIV-1 antibody. Plasma HCV RNA was quantified for each sample with the use of the COBAS Ampliprep/TaqMan real-time reverse-transcriptase polymerase-chain-reaction assay, version 2.0 (Roche Molecular Diagnostics), which has a lower limit of quantification of 15 IU per milliliter. HIV infection was defined as positive test result with the use of a third-generation HIV enzyme immunoassay (VITROS Anti-HIV 1+2 Assay, Ortho Clinical Diagnostics).

Laboratory Analysis

Hematologic and biochemical studies were conducted via automatic analyzer with SYSMEX XN 1000 (Sysmex Coorporation - Kobe, Japan). Serum thyroxine and thyrotropin were measured with use of an automated immunoassay with chemiluminescence detection Roche Cobas 8000 modular analyzer (Roche Diagnostics GmbH, Mannheim, Germany) and commercial reagents.

Statistical Analysis

Analyses were conducted with the use of SAS software, version 9.2 (SAS Institute), and R software, version 2.15.1 (R Project for Statistical Computing). We used the chi-square test and Pearson correlation tests test to compare demographic variables and laboratory parameters between study groups. P values of less than 0.05 were considered to indicate statistical significance.

RESULTS

The median age of the Afghan refugees was 34 years (interquartile range, 18 to 65), 58% were men, and all of them resided in Giresun city. Median age of control subjects was 36 years (ranged from 17-78). Control group (400 subjects; 200 of them were women) were selected from healthy Turkish subjects from Giresun city. There was no statistically significant difference between groups in terms of age and gender (all $P > 0.05$).

A total of 2.8% (11 patients; 7 female) of control subjects tested positive for HBs antigen. Other hand, 5.8% (23 subjects; 13 female) of 403 refugees had seropositive for HBs antigen as shown in Table 1. There was no significant difference between the refugee group and the Turkish control group with respect to the overall prevalence of HBV infection ($P = 0.106$).

On study entry, 1.2% of control subjects (5 subjects; 3 of them were female) had seropositive for anti-HCV antibody. Among Afghan refugees, 2.3% of subjects (9 patients; 5 of them were female) tested positive for both anti- HCV antibody and HCV RNA. There was no significant difference between the refugee group and the Turkish group in the mean percentage of subjects who had seropositive results for anti-HCV antibody ($P = 0.403$).

Table 1. *Seroprevalance of HBV, HCV, HIV*

	HBsAg	Anti-HCV/HCV RNA	HIV-RNA
Giresun Citizens (200 male-200 female)	11 (7 female)	5 (3 female)	0
Afghan Refugees (233 male-170 female)	23 (13 female)	9 (5 female)	9 (6 female, 3 male)

A total of 803 study subjects screened for anti-HIV antibody. At the end of analysis, no control subjects tested positive for HIV infection who selected from Turkish citizens resided in the Giresun city. Other hand, 9 refugees (2.3%) had positive test results for both anti-HIV antibody and HIV- RNA. HIV viral-load assays were also performed in all patients. There was significant difference between two groups in the percentage of subjects with HIV infection (P = 0.005).

The mean serum TSH level was higher in refugees than in control subjects (3.5 ± 10.8 versus 2.1 ± 1.7 μg per deciliter, P = 0.019) When age and sex were controlled for in a multivariate analysis, elderly ages were associated with a lower levels of TSH but gender status was not. In addition, the mean serum T4 level was not statistically significant between Afghans and Turks (1.18 ± 0.77 versus 1.13 ± 0.33 μg per deciliter, P = 0.31).

Other laboratory test results of Afghan refugees showed significantly lower serum ALT levels and increased hemoglobin levels in comparison to healthy Turkish controls (19 ± 12 versus 22 ± 24 unit per liter, P = 0.018; 13.9 ± 1.8 versus 12.8 ± 1.9 gram per deciliter, P = 0.001). Baseline characteristics of the study subjects showed in the Table 2.

DISCUSSION

The results of this population based study showed that the prevalence of HIV infection was higher than those naive Turkish population at the coast of Black sea. We also demonstrated a positive correlation between HCV and HIV infections particularly among afghan refugee women. Furthermore, we also detected higher TSH levels in Afghan refugees than those Turkish counterparts. Interestingly, both of HBV and HCV infection prevalence of Afghan immigrants were similar to Turkish subjects.

HBV infection is associated with cirrhosis and hepatocellular carcinoma. Although preventive efforts can reduce the incidence of HBV infection, refugees

Table 2. *The results for the two groups according to biochemical parameters*

		N	Mean	Std. Dev.	Min.	Max.
Hgb g/dl	Giresun citizens	400	12,8915	1,91556	7,80	17,60
	Afghan refugees	403	13,9404	1,85452	8,00	19,00
	Total	803	13,4179	1,95573	7,80	19,00
Glukoz mg/dl	Giresun citizens	363	111,43	45,353	11	427
	Afghan refugees	305	105,82	41,339	11	401
	Total	668	108,87	43,624	11	427
AST U/L	Giresun citizens	358	23,16	15,747	10	146
	Afghan refugees	324	22,38	10,182	10	93
	Total	682	22,79	13,391	10	146
ALT U/L	Giresun citizens	360	22,87	24,151	4	255
	Afghan refugees	329	19,33	12,627	4	103
	Total	689	21,18	19,583	4	255
Albumin g/dl	Giresun citizens	82	4,3530	,53092	2,80	5,10
	Afghan refugees	101	4,4175	,85999	,59	5,30
	Total	183	4,3886	,72996	,59	5,30
Kreatinin mg/dl	Giresun citizens	360	1,1808	6,15795	,34	117,00
	Afghan refugees	331	,8300	1,40057	,30	26,00
	Total	691	1,0128	4,54956	,30	117,00
T4 ng/dl	Giresun citizens	297	1,1334	,33771	1,00	3,00
	Afghan refugees	139	1,1871	,77617	,00	9,00
	Total	436	1,1505	,51899	,00	9,00
TSH μU/ml	Giresun citizens	324	2,1052	1,77161	,01	15,81
	Afghan refugees	181	3,5508	10,82126	,01	100,00
	Total	505	2,6233	6,65689	,01	100,00

have still a key role for disease transmission, not only in Western countries but also in developing world. Thus, the prevention of HBV transmission is the most effective way to reduce the global burden of HBV infection particularly among refugees (8). A previous study from northern part of Turkey reported that overall Hbsag prevalence was 4%. The same study showed 4.4% HBsAg prevalence with male group, 3.6% with female group and there was significant gender difference between the two groups (9). Despite available preventive approaches, refugees often experience symptoms and complications of communicable diseases such as HBV infection. A study from Pakistan reported that seroprevalence of HBs Ag among Afghan refugees living in the camps was 8.3% (5). While the study among refugees arriving from Afghanistan into the Pakistan, found a seroprevalence as high as 10.1% (10). Focusing on the link between the Afghan immigration and HBV infection we tested subjects for presence of HBs seropositivity. At the final analysis, there had no significant difference between groups in terms of the seroprevalence of HBs antigen. Lower seroprevalence of HBV infection may have been due to higher socioeconomic status of the refugees.

We also investigated the prevalence of HCV infection profiles of Afghan refugees and their healthy counterparts to study whether the risk of HCV infection was higher among refugees or not. Hepatitis C virus (HCV) is one of the most common hepatotrophic infections and the predominant risk factors for HCV acquisition are injection-drug use; blood transfusion before 1992, high lifetime number of sexual partners, and iatrogenic transmission, including through dialysis (11). The seroprevalence of HCV has reportedly been as 0-1% in Turkey and 1-2% in Afghanistan (12, 13).

In our study, the seroprevalence of anti-HCV in Afghan refugees was determined to be similar to Turkish citizens. Providing evidence of high similarity with other studies (10, 14). We showed that seroprevalence of HBV and HCV among Afghan refugees was found to be similar to those in Turkish citizens; however, HIV infection was more frequent than Turkish counterparts.

Turkish community have also historically a very low prevalence of human immunodeficiency virus (HIV) infection due to traditional rules. In studies conducted in Turkey, the seroprevalence of anti-HIV has been established as 1% in the 0-18 years range. According to the recent studies, there were 13,181 HIV-positive patients in Turkey in 2016, and broadly 2500 new cases are diagnosed annually in the country (15).

Two previous studies also addressed HIV prevalence among Afghan refugees attending primary care clinics in Pakistan and reported HIV rates in individuals from Afghanistan of as high as 6% (10, 16).

Other research from Afghanistan showed that the prevalence of HIV infection was as low as 0.063%, but this study conducted among younger Afghan army soldiers (6).

Higher prevalence of HIV infection were probably a result of conditions related to refugee status including lack of infrastructure, overcrowded camps, insufficient health care systems and low economic income, although increased sexual activity among refugees may also have contributed. Although the effectiveness of prevention efforts for HIV infection remains uncertain, our findings are crucial to understanding whether the current evidence-based interventions are sufficient to reduce HIV infection and to guide screening refugees. Additionally, these findings prompt the need for prospective investigation into the potential benefit of spreading HIV infection among Afghan refugees.

Iodine deficiency is well known and important reason for goiter. It is also shown that iodine deficiency results in mild TSH elevation and reduction in thyroid hormone serum levels. Iodine deficiency was seen more in cases with hypothyroidism, while excess of iodine was observed to be more frequent in hyperthyroid patients (17). Iodine replacement program in some countries was shown to be reduction of mean TSH value of the people (18). Other hand, endemic goiter is now the most common type of thyroid disease diagnosed in Afghanistan. In the current study, the higher levels of TSH in immigrants from Afghanistan were probably due to their geographic localization. That means it is close to Himalaya mountain region well known iodine deficient mountain area (19). On the other side Giresun is a coastal province to the Black Sea. People here consumes iodinated sea food and also last decade's iodination programs of the food is well done.

The most common liver diseases are nonalcoholic fatty liver disease (NAFLD), alcoholic liver disease, and viral hepatitis among the population. Elevated liver enzymes levels (mainly ALT) are positively associated with the prevalence of NAFLD (20). For patients suspected to have NAFLD because of elevated liver enzymes transabdominal ultrasound may confirm the presence of hepatosteatosis (21).

In the current study, the mean liver transaminase levels of refugees was lower than Turkish citizens, which suggests that prevalence of NAFLD substantially low among Afghans.

This study has several limitations. First, individual data, marital status, location of born places, both of illicit and intravenous drug use and sexual behaviors were not reported by the participants and may be subject to social desirability and other biases. Second, due to retrospective nature of the study we did not perform radiologic techniques to show hepatobiliary system

and thyroid tissue. Furthermore, an important consideration is whether our estimates of prevalence of HBV, HCV and HIV infections can be generalized entire the Afghan population.

Higher rates of HIV infection may have been associated with infrastructure of refugee camps and health care systems of residential areas of refugees in Afghanistan. Unexpected higher rates in the incidence of HIV infection indicate a need to strengthen prevention efforts to treat immigrant women, including improvement health care systems as well as long-term surveillance programs. There will be also unmeasured indirect costs, including loss of socioeconomic support for both refugee women and their families inside the traditional Turkish town. Moreover, our comprehensive analysis identified several targets for refugee trials. Additional studies are needed to further define the characteristic features of Afghans.

CONCLUSION

Immigration may lead to spread of some infections especially HBV, HCV, and HIV. We need further investigations to find out the risk of infections that originated from immigration.

Abbreviations

HBV — Hepatitis B virüs infection
HCV — Hepatitis C virüs infection
HIV — Human immunodeficiency virus
HBsAg — Hepatitis B surface antigen
Anti HBs — Hepatitis B surface antibody
AntiHBc — Hepatitis B core antibody
TSH — Thyroid stimulating hormone
NAFLD — Nonalcoholic fatty liver disease
AIDS — Acquired immune deficiency syndrome
ALT — Alanine aminotransferase
RNA — Ribonucleic acid

DECLARATION OF INTEREST

The autors declare that there are no conflicts of interests.

Sažetak

SKRINING ZA HEPATITIS B I C SEROPREVALENCU I PREVALENCA HIV INFEKCIJE MEĐU AVGANISTANSKIM IZBEGLICAMA KOJE SU 2018. GODINE STIGLE U OBALSKO PODRUČJE TURSKE: SISTEMATSKA ANALIZA

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Uvod: Prethodne studije su pokazale da je status izbeglice povezan sa različitim pogoršanim efektima na ljudsko zdravlje uključujući veću rasprostranjenost hepatitis B, C I HIV infekcija. U ovoj studiji naš je cilj da premostimo jaz između avganistanskih imigranata i turske populacije time što ćemo identifikovati HBV, HCV I HIV profile. Pored toga, prikupljen je veliki broj laboratorijskih parametara za sve učesnike, uključujući rezultate hematološkog i biohemijskog testa. **Materijali i metode:** Izvršili smo retrospektivni pregled laboratorijskih evidencija u tercijarnom centru u severnoj Turskoj od 1. Januara 2018. godine do 15. Aprila 2018. godine. Naša studija populacije zasnovana je na bolničkim podacima od 403 avganistanske izbeglice i 400 turskih građana.

Rezultati: Izbeglice iz Avganistana su imale veću anti-HIV seropozitivnost od turskih građana ($p < 0.05$). Nije bilo razlike između dve grupe prema HbsAg i anti-HCV seropozitivnosti. Takođe, avganistanske izbelice su imali statistički niže nivoe ALT, veće nivoe hemoglobina i viši srednji TSH nivo ($p < 0.05$). Srednja vrednost T4 nije pokazala značajnu razliku između ove dve grupe.

Zaključak: Potrebna su nam dodatna istraživanja ne bi li pronašli rizike infekcija koji potiču od imigracije.

Ključne reči: Imigranti, infektivne bolesti, virusni hepatitis, AIDS.

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VAGINAL HYSTERECTOMY COMPARED TO ABDOMINAL AND LAPAROSCOPIC HYSTERECTOMIES IN PATIENTS WITHOUT UTERINE PROLAPSE

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Abstract: **Introduction:** Except for the uterine prolapse indication, vaginal hysterectomy has been less popular than abdominal hysterectomy because the latter is considered safer and easier and surgeons often lack sufficient experience on the former. This study aims at comparing a group of patients without prolapse who underwent vaginal hysterectomy to another group of patients who underwent abdominal and laparoscopic hysterectomies with respect to intraoperative and early postoperative complications. **Materials and Methods:** We retrospectively reviewed the files of patients who presented to the gynecology outpatient clinic of Ondokuz May2s University (OMU), Turkey, between January 2013 and February 2018 and for whom hysterectomy was decided due to benign indications other than uterine prolapse. A total of 105 patients, 35 from each of the groups who underwent abdominal, laparoscopic and vaginal hysterectomies, were included in the study. The vaginal hysterectomy group was compared to the abdominal and laparoscopic hysterectomy patient groups with respect to duration of operation, decrease in hematocrit, blood transfusion, duration of hospitalization, hospital expenses, postoperative pain, wound site infection, and complications of intestine, bladder and ureter. **Results:** No statistically significant differences were found between the demographic characteristics of the groups. Vaginal hysterectomy was shown to be superior to laparoscopic and abdominal hysterectomies with respect to mean duration of operation ($p < 0.005$), decrease in hematocrit showing the amount of bleeding ($p < 0.005$), duration of hospitalization ($p < 0.005$), hospital expenses ($p < 0.005$) and amount of postoperative analgesic need ($p < 0.005$). Wound site infection was found more in abdominal hysterectomy than in vaginal and laparoscopic hysterectomies ($p < 0.005$). No statistically significant difference was found between vaginal, abdominal and laparoscopic hysterectomies with respect to blood transfusion and complications of intestine, bladder and ureter ($p > 0.005$). **Conclusion:** The most important factor in choosing a hysterectomy method is the experience of the surgeon. However, vaginal hysterectomy should be the primarily preferred method, if possible, for being more advantageous in many respects.

Key words: Hysterectomy, Minimal invasive surgery, Vaginal hysterectomy.

INTRODUCTION

Hysterectomy occupies a large portion of the routine practices of gynecologists (1). It is a major gynecological surgical operation performed most frequently after cesarean section operations (2). According to the records of the Disease Control and Prevention Center in the United States of America (USA), hysterectomy has been applied to 8.6 million women over 15 years of age between 1980 and 1993 (3). While it is estimated that hysterectomy will be administered to approximately 20% of the women aged around 55 in the United Kingdom, the rate of hysterectomy in the age interval of 40-70 is calculated to be 15% in Italy (4, 5). The number of hysterectomies is approximately 20000 a year in Australia and approximately 10000 in Finland (6, 7). Although there is no figure available for Turkey, we think that these numbers are also applicable to our country. Hysterectomy can be performed abdominally, vaginally, laparoscopically, robotically or using a combination of various techniques as in laparoscopy-assisted vaginal hysterectomy (8). Based on the meta-analyses made by Cochrane in recent years, the American

College of Obstetrics and Gynecology (ACOG) recommends vaginal hysterectomy to be the first choice in benign diseases (9, 10). Despite this, the 2003 records in the USA show that 66.1% of hysterectomies were abdominal, 21.8% vaginal and 11.8% laparoscopic (8). Abdominal hysterectomy is more popular because a large abdominal incision is easier and surgeons are not so confident when performing a vaginal hysterectomy (11). Vaginal hysterectomy should always be the first choice as long as there is no contraindication in women who had a delivery (12). Vaginal hysterectomy is a surgical intervention that involves no visible scar tissue and thus does not raise any esthetic concern and its postoperative period is rather comfortable (13). Since there is no visible scar tissue, it is obviously superior also in terms of wound site infection. Considering that intraoperative bleeding is less in experienced hands, hospitalization and recovery times are shorter, postoperative pain is milder and the cost is lower, the technique to be primarily chosen for the patient should be vaginal hysterectomy (14).

Laparoscopic hysterectomy is also superior to abdominal surgery and these patients also return to their daily lives in a short time like the ones who are undergone vaginal hysterectomy (15, 16). However, compared to abdominal and vaginal hysterectomies, the duration of surgery is the longest in laparoscopic hysterectomy and intraoperative wounding, especially that of the urinary system, is more common compared to the other methods (17). Additionally, laparoscopic hysterectomy is the most expensive technique as compared to abdominal and vaginal hysterectomies (10). There are no studies showing the superiority of robotic or single-port hysterectomy to the conventional laparoscopic hysterectomy (12). There is still no consensus among surgeons as to which method is the most appropriate (12, 18). There are many randomized studies comparing the outcomes of hysterectomy types (18). The decision on the surgical technique to be chosen depends on the training and experience of the surgeon, the indication of the operation, the size and weight of the uterus and the number of past abdominal operations (19). In this study, 35 patients without prolapse who underwent vaginal hysterectomy in our clinic due to benign hysterectomy indication between January 2013 and February 2018 were compared to patients who underwent abdominal and laparoscopic hysterectomies with respect to intraoperative and postoperative complications.

MATERIAL AND METHODS

The outcomes of the patients without prolapse who presented to the gynecology outpatient clinic of the Gynecology and Obstetrics Clinic of Ondokuz Mayıs University (OMU) and underwent hysterectomy due to benign indication were compared with respect to hysterectomy types (vaginal, abdominal and laparoscopic) in this study. **The objective** of the study was to compare the preoperative, intraoperative and postoperative outcomes of these three groups of operated patients in terms of duration of operation, decrease in hematocrit, duration of hospitalization, hospital expenses, need for postoperative analgesia, complications of bladder and ureter, wound site infection, complications of intestine and blood transfusion. The files of the patients who underwent hysterectomy between January 2013 and February 2018 were reviewed retrospectively. There were a total of 2442 hysterectomy cases between these dates and 1789 of these were found to undergo abdominal, 227 vaginal and 426 laparoscopic hysterectomies. In the study, 35 patients without prolapse who underwent vaginal hysterectomy were compared to two separate groups of 35 patients each who had the same characteristics and underwent abdominal and laparoscopic hysterectomies. The indications of hysterectomy consisted of benign gynecological reasons in the study. Those who had genital system malignity were excluded from the study. Indications associated with pelvic relaxation such as genital prolapse and cystocele were also left out. The study included patients with indications of cervical intraepithelial neoplasia, endometrial hyperplasia/polyp, adnexal mass, myoma uteri, adenomyosis, dysfunctional uterine bleeding (DUB), and postmenopausal bleeding. Demographic parameters including age, BMI, gravida, parity, past abdominal surgery and American Society of Anesthesiologists (ASA) scores were compared. The cases were managed by an experienced surgeon and two assistant surgeons. All patients were given the same premedication and operated under general anesthesia. The intestinal cleanse of all patients was performed using Sodium Dihydrogen Phosphate + Disodium Hydrogen Phosphate. During their operations, all patients were administered intravenous (IV) 2 gm cefazolin sodium in 1000 milligram (mg) ampoules. The prophylactic anti-biotherapy was continued with 2 x 1 gm of IV cefazolin sodium at postoperative day 1. All laparoscopic procedures were carried out using video monitoring equipment in modified lithotomy position. A laparoscope with 10-mm panoramic view (StorzGmBH, Germany) was connected to the standard sub-umbilical region. Subsequently, trocars with 5-mm flap-valves were placed. All instruments used during the laparoscopic procedures were reusable. All vaginal hysterectomies were completed using Liga Sure dolphin 5 mm 37 centimeter (cm) LS1500 (COVIDIEN, USA) in lithotomy position. All abdominal hysterectomies were

performed with standard type-1 hysterectomy technique and a Foley catheter was used for bladder drainage for postoperative 24 hours. A gauze stype was vaginally placed after the operation in patients who underwent vaginal hysterectomy and it was removed 24 hours later. In all operations, the time lapsed from the first surgical incision to the completion of all surgical procedures and closure of the incision site was calculated as the "duration of operation". All pieces sent to the pathology were weighed and noted. The analgesia applied when necessary in the postoperative period was given according to a certain schedule. This schedule involved 50 mg of intravenous (IV) Dolantin in 4-hour intervals within the first postoperative 12 hours, then 75 mg of intramuscular (IM) or IV diclofenac sodium or 100 mg of diclofenac sodium in the form of oral tablets. The total analgesic dose given to the patients and the time in which they were in need of analgesics were calculated. The hematocrit value of each patient was measured at preoperative and postoperative day 2 to calculate the blood lost during the operation. The duration of hospitalization was taken as the number of days from the day of operation to the day of discharge. The cost analysis for each patient was based on the data obtained from the OMU system records. Since preoperative preparation was the same for every patient, it was excluded from the comparative cost analysis. The three groups of patients who had abdominal, vaginal and laparoscopic hysterectomies were compared with respect to injuries of major organs such as intestines, bladder and ureters, decrease in hematocrit, blood transfusion, duration of operation, duration of hospitalization, hospital expenses, postoperative pain, and wound site infection. This study was conducted after having been found ethically appropriate by the decision of Samsun OMU Clinic Trials Ethics Committee numbered 111 and dated 15 March 2018. The data obtained were analyzed on the SPSS (Statistics Program for Social Sciences) version 20.0 and R programs. The One Way Analysis of Variance (ANOVA) [Kruskal Wallis] was used to identify the differences within the groups being studied, and the Chi-Square Test, Fisher Exact Test and frequency analyses to show the relationships and differences between the variables. Values of $p < 0.05$ were considered to be significant.

RESULTS

From the patients who presented to our hospital between January 2013 and February 2018, a total of 105 patients with similar demographic characteristics, 35 from each of the groups who underwent vaginal, abdominal and laparoscopic hysterectomies due to benign indications other than prolapse, were included in the study. The mean age of the patients who underwent vaginal hysterectomy was 50.91, their mean body mass index (BMI) 30.3, mean gravida 4.42, mean parity 3.48 and mean ASA score 1.65; the mean age of the patients who underwent abdominal hysterectomy was 51.05, their mean BMI 30.89, mean gravida 4.11, mean parity 3.42 and mean ASA score 1.51; the mean age of the patients who underwent laparoscopic hysterectomy was 50.08, their mean BMI 30.02, mean gravida 3.71, mean parity 2.62 and mean ASA score 1.60. The number of past abdominal operations was calculated to be 12 (30%) for vaginal hysterectomy, 13 (32.5%) for abdominal hysterectomy and 15 (37.5%) for laparoscopic hysterectomy. The age factor was observed not to have any significant effect on the surgical methods used ($p > 0.05$). There was no significant correlation between the surgical methods used and BMI ($p > 0.05$) nor there was any significant correlation between the other variables (gravida, parity and ASA score) and the surgical methods ($p > 0.05$). The number of patients who had undergone a past abdominal operation and underwent vaginal hysterectomy was 12 (30%), the number of those who underwent abdominal hysterectomy was 13 (32.5%) and the number of those who underwent laparoscopic hysterectomy was 15 (37.5%) and there was no correlation between this parameter and the surgical methods ($p > 0.05$). The demographic characteristics of the patients by their hysterectomy types are summarized in Table 1. The indications for all these three groups were cervical intraepithelial neoplasia,

Table 1. *Demographic characteristics of patients with respect to the hysterectomy types*

Factor	Vaginal Hysterectomy	Abdominal Hysterectomy	Laparoscopic Hysterectomy	P value
Age	50.91 (37-72)	51.05 (38-69)	50.08 (35-70)	.869
BMI	30.38 (20-47)	30.89 (23-49)	30.02 (19-44)	.826
Gravida	4.42 (2-12)	4.11 (1-12)	3.71 (0-16)	.099
Parity	3.48 (2-8)	3.42 (1-10)	2.62 (0-10)	.062
ASA score	1.65 (1-3)	1.51 (1-3)	1.60 (1-3)	.515
Past Abdominal Operation	12 (30%)	13 (32.5%)	15 (37.5%)	.821

endometrial hyperplasia/polyp, adnexal mass, myoma uteri, adenomyosis, dysfunctional uterine bleeding(DUB), and postmenopausal bleeding. No significant correlation was seen between surgical indications and surgical types ($p > 0.005$). In the patient group who were operated using the vaginal hysterectomy method, the number of patients with the indication of cervical intraepithelial neoplasia was 3 (8.6%), with the indication of endometrial hyperplasia/endometrial polyp was 9 (25.7%), with the indication of adnexal mass was 1 (2.9%), with the indication of myoma uteri was 4 (11.4%), with the indication of adenomyosis was 4 (11.4%), with the indication of DUB was 6 (17.1%) and with the indication of postmenopausal bleeding was 8 (22.9%). In the patient group who were operated using the abdominal hysterectomy method, the number of patients with the indication of cervical intraepithelial neoplasia was 3 (8.6%), with the indication of endometrial hyperplasia/endometrial polyp was 10 (28.6%), with the indication of adnexal mass was 1 (2.9%), with the indication of myoma uteri was 3 (8.6%), with the indication of adenomyosis was 5 (14.3%), with the indication of DUB was 5 (14.3%) and with the indication of postmenopausal bleeding was 8 (22.9%). Finally, in the patient group who were operated using laparoscopic hysterectomy, the number of patients with the indication of cervical intraepithelial neoplasia was 4 (11.4%), with the indication of endometrial hyperplasia/endometrial polyp was 9 (25.7%), with the indication of adnexial mass was 1 (2.9%), with the indication of myoma uteri was 4 (11.4%), with the indication of adenomyosis was 3 (8.6%), with the indication of DUB was 7 (20%) and with the indication of postmenopausal bleeding was 7 (20%) (Table 2). The duration of operation was calculated as the time lapsed from the first surgical incision to the closure of the incision site. The mean duration of operation was 37.54 min. for vaginal hysterectomy, 46.43 min. for abdominal hysterectomy and 156.63 min. for laparoscopic hysterectomy. There were significant differences between duration of operation and the three different types of operations ($p < 0.005$). The estimated amount of blood loss was calculated using the mean drop in hematocrit by measuring the patients' amount of hematocrit at preoperative and postoperative day 2. The mean drop in hematocrit was found to be 3.46% in vaginal hysterectomy, 7% in abdominal hysterectomy and 7% in laparoscopic hysterectomy. The drop in hematocrit differed significantly among the surgical methods ($p < 0.005$). It was concluded that the surgical method with the lowest hematocrit drop was the vaginal hysterectomy method (3.46%). Duration of hospitalization was found to differ among surgical methods; there were significant differences between the vaginal hysterectomy method and the abdominal hysterectomy and laparoscopic hysterectomy surgical methods ($p < 0.05$). The mean duration of hospitalization was 2 days in vaginal hysterectomy, 5 days in abdominal hysterectomy and 4 days in laparoscopic hysterectomy. No significant difference was observed between the abdominal hysterectomy and laparoscopic hysterectomy surgical methods with respect to duration of hospitalization ($p > 0.05$). The surgical method that had the shortest hospitalization time was the vaginal hysterectomy method (two days). A statistically significant difference was found between duration of hospitalization and surgical types ($p < 0.005$). Significant differences were observed between postop analgesic amount and the three different surgical types. It was concluded that the surgical type that necessitated the smallest amount of analgesics for the patients was the vaginal hysterectomy method (two days). The postop amount of analgesics differed significantly between the vaginal hysterectomy method and the abdominal hysterectomy and laparoscopic hysterectomy surgical methods ($p < 0.05$). The mean postoperative analgesic need was 2 days in vaginal hysterectomy, 3 days in abdominal hysterectomy and 3 days in laparoscopic hysterectomy. A statistically significant difference was found between the three groups ($p < 0.005$). A difference was observed between hospital expenses and surgical methods. A significant difference was seen between

Table 2. *Indications for Operation Types*

INDICATIONS	Vaginal Hysterectomy	Abdominal Hysterectomy	Laparoscopic Hysterectomy	p
CervicalIntraepithelial Neoplasia	8.6% (n = 3)	8.6% (n = 3)	11.4% (n = 4)	0.999
Endometrial Hyperplasia/Endometrial Polyp	25.7% (n = 9)	28.6% (n = 10)	25.7% (n = 9)	
Adnexialmass	2.9% (n = 1)	2.9% (n = 1)	2.9% (n = 1)	
Myoma Uteri	11.4% (n = 4)	8.6% (n = 3)	11.4% (n = 4)	
Adenomyosis	11.4% (n = 4)	14.3% (n = 5)	8.6% (n = 3)	
Dysfunctional Uterine Bleeding	17.1% (n = 6)	14.3% (n = 5)	20% (n =7)	
Postmenopausal Bleeding	22.9% (n = 8)	22.9% (n = 8)	20% (n = 7)	

the vaginal hysterectomy method and the laparoscopic hysterectomy surgical method ($p < 0.05$). There was also a significant difference between the abdominal hysterectomy method and the laparoscopic hysterectomy surgical method ($p < 0.05$). No significant difference was seen between the abdominal hysterectomy and vaginal hysterectomy surgical methods with respect to hospital expenses ($p > 0.05$). The surgical method with the lowest hospital expenses was vaginal hysterectomy (1591.47 Turkish Liras (TL)) and this was found statistically significant ($p < 0.005$). The mean cost was calculated to be TL1.591,47 for vaginal hysterectomy, TL1.855,70 for abdominal hysterectomy and TL 4.230,19 for laparoscopic hysterectomy. As for wound site infection, there were no patients who had wound site infection among patients who underwent vaginal and laparoscopic hysterectomies and 3 patients among those who underwent abdominal hysterectomy. A statistically significant difference was found between the surgical types with respect to wound site infection ($p < 0.005$). In the abdominal hysterectomy method, wound site infection occurred in 8.6% of the patients, which was found to be significantly high ($p < 0.05$). While there were no bladder or ureter complications in the patients who underwent vaginal hysterectomy, ureter complications were seen in 2 patients in abdominal hysterectomy and 3 patients in laparoscopic hysterectomy. There was no statistically significant difference between the three groups ($p > 0.05$). No intestinal complications were seen in the patients who underwent vaginal hysterectomy and abdominal hysterectomy, where as 1 patient had intestinal complication in the laparoscopic hysterectomy group. No significant difference was found between the hysterectomy types with respect to intestinal complications ($p > 0.005$) (Table 3). Generally speaking, there was no statistically significant difference between the surgical methods with respect to intestinal complications, bladder and ureter complications and blood transfusion ($p > 0.05$). The number of patients who had blood transfusion was 1 in vaginal hysterectomy, 5 in abdominal hysterectomy and 2 in laparoscopic hysterectomy. No significant difference was found between the surgical types with respect to blood transfusion ($p > 0.05$).

DISCUSSION

Vaginal hysterectomy is a minimally invasive surgery involving few complications and morbidities and no scar tissue. Except for serious adhesive and large mass involving conditions such as severe endometriosis, pelvic inflammatory disease or adnexal pathology, vaginal hysterectomy is recommended in many studies as the method of first choice in patients for whom hysterectomy is decided due to benign indications (8, 9, 11, 12, 13, 20). In their two studies made in 1990 and 2002, Figueredo Netto O et al. have shown that prolapse is not the basic condition for vaginal hysterectomy and after applying anesthesia, uterus can be pulled down and vaginal hysterectomy can be performed with success (12, 21) Kumar et al. administered vaginal hysterectomy to 80 patients without prolapse and achieved a 95% success rate (22). These studies are supportive of our results. In their study with 250 patients, Doucette et al. administered vaginal hysterectomy to patients with common contraindications such as large uterus, nulliparity, past cesarean section and past laparotomy and argued that such contraindications should be considered rare contraindications (23). Kovac et al. also administered vaginal hysterectomy to patients other surgeons thought were not suitable for vaginal hysterectomy and achieved a 91% success rate (24). In a recent prospective study conducted by Ursuleanu et al., 816 patients, 56% of whom were nulliparous and 69%

Table 3. *Results of from blood transfusion to operation duration for Operation Types*

Factor	Vaginal Hysterectomy	Abdominal Hysterectomy	Laparoscopic Hysterectomy	P value
Duration of Operation	37.54 (27-55)	46.43 (36-70)	156.63 (125-200)	.000
Decrease in hematocrit	3.46 (0-8)	7.00 (3-13)	7.00 (3-11)	.000
Duration of hospitalization	2 (1-5)	5 (3-8)	4 (3-17)	.000
Hospital expenses (TL)	1.591,47 (996, 63-3.405,83)	1.855,70 (1.268,45-2.822,13)	4.230,19 (2.010,95-8.039,10)	.000
Postop analgesia need	2(1-4)	3 (2-6)	3(2-14)	.000
Complications of bladder and ureter	0% (n = 0)	5.7% (n = 2)	8.6% (n = 3)	.365
Wound site infection	0% (n = 0)	8.6% (n = 3)	0% (n = 0)	.046
Intestinal complications	0% (n = 0)	0% (n = 0)	2.9% (n = 1)	1.00
Blood transfusion	2.9% (n = 1)	14.5% (n = 5)	5.7% (n = 2)	1.00

with past cesarean section, underwent vaginal hysterectomy and no increase in complications was found at the end of the study (25). Compatible with the literature, vaginal hysterectomy was administered successfully also in our study to patients with past uterine surgery and to those who were nulliparous. These results show that past surgical operations including cesarean section do not constitute a contraindication for a vaginal approach in experienced hands. Some studies in the literature indicate that although vaginal hysterectomy has many superior aspects, the reason for its being used less in daily practice is the lack of training and experience. Tue et al. has conducted a retrospective study concerning this situation in America. They reviewed 94.599 patients who underwent hysterectomy between 2000 and 2005. Tue et al. found in their study that abdominal route was preferred at a rate of 82% in hospitals providing training and showed that vaginal hysterectomy was taught less to the new generation of gynecologic surgeons (26). Varma et al. adopted a positive approach to vaginal hysterectomy in their study and raised the rate of vaginal hysterectomy from 32% to 95% without increasing morbidity at the end of their 5-year study (27) We compared in our study the patients without prolapses who underwent vaginal hysterectomy and abdominal and laparoscopic hysterectomies in terms of duration of operation, decrease in hematocrit, cost, duration of hospitalization, postoperative amount of analgesia, need for blood transfusion, wound site infection, and complications of intestines, bladder and ureters and found vaginal hysterectomy advantageous in many respects. The studies in the literature have also shown that, with an operation time ranging between 30 and 140 min., vaginal hysterectomy has a shorter operation time than those of abdominal and laparoscopic hysterectomies (28). Cochrane compared the duration of operation in vaginal, laparoscopic and abdominal hysterectomies in the meta-analysis they made in 2015 with the inclusion of 5102 patients. They showed that laparoscopic hysterectomy, a minimally invasive surgery like vaginal hysterectomy, had the longest operation time (29) Similar to these results, we also found in our study that, with a mean operation time of 37.54 min., the patients to whom we administered vaginal hysterectomy had a shorter operation time than those of abdominal and laparoscopic hysterectomies. Even though some studies have reported that vaginal hysterectomy causes more blood loss (17), many other studies in the literature defend that vaginal hysterectomy is an operation causing the least amount of bleeding (16). We also showed in our study that the amount of bleeding was the least. A majority of the studies in the literature have found that the operation with the highest cost is laparoscopic hysterectomy due to the prices of the materials used during the operation. No significant difference has been found between abdominal and vaginal hysterectomies with respect to cost (23). However, with a mean cost of TL 1.591.47, vaginal hysterectomy was found to be a more cost effective technique than abdominal and laparoscopic hysterectomies in our study. A large portion of the studies in the literature have found that vaginal and laparoscopic hysterectomies, which are minimally invasive surgeries, are superior to abdominal hysterectomy with respect to duration of hospitalization. The mean duration of hospitalization was calculated to be 2 days for vaginal hysterectomy in our study. Compatible with the literature, vaginal hysterectomy was shown to be superior to abdominal and laparoscopic hysterectomies in terms of duration of hospitalization. In most of the studies in the literature, the postoperative need for analgesics has been shown to be twice as much in abdominal hysterectomy as in vaginal and laparoscopic hysterectomies (23). This is due to the abdominal incision and the procedure itself. As the tissue trauma increases, the need for analgesia also increases. Similar to the literature, the need for analgesics in our study was calculated to be 2 days on the average for vaginal hysterectomy, showing its superiority to laparoscopic and abdominal hysterectomies. In almost all of the studies in the literature, the technique that was found to have the highest risk of wound site infection was abdominal hysterectomy due to the abdominal incision involved in it (23). Similarly, laparoscopic hysterectomy has been also shown to involve a higher risk of infection than vaginal hysterectomy, however small the difference may be (23). Unlike the literature, we did not find any significant difference between laparoscopic and vaginal hysterectomies with respect to wound site infection in our study, but found vaginal hysterectomy superior to abdominal hysterectomy as in the literature. A large portion of the studies in the literature have shown that laparoscopic hysterectomy is twice as risky as abdominal and vaginal hysterectomies with respect to complications of bladder and ureter (23); moreover, the intestinal perforation rate is thought to increase during laparoscopic port entries (13). Shown as the most invasive technique in the literature, abdominal hysterectomy has the highest probability of requiring blood transfusion (23). Unlike the data in the literature, we did not find in our study any significant difference between abdominal, laparoscopic and vaginal hysterectomies in terms of blood transfusion or complications of the bladder, ureters and intestines. Vaginal hysterectomy was found superior to laparoscopic and abdominal hysterectomies with respect to duration of operation, decrease in hematocrit, duration of hospitalization, and postoperative need for analgesics. Older patients and those with higher anesthe-

tic ASA scores due to their medical diseases usually tolerate vaginal hysterectomy better than abdominal and laparoscopic hysterectomies (23). Operations of highly obese patients make vaginal, abdominal and laparoscopic hysterectomies technically difficult, but such difficulty is less in vaginal hysterectomy (23). Additional conditions associated with vaginal wall relaxation such as cystocele and rectocele can be repaired more easily through the vaginal route (23). Vaginal hysterectomy requires a shorter operation time than abdominal and laparoscopic hysterectomies (15). Vaginal hysterectomy has been evidenced to have a lower cost than laparoscopic hysterectomy, but there are no studies comparing its cost to that of abdominal hysterectomy. The probability of ureter injury is the least in vaginal hysterectomy and the most in laparoscopic hysterectomy (13). Similar to our study, vaginal hysterectomy has been found to be safer, its postop pain to be less, duration of hospitalization to be shorter, patient satisfaction to be higher and its cost to be less as compared to the other methods in both the broad-scale Cochrane meta-analysis and the eVALute study (10). The major limitation of our study was that it was planned as a retrospective study, but it may serve as a guide for larger randomized controlled studies that may be conducted to clearly show the superiority of vaginal hysterectomy in patients without uterine prolapse.

CONCLUSION

For many years, vaginal hysterectomy has been delimited with the indication of uterine prolapse. Many studies in the literature support the fact that the vaginal hysterectomy method can be preferred to other methods in also benign indications without prolapse. When compared to laparoscopic and abdominal hysterectomies, vaginal hysterectomy is more advantageous in duration of operation, amount of bleeding, cost, duration of hospitalization, wound site infection, intraabdominal adhesion and postop analgesia need. Adequate training should be provided about the practice of vaginal hysterectomy particularly in uteruses without prolapses during the specialization courses in training hospitals and hysterectomy through vaginal route should be promoted.

Abbreviations:

OMU — OndokuzMayıs University
ACOG — American College of Obstetrics and Gynecology
USA — United States of America
ASA — American Society of Anesthesiologists
IM — Intramuscular
IV — Intraveous
SPSS — Statistics Program for Social Sciences
ANOVA — One Way Analysis of Variance
BMI — body mass index
DUB — dysfunctional uterine bleeding
TL — Turkish Liras

DECLARATION OF INTEREST

The authors declare that there are no conflicts of interest.

Sažetak

VAGINALNA HISTEREKTOMIJA U POREĐENJU SA ABDOMINALNOM I LAPAROSKOPSKOM HISTEREKTOMIJOM KOD PACIJENTKINJA BEZ PROLAPSA UTERUSA

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Uvod: Osim indikacije za prolaps materice, vaginalna histerektomija je bila manje popularna od abdominalne histerektomije zato što je abdominalna histerektomija smatrana za bezbedniju i lakšu, a hirurzima često manjka dovoljno iskustva za vaginalnu histerektomiju. Ova studija ima za cilj da uporedi grupu pacijentkinja bez prolapsa uterusa, koje su imale vaginalnu histerektomiju sa drugom grupom pacijentkinja koje su imale abdominalnu i laparaskopsku histerektomiju u odnosu na intraoperativne i rane postoperativne komplikacije.

Materijal i metode: Retrospektivno smo pregledali kartone pacijentkinja sa ginekološke klinike Univerziteta Ondokuz Mayıs, u Turskoj, između januara 2013 i februara 2018, kod kojih je urađena histerektomija zbog benignih indikacija, izuzev prolapsa materice. U studiju je uključeno ukupno 105 pacijentkinja, 35 iz svake od grupa koje su imale abdominalnu, lapara-

skopsku i vaginalnu histerektomiju. Grupa sa vaginalnom histerektomijom je upoređivana sa grupom sa abdominalnom i laparaskopskom histerektomijom u smislu trajanja operacije, smanjenja hematokrita, transfuzije krvi, trajanja hospitalizacije, bolničkih troškova, postoperativnog bola, infekcija rane, kao i komplikacija creva, bešike i uretera.

Rezultati: Nisu pronađene statistički značajne razlike između demografskih karakteristika grupa. Pokazano je da je vaginalna histerektomija superiornija u odnosu na laparaskopsku i abdominalnu histerektomiju u smislu trajanja operacije ($p < 0.005$), smanjenje hematokrita pokazuje količinu krvarenja ($p < 0.005$), trajanja hospitalizacije ($p < 0.005$), bolničkih troškova ($p < 0.005$), i količine potrebnih postoperativnih analgetika ($p < 0.005$). Infekcija rane je češća kod abdominalne histerektomije nego kod vaginalne i laparoskopske ($p < 0.005$). Nije pronađena statistički značajna razlika između vaginalnih, abdominalnih i laparaskopskih histerektomija u odnosu na transfuziju krvi i komplikacije creva, bešike i uretera ($p > 0.005$).

Zaključak: Najvažniji faktor u odabiru metode histerektomije jeste iskustvo hirurga. Međutim vaginalna histerektomija bi trebala biti primarno poželjna metoda, ako je moguće, jer je u mnogim pogledima povoljnija.

Ključne reči: Histerektomija, minimalno invazivna hirurgija, vaginalna histerektomija.

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ELECTROSURGICAL MICRONEEDLE VERSUS SCALPEL SKIN INCISIONS IN THE FACIAL REGION

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Abstract: **Objective:** Electrosurgery is widely used in surgical procedures, but mainly for subcutaneous and deep layer dissections. The aim of this study was to clinically evaluate the results of routine use of electrosurgical microneedle in performing skin incisions in the facial regions. **Material and methods:** Eighty patients with both benign and malignant skin lesions in the facial regions undergoing surgery were enrolled in this study. In group A comprising 40 patients, cold steel surgical scalpel N° 15 was used for the surgical procedure. Electrosurgical microneedle with 0.06 mm tip radius and generator unit *KLS Martin Electrosurgical Unit ME MB 2* set on cutting mode, power 12 W was used for performing the surgery in group B including the same number of patients. Differences between incision time, excision time, blood loss and the wound related complications were evaluated. **Results:** The two groups did not significantly differ in the speed of incision and speed of excision although both the speed of incision and the speed of excision were found to be slightly faster in the electrosurgery group. There was significantly less blood loss in the electrosurgery group compared with the scalpel group.Statistical analysis did not confirm as significant the difference in complications between the two groups although most of the complications were associated with the patients operated with scalpel. **Conclusion:** Electrosurgery presents safe and effective way of work. In that manner, it is very important to choose the right generator unit's settings and the right type of electrode.

Key words: surgical scalpel, electrosurgery, facial regions.

INTRODUCTION

Surgical scalpel is the most widely used cutting instrument in surgery. The incisions made with the scalpel are sharp and very precise causing only mechanical injury to the tissue together with profound bleeding. Different types of scalpel are used for different procedures in surgery (1, 2).

However, over the years different alternative ways for cutting the skin have been developed with electrosurgery being the most popular one (3). Electrosurgery involves the passage of high frequency alternating electrical current in the tissues to produce the effect of cutting or coagulation (3, 4).

In recent years there has been a huge improvement in the design of electrosurgical devices thus making electrosurgery safe and effective method for work. But although it is widely used in surgical procedures, mainly for subcutaneous and deep layer dissections its use on skin has been precluded by the fear of complications like delayed wound healing and surgical site infections (4). In that manner it is very important to choose the right generator unit's settings and the right type of electrode.

In order to achieve the effect of the scalpel, pure cut mode with the generator unit output power set on the lowest power that can produce the effect of cutting combined with an electrode in form of needle or microneedle should be used for cutting the skin (5, 6). The microneedle electrode with the tip radius of 0.06 mm is used for performing fine surgical procedures (1, 7, 8).

The aim of this study was to clinically evaluate the results of routine use of electrosurgical microneedle in performing skin incisions in the facial regions.

MATERIALS AND METHODS

Eighty patients with both benign and malignant skin lesions in the facial regions undergoing surgery were enrolled in this study. The patients were recruited

from the University Clinic for Plastic and Reconstructive Surgery, Medical Faculty, Ss. Cyril and Methodius University in Skopje, Macedonia, in the time interval between September 2017 to September 2018.

Patients were randomized in two groups using the envelope randomization method. Each group included 40 patients. In group A cold steel surgical scalpel N° 15 was used for the surgical procedure whereas electrosurgical microneedle with 0.06 mm tip radius and generator unit *KLS Martin Electrosurgical Unit ME MB 2* set on cutting mode, power 12 W was used for performing the surgery in group B. Electrosurgery was used for hemostasis during the dissection process in both groups using the same generator unit set on coagulation mode power 20 W.

Surgical procedures were performed under local infiltrative anesthesia (lidocaine 1% with adrenalin) as to standard practice.

In each surgical procedure the proposed skin excision was marked. When the excision was a circle its perimeter was calculated using the standard formula and when the excision was an ellipse its perimeter was calculated using the Ramanujan formula. The time required to complete the incision was calculated. The incision included cutting of the epidermis and dermis. Incision was considered completed when hypodermis was reached. The perimeter in millimeters divided by the time in seconds gave the speed of incision movement (mm/s).

Only the tip of the microneedle was allowed to come in contact with the proposed incision line while the sides of the microneedle were not allowed to touch the skin edges at any time. To avert the skin edges away as cutting precedes, the surgeon and assistant applied mild traction pressure on either side of the skin incision.

The time needed to complete the excision was calculated. In all the cases only skin and superficial part of the subdermal tissue were excised. The excision was considered completed with the completion of the haemostasis.

Blood loss was also calculated. First dry gauze swabs were measured and then the gauze swabs soaked with blood. The difference between the two measurements was considered the total blood loss. One gram of blood was regarded as equivalent of 1ml of blood. No suction evacuation of blood was done while making the skin incision.

On completing total skin excision, the vitality of the skin was evaluated by checking its color and blood supply. Wound edges were inspected for any thermal trauma in form of fulguration and dermal peeling.

At the termination of the operation the postoperative defect was closed in manner of direct closure where there was no tension or with the use of local skin flaps in order to release the tension. Wound closure was achieved in two layers with interrupted sutures. The subcutis was sutured with 3/0 Polyglactin 910 while the skin was sutured with silk fibroin 4/0.

Wound complications occurring at any stage after the operation and at one month follow up were recorded. Each wound was inspected for wound healing complications comprising wound infection, dehiscence, necrosis, and haematoma.

All the patients were informed about the nature of the skin incision and written informed consent was signed.

RESULTS

Statistical analysis of the data was performed using the statistical program Statistics for Windows 7,0. A value of $p < 0,05$ was considered statistically significant.

Both groups of patients were homogenous according to the sex structure ($p = 0.64$). The mean age of the patients in group A was 61.45 ± 19.8 and the mean age of the patients in group B was 69.03 ± 11.9.

The indication for surgery in terms of underlying diagnosis did not differ significantly between the groups and malignancy was diagnosed in majority of patients in each group.

The velocity of incision was analyzed in mm/s from the start of cutting till completing the incision. The speed of incision when steel scalpel was used ranged 2.6 ± 1.1 mm/s while the speed of incision when microneedle electrosurgery was used ranged 2.95 ± 1.2 mm/s. The speed of incision although not significantly was found to be slightly faster in the group B (2.6 ± 1.1vs 2.95 ± 1.2; $p = 0.17$) (Table 1).

The speed of excision was also analyzed. Excision included excision of skin and superficial part of the subcutaneous tissue. Excision was considered completed with the completion of the hemostasis. The speed of the excision was registered as non-significantly faster in group B in our study (1.74 ± 1.1 vs. 1.97 ± 1.0; $p = 0.33$) (Table 2).

Table 1. *Speed of Incision*

Groups	Speed of incision (mm/s)			p value
	n	**mean ± SD**	**min - max**	
Scalpel	40	2.6 ± 1.1	0.7 – 5.1	0.17ns
Microneedle	40	2.95 ± 1.2	0.7 – 6.3	

p (Student t-test)

Table 2. *Speed of Excision*

Groups	Speed of excision (mm^2/s)			p value
	n	**mean ± SD**	**min - max**	
Scalpel	40	1.74 ± 1.1	0.4 – 6.7	0.33ns
Microneedle	40	1.97 ± 1.0	0.5 – 5.1	

p (Student t-test)

Table 3. *Blood Loss*

Groups	Blood loss (ml/mm^2)			p value
	n	**mean ± SD**	**min - max**	
Scalpel	40	0.017 ± 0.013	0.003 – 0.062	0.00089sig
Microneedle	40	0.009 ± 0.006	0.002 – 0.03	

p (Student t-test)

Table 4. *Complications in general*

Complications in general	Treatment			p value
	n	**Scalpel**	**Microneedle**	
No	62	30 (75%)	32 (80%)	0.59 ns
Yes	18	10 (25%)	8 (20%)	

p (Chi-square test)

Table 5. *Complications*

Complications	Treatment			p value
	n	**Scalpel**	**Microneedle**	
Infection				
No	77	40 (100)	37 (92.5)	[b]0.24 ns
Yes	3	0	3 (7.5)	
Hematoma				
No	75	36 (90)	39 (97.5)	[b]0.36 ns
Yes	5	4 (10)	1 (2.5)	
Delayed wound healing				
No	67	31 (77.5)	36 (90)	[a]0.13ns
Yes	13	9 (22.5)	4 (10)	
Dehiscence - partial				
No	69	32 (80)	37 (92.5)	[a]0.1 ns
Yes	11	8 (20)	3 (7.5)	
Necrosis				
No	71	33 (82.5)	38 (95)	[b]0.15 ns
Yes	9	7 (17.5)	2 (5)	

[a]p (Chi-square test) [b]p (Fisher exact, two tailed)

When the blood loss was measured as ml/mm^2 there was significant difference between the two groups for the value p = 0.00089. The mean blood loss was significantly lower in the group of patients operated with electrosurgery (0.009 ± 0.006 vs 0.017 ± 0.013) (Table 3).

Results of this study showed that complications had 25% of the patients in the scalpel group and 20% of the patients in the microneedle group. Statistical analysis did not confirm as significant the difference in complications between the two groups (p = 0.59) (Table 4).

The patients in both groups did not significantly differ in the postoperative complications (p > 0.05), although of the complications were associated with the patients operated with scalpel (Table 5).

Macroscopic signs for thermal trauma as charcoal effect together with dermal peeling was noticed in two patients and only dermal peeling in only one patient. Prolonged wound healing and partial wound dehiscence was noticed in only one patient, one of the patients with signs of fulguration and dermal peeling.

In our study the postoperative complications were not significantly associated with smoking (p = 0.54).

DISCUSSION

Wound healing of the skin after surgical incision is a primary factor affecting patient morbidity and recovery time. Although electrosurgical instruments are used increasingly for making deep layer incisions and tissue dissection, concerns about excessive scaring, high wound infection rate and poor wound healing have restricted the widespread use of electrosurgery for skin incisions.

Improvements in the design of electrosurgical devices have created generators that produce pure sinusoidal cut waveforms that cause minimal thermal damage to the tissue. This coupled with specialized cutting tips like microneedle can make a skin incision that does not differ from scalpel incision.

Several previous studies have investigated the use of electrosurgery in skin opening. Most were connected with general surgery and mainly for abdominal and thoracic skin incisions. They have shown that there is no difference in the wound healing between the wounds created with steel scalpel and the wounds created with electrosurgery (10-19).

The study of Sheikh B. et al. recommend the use of microneedle electrosurgery surgery in all neurosurgical procedures especially when blood loss has significant importance, such as in paediatric cases (20).

Similar results were shown in the study of Kumar and al. which analyses the outcome of patients following use of scalpel and electrosurgery in elective skin incisions of head and neck cancer. Due to the reduced blood loss and shorter operative time they strongly recommend the use of electrosurgery in these group of patients.

In our study the two groups did not differ significantly in the both incisional and excisional speed although both the incisional and excisional time were faster in the electrosurgery group. There was significantly less blood loss in the electrosurgery group compared with the scalpel group. There is no change in wound complications rate in the electrosurgery group. More over in our study most of the complications were associated with the patients operated with scalpel.

On the base of this study it is suggested that the skin may be safely incised with electrosurgery. Furthermore, the recent increase in blood borne disease makes exclusion of the scalpel from the operative field an attractive option and the role of scalpel in making incisions may be completely taken over by the electrosurgery.

CONCLUSION

Electrosurgery is safe and effective way of performing elective surgical procedures in the facial region. The findings of this study support the use of microneedle in surgical procedures concerning the facial region.

DECLARATION OF INTEREST

The authors declare that there are no conflicts of interests.

This study was done as a part of a more extended PhD thesis.

Sažetak

POREĐENJE ELEKTROHIRURŠKIH KOŽNIH INCIZIJA MIKROIGLOM I KOŽNIH INCIZIJA SKALPELOM U PREDELU LICA

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Uvod: Elektrohirurgija se široko koristi u hirurškim procedurama, ali uglavnom za potkožne i duboke disekcije. Cilj ove studije bio je da se klinički proceni rezultat rutinskog korišćenja elektrohirurške mikrogle za kožne incizije u predelu lica. **Materijal i imetode:** U studiju je uključeno osamdeset pacijenata sa benignim i malignim lezijama kože u predelu lica koji su operisani. U grupi A, koja se sastojala od 40 pacijenata, korišćen je hirurški skalpel broj 15. Grupa B je imala isti broj pacijenata i tu je korišćen elektrohirurška mikroigla sa radijusom 0.06 mm i generatorskom jedinicom KLS Martin Electrosurgical Unit ME MB2 postavljen na režim sečenja, snage 12 W. Vrednovane su razlike između vremena incizije, vremena ekscizije, gubitka krvi i komplikacija vezanih za ranu. **Rezultati:** Dve grupe se nisu značajno razlikovale u brzini incizije i ekscizije, iako su se ove dve vrednosti pokazale nešto brže u grupi gde je korišćena elektrohirurška mikroigla. Bilo je značajno manje gubitka krvi u grupi B u poređenju sa grupom gde je korišćen skalpel. Statistička analiza nije potvrdila značajnu razliku u komplikacijama između dve grupe, iako je većina komplikacija bila povezana sa pacijentima kod kojih je korišćen skalpel. **Zaključak:** Elektrohirurgija predstavlja bezbedan i efikasan način rada. Važno je odabrati odgovarajuće postavke generatorske jedinice i odgovarajući tip elektrode.

Ključne reči: hirurški skalpel, elektrohirurgija, region lica.

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EFFECT OF SUGAMMADEX AND NEOSTIGMINE ON BLOOD GLUCOSE LEVEL: A PROSPECTIVE RANDOMIZED CONTROLLED TRIAL

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Abstract: **Objectives:** Sugammadex is offered as a recent alternative to cholinesterase inhibitors in reversing neuromuscular block. Sugammadex is a cyclodextrin molecule that is consisted of bounded sugar molecules. Given its chemical structure, sugammadex may increase blood glucose levels. We aimed to investigate the effect of sugammadex on blood glucose and compare sugammadex to the conventional reverse agent Neostigmine. **Methods:** Sixty patients undergoing abdominal surgery under general anesthesia were included in this study. The patients were randomly divided into two groups: Group N (n = 30) and Group S (n = 30). At the end of the surgery 50 μg/kg Neostigmine and 20 μg/kg atropine was administered for the patients in Group N and 2 mg/kg sugammadex was administered for the patients in Group S. Blood glucose levels were measured at 15 minutes before (T1) and at 30th minute of surgery (T2). Blood glucose levels were recorded 30 minutes (T3), 2 hours (T4) and 4 hours (T5) after administration of the reversing agent. **Results:** Blood glucose levels that were measured at T3, T4 and T5 were significantly higher in Group S compared to Group N ($p < 0.05$). We consider that sugammadex contains glucose molecules and does not bind to plasma proteins, may cause an increase in blood glucose level and this increase may be associated with chemical structure of sugammadex rather than surgical stress.

Key words: Neuromuscular block reverse, Sugammadex, Neostigmine, blood glucose level.

INTRODUCTION

Blood glucose level effects mortality and morbidity in the perioperative period. Surgical stimulus is among the most important factors that affect the metabolic and endocrine system response during surgery. Blood glucose level is increased by surgical stimulus that influences insulin and glucagon release. Increase in blood glucose levels is a factor that directly effects wound healing negatively and may prolong length of hospital stay (1, 2). Neuromuscular blocking agents are frequently used in general anesthesia in order to facilitate endotracheal intubation and provide muscle relaxation during the surgery. Non-depolari- zing neuromuscular blockers, which are also known as muscle relaxants, block the binding of neurotransmitters to nicotinic acetylcholine receptor at the neuromuscular junction of motor neurons and paralyze the muscles. Cholinesterase inhibitors such as neostigmine are the most commonly used agents in anesthesiology practice to reverse effects of non-depolarizing neuromuscular blockers. Neostigmine provides acetylcholine accumulation in neuromuscular junction by inhibiting acetyl-cholin-esterase. This promotes neuromuscular transmission in the synapse and helps return of normal muscle function (3, 4, 5).

Sugammadex is an excellent alternative to the conventional decurarisation process performed with cholinesterase inhibitors. Sugammadex reverses deep rocuronium-induced neuromuscular block safely and rapidly without resulting in anticholinergic side effects. Sugammadex ensures elimination of non-depolarizing muscle relaxants such as rocuronium and vecuronium via the kidneys without being metabolized (6, 7, 8). Sugammadex is a modified gamma-cyclodextrin which makes steroidal non-depolarizing muscle relaxants inactive by encapsulating them. Gamma-cyclodextrin is consisted

of eight glucose units. "Su" refers to sugar and "gammadex" refers to the structural molecule gamma-cyclodextrin (9, 10).

Our hypothesis was sugammadex might increase blood glucose levels given its chemical structure. We aimed to assess the effect of sugammadex on blood glucose and compare sugammadex to the conventional reverse agent Neostigmine.

MATERIAL AND METHODS

This study is designed as a prospective, randomized, controlled clinical research. It was approved by Clinical Research Ethics Committee of Kocaeli University. Written informed consents have been obtained from all patients that participated in the study. We enrolled 60 patients, aged between 18-65 years with American Society of Anesthesiologists (ASA) class I-II-III who were planned to undergo abdominal surgery under general anesthesia. The patients who had diabetes mellitus and other endocrine diseases (such as hyperthyroidism, hypothyroidism, renal-hepatic enzyme disorders, pregnancy and lactation) causing abnormal glucose metabolism or the patients using drugs (such as steroids, beta-blockers, insulin, sulfonylurea) which may effects glucose metabolism and patients who had alcohol usage in the past week were excluded from the study. The patients were randomized into two groups using a computerized randomization program. Thirty patients were included in the Neostigmine group (Group N) and 30 patients were included in the sugammadex group (Group S).

All patients were held nil per os for 8 hours. After cannulation with 18-20 Gauge intravenous catheter, infusion of 0.9% normal saline was started. The patients did not receive any glucose-containing intravenous fluids and were not fed during the first 4 hours of the postoperative period. The patients were premedicated with 0.03 mg/kg midazolam and 1 μg/kg fentanyl before the surgery. Electrocardiography (ECG), heart rate (HR), non-invasive measurement of systolic arterial pressure (SAP), diastolic arterial pressure (DAP), mean arterial blood pressure (MAP), pulse oxymetry (SpO2), and end-tidal carbon dioxide pressure (EtCO2) was monitored in the operating room. A train of four (TOF) device (Watch S, Organon) was used to measure the level of neuromuscular block.

For anesthesia induction, 5 mg/kg intravenous sodium thiopental, was administered to all patients. Muscle relaxation was achieved using 0.6 mg/kg intravenous rocuronium bromide. When maximum neuromuscular block occurred (TOF ratio = 0.0), the patient was intubated. The maintenance course of anesthesia was continued with intravenous infusion of 0.05 μg/kg/min remifentanil and inhalation of 2% sevoflurane in a mixture of 50% Oxygen and 50% Nitrous oxide. All patients received 1 mg/kg of dexketoprofen for postoperative analgesia, 30 minutes before the end of the surgery. After the surgery was completed, 50 μg/kg of neostigmine and 20 μg/kg of atropine were given for the patients in Group N and 2 mg/kg of sugammadex in Group S to reverse the neuromuscular block of rocuronium. The patients were extubated after maximum muscle strength was achieved (TOF ratio > 0.9).

The blood glucose levels of the patients were measured using a glucometer (Optium®, Abbott laboratories, USA) with strip (Medisense®, Abbott laboratories, UK). Blood glucose levels were measured 15 minutes preoperatively (T1) and at 30th minute intraoperatively (T2). Blood glucose levels were also recorded 30 minutes (T3), 2 hours (T4) and 4 hours (T5) after the administration of reverse agents. SAP, DAP, MAP, HR, SpO2, EtCO2 were recorded at the same time. Duration of surgery was also recorded which was defined as: "The time measured starting from the first incision of the skin until the end of closing sutures of the skin."

Descriptive statistics (mean, standard deviation) were used to summarize data. Two-way analysis of variance (ANOVA) test was used for repeated measurements to find differences between the groups. Bonferroni paired t-test was used for paired comparisons within the groups. Independent sample t-test was used for the characteristics of the patients, and also Fisher's exact test was used for nominal values. Statistical significance was considered as $p < 0.05$ in the two-tailed tests.

RESULTS

There were no statistically significant difference between the groups in terms of gender, age, weight, duration of surgery, ASA, and comorbid diseases ($p > 0.05$) (Table 1). The distribution of types of surgery in two groups was stated in Table 2.

Table 1. *The characteristics of the patients*

	Sugammadex Group (n = 30)	Neostigmine Group (n = 30)	P value
Gender (Male/Female)	11/19	21/9	0.70 *
Age (years)	56.13 ± 8.38	52.20 ± 11.92	0.14 **
Weight (kg)	69.57 ± 12.01	69.47 ± 12.71	0.97 **
Duration of Surgery (min)	106.50 ± 31.89	98.83 ± 32.04	0.35 **
ASA (I/II/III)	6/13/11	9/15/6	0.12 *
Comorbid Disease (Yes/No)	22/8	15/15	0.06 *

p: The two-tailed significance test, ASA: The American Society of Anesthesiologists Anesthesia Risk Scoring
*The Fisher's exact test. **The independent sample t-test.

Table 2. *Types of surgery performed in two groups*

Types of surgery	Sugammadex Group (n = 30)	Neostigmine Group (n = 30)
Total abdominal hysterectomy and bilateral salpingooferectomy	13	12
Excision of liver or pancreatic cysts	1	2
Oophorectomy	5	4
Exploration of abdominal masses	2	1
Partial or total colectomy	8	7
Partial or total gastrectomy	1	2
Myomectomy	0	2

Table 3. *The blood glucose levels (mg/dL) in two groups*

	Sugammadex Group	Neostigmine group	p
T1	105,77 ± 20,29	107,33 ± 14,14	0,742
T2	115,20 ± 15,05	111,87 ± 17,66	0,441
T3	146,20 ± 30,67	127,47 ± 23,00	0,008*
T4	143,03 ± 29,01	124,70 ± 22,57	0,007*
T5	141,37 ± 31,19	125,53 ± 27,27	0,034*

T1: 15 minutes preoperatively; T2: 30 minutes intraoperatively; T3: 30 minutes after administration of the reversing agent; T4: 2 hours after administration of the reversing agent; T5: 4 hours after administration of the reversing agent. * $p < 0.05$

When the blood glucose levels were compared between the groups, there was no significant difference at T1 and T2 between the two groups. Blood glucose levels were significantly higher at T3, T4 and T5 in the Sugammadex group compared to those in Neostigmine group ($p < 0.05$) (Figure 1). Blood glucose levels measured at T1, T2, T3, T4, T5 and p values in both groups

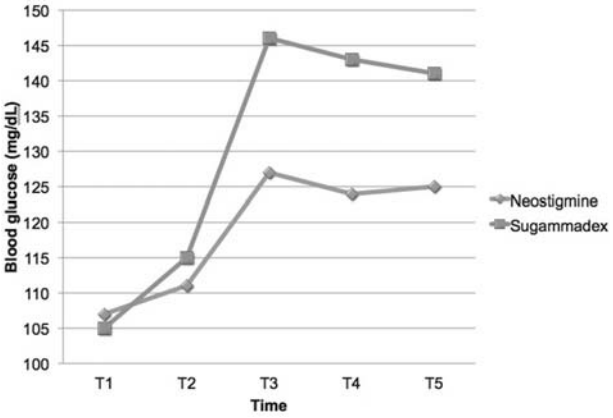

Figure 1. *Graphical comparison of mean blood glucose levels (mg/dL) in two groups. T1: 15 minutes preoperatively; T2: 30th minute intraoperatively; T3: 30 minutes after administration of the reversing agent; T4: 2 hours after administration of the reversing agent; T5: 4 hours after administration of the reversing agent*

were shown in Table 3. Heart rate, non-invasive measurement of systolic arterial pressure, diastolic arterial pressure, mean arterial blood pressure, oxygen saturation and end-tidal carbon dioxide pressure values were shown in Table 4.

DISCUSSION

The current study compared the effect of sugammadex on blood glucose levels to neostigmine in patients who underwent abdominal surgery. We determined a significant increase in glucose levels when sugammadex was used. Efficacy and safety of sugammadex was excessively studied before, but to our knowledge, there is no study showing the effect of sugammadex on perioperative blood glucose levels (11).

Table 4. *The hemodynamic values measured in two groups*

		T1	T2	T3	T4	T5
SAP (mm/Hg) mean ± SD	Group S	143.0 ± 23.59	120.57 ± 18.35	133.33 ± 22.74	138.47 ± 26.72	134.43 ± 24.09*
	Group N	136.47 ± 26.85	126.73 ± 17.68	141.0 ± 18.95	123.23 ± 17.04	115.87 ± 17.16*
DAP (mm/Hg) mean ± SD	Group S	83.07 ± 16.97	69.77 ± 14.71	75.13 ± 12.33	78.73 ± 9.57	74.03 ± 8.63*
	Group N	77.93 ± 10.63	74.5 ± 13.59	79.67 ± 13.35	74.0 ± 13.25	68.57 ± 11.23*
MAP (mm/Hg) mean ± SD	Group S	103.83±21.91	87.23±16.0	93.2±13.45	98.63±9.49	95.0±10.32*
	Group N	98.2 ± 17.27	88.6 ± 14.28	104.13 ± 14.59	91.37 ± 14.61	84.13 ± 12.35*
HR (beat/min) mean ± SD	Group S	89.7 ± 17.14	82.73 ± 17.35	87.3 ± 15.27	90.53 ± 14.02	90.7 ± 14.33
	Group N	87.6 ± 14.71	77.67 ± 10.99	83.6 ± 19.12	80.17 ± 18.48	87.87 ± 17.77

T1: 15 minutes preoperatively; T2: 30th minute intraoperatively; T3: 30 minutes after administration of the reversing agent; T4: 2 hours after administration of the reversing agent; T5: 4 hours after administration of the reversing agent

SAP: Systolic arterial pressure; DAP: Diastolic arterial pressure; MAP: Mean arterial pressure; HR: Heart rate; N: Neostigmine; S: Sugammadex; SD: Standard deviation.

* $p < 0.05$ between the groups

There are many factors that may influence blood glucose during and after a surgery. These factors include preoperative increased catabolic hormones due to dehydration, hunger, fear, perioperative bleeding, hypothermia, hypoxia, hypercapnia, pain, immobility, hypoxia, infection and circadian rhythm changes. The levels of adrenocorticotropic hormone and cortisol are elevated at the beginning of surgery, and then catecholamines, glucagon and growth hormone are released. Insulin secretion is reduced and insulin resistance often develops during surgical trauma (12, 13). Perioperative blood glucose level is elevated as a result of all of these reasons.

Sugammadex is the first selective neuromuscular relaxant drug binding agent, which is used to reverse the effects of non-depolarizing neuromuscular blockers. Decurarisation with sugammadex is a new approach to safely and rapidly reverse vecuronium or rocuronium-induced neuromuscular block. Sugammadex is a cyclodextrin and cyclodextrins contain 6-12 glucose units. Sugammadex does not bind to plasma proteins and erythrocytes. It does not produce any metabolite and is usually excreted unchanged with encapsulated neuromuscular blocker drug in urine within 24 hours. No major adverse effect of sugammadex was reported previously. Minor and common adverse effects reported include non-specific hypotension and cough at the end of the operation due to light anesthesia. Uncommon side effects are allergic reactions and return of muscle relaxation after the operation (14, 15, 16).

We hypothesized blood glucose level might increase due to the presence of free sugammadex in plasma and we noted a significant increase compared to neostigmine shortly after drug administration and after withdrawal of the endotracheal tube. This can be explained in two ways: stress response such as reaction to the endotracheal tube, agitation due to fast awakening as a result of the rapid reversal effect of sugammadex may be the reason of high blood glucose levels when sugammadex was used. In accordance with the literature, we considered that increase in blood glucose at early postoperative phase was associated with fast and efficient decurarisation provided by sugammadex (16-19). The second reason can be addressed as blood glucose levels are elevated due to the chemical structure of sugammadex. We evaluated blood glucose levels at 2 and 4 hours after extubation to distinguish between the two reasons. The blood glucose levels were significantly higher at 30th minute after extubation compared to glucose levels in the preoperative and intraoperative period in Sugammadex and Neostigmine groups. Thus, we considered increase of blood glucose at 30th minute after extubation may be associated with early postoperative stress. However, the blood glucose levels were also significantly higher 2 and 4 hours after endotracheal extubation in sugammadex-treated patients. We concluded that this situation was associated with the chemical structure of sugammadex.

The effect of sugammadex on blood glucose levels was studied among diabetic rats previously (20). Sugammadex was administered at different doses to control rats and diabetic rats. Serum glucose levels were found significantly higher in diabetic rats however there was no difference between diabetic rats that sugammadex was not given and sugammadex-treated diabetic rats. The effect of sugammadex on serum glucose has not been fully understood as expected because sugammadex-treated rats were diabetic. It is noteworthy that, reversal of neuromuscular block using sugammadex showed no difference in diabetic patients versus general population (21).

In conclusion, blood glucose levels were higher after administration of sugammadex compared to neostigmine in acute post-operative period. We consider that sugammadex contains glucose molecules and does not bind to plasma proteins may cause an increase in blood glucose level and this increase may be associated with chemical structure of sugammadex rather than surgical stress of patients.

DECLARATION OF INTEREST

The authors declare that there are no conflicts of interests.

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Sažetak

EFEKAT SUGAMADEKSA I NEOSTIGMINA NA NIVO GLUKOZE U KRVI: PROSPEKTIVNO RANDOMIZOVANO KONTROLISANO ISPITIVANJE

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Uvod: Sugamadeks se koristi kao alternativa inhibitorima holinesteraze kod reverzibilnog neuromuskularnog bloka. Sugamadeks je molekul ciklodekstrina koji se sastoji od međusobno povezanih molekula šećera. Shodno hemijskoj strukturi, sugamadeks može povećati nivo glukoze u krvi. Cilj nam je bio da istražimo efekat sugamadeksa na nivo glukoze u krvi i uporedimo sugamadeks sa konvencionalnim neostigminom. **Metode:** Šezdeset pacijenata, podvrgnutih srednjeročnoj abdominalnoj operaciji pod opštom anestezijom, uključeno je u ovu studiju. Pacijenti su nasumično podeljeni u dve grupe: Grupa N (n = 30) i Grupa S (n = 30). Doza od 50 μg/kg neostigmina i 20 μg/kg atropina je data pacijentima iz Grupe N, a 2 mg/kg sugamadeksa je data pacijentima iz Grupe S. Nivo glukoze u krvi meren je 15 minuta pre (T1) i 30og minuta operacije (T2). Nivo glukoze u krvi je takođe merena 30 minuta (T3), 2h (T4) i 4h (T5) posle administracije reverzibilnog agensa.

Rezultati: Nivoi glukoze u krvi mereni u vremenu T3, T4, T5 su bili značajno viši u Grupi S u poređenju sa Grupom N ($p < 0.05$). Smatramo da sugamadeks koji sadrži molekule glukoze i ne vezuje se za proteine plazme, može izazvati povećanje nivoa glukoze u krvi i ovo povećanje može biti povezano sa hemijskom strukturom sugamadeksa pre nego sa operacijom izazvanim stresom pacijenata.

Ključne reči: reverzibilni neuromuskularni blok, sugamadeks, neostigmin, nivo glukoze u krvi.

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Original article

CALCIURIA IN CHILDREN WITH PRIMARY MONO-SYMPTOMATIC NOCTURNAL ENURESIS

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Abstract: **Introduction:** The prevalence of idiopathic hypercalciuria (IH) in healthy pediatric population ranges from 3.0% to 7.0%. There is insufficient data about IH in children with mono-symptomatic enuresis. **The aim** of this study was to examine calcium excretion in urine (UCa) in patients with primary mono-symptomatic nocturnal enuresis (PMNE). **Methods:** In patients with PMNE, aged 5 to 17 years, IH was determined in 24-h urine and from second morning spot urine. The completeness of the 24-h urine collections was estimated via measuring 24h-urine creatinine excretion (UCr) of 0.1–0.2 mmol/kg/24h. **Results:** Sixty patients with PMNE, 32 males and 28 girls, median age of 9 years were enrolled in the study. Only 41.7% patients successfully completed 24 h urine collection. IH, defined as 24-h UCa > 0.1 mmol/kg body weight, was diagnosed in 12% of the patients, while when defined as UCa/UCr > 0.8 mmol/mmol in children 5-7 years and > 0.6 mmol/mmol in those > 7 years, IH was 8.3% and 6.7% from 24h- urine and spot urine, respectively. **Conclusion:** Children and adolescents with PMNE are in risk of hypercalciuria. Therefore, it is useful to examine 24 hours of urine calcium excretion in these patients.

Key words: Idiopathic hypercalciuria; collection of 24h-urine; enuresis.

INTRODUCTION

Nocturnal enuresis or bedwetting is an involuntary voiding during sleep in children aged more than 5 years. It is a primary when children have never achieved six months of continuously dry nights, or it is a secondary which occur after at least 6 months of nighttime voiding control. Nocturnal enuresis is common in children. However, its prevalence decreases with increasing age of the child. The Avon Longitudinal Study of Parents and Children found that the prevalence of bedwetting < 2 nights per week is 30% at age of 4.5 years and 8% at 9.5 years, and the prevalence of bedwetting ≥ 2 nights per week is 8% at 4.5 years and 1.5% at 9.5 years (1). In another studies, about 10% of all 7-yr-old children, 5% of all 10-yr-olds and 0.5–1% of adults were affected more than three times bedwetting per week (2, 3).

Nocturnal enuresis is very distressing condition that can have a deep impact on the child/young person's behavior and on their emotional and social life (4, 5). It also disturbs a quality of life among the parents or guardians (6).

According to the Standardization Committee of the International Children's Continence Society (ICCS) the term mono-symptomatic nocturnal enuresis (MNE) signifies that children have enuresis only when asleep while the term non-mono-symptomatic nocturnal enuresis (NMNE) describes the symptoms of children who have urinary incontinence at night and also have day time voiding symptoms (7). An estimated 80 percent of children with nocturnal enuresis have MNE form.

The pathophysiology of primary MNE (PMNE) is complex and so far it has not yet been fully clarified. An altered circadian profile of antidiuretic hormone, arousal failure and delayed urinary bladder maturation are the best studied pathophysiological factors (8).

Kamperis et al. documented that polyuric patients with MNE refractory to desmopressin treatment excrete larger amounts of sodium and urea at night compared with healthy controls and nonpolyurics MNE patients despite a normal the circadian rhythm of sodium-regulating hormones such as atrial natriuretic peptide, angiotensin II, aldosterone, and renin levels but may be secondary to augmented urinary prostaglandin E2 (PGE2) excretion (9). Some authors found idiopathic hypercalciuria (IH) to be more common in children with PMNE than in children without nocturnal enuresis and for this reason they assume that IH could be one of the contributing pathophysiologic factor to PMNE (10, 11, 12).

Considering 24 h-variations in urine calcium excretion, the diagnosis of hypercalciuria is most accurately determined from the urine collected for 24 h. This is usually difficult to achieve in children who have nocturnal enuresis. In situations where 24h-urine collection is not possible, random urine measurements are implemented, using spot urine ratio of the calcium and creatinine and comparing it with its age-related reference values (10, 13).

The aim of this study was to examine calcium excretion in urine collected for 24 hours and from the second morning spot urine in children and adolescents with PMNE, and to estimate the frequency of hypercalciuria.

MATERIAL AND METHODS

All consecutive children and adolescents referred from September 2017 to May 2018 to Pediatric Hospital in Novi Pazar (a city located in the Raška District of southwestern Serbia), due to nocturnal enuresis, were considered to be included in this study. Inclusion criteria for the study were: 1) Patients with PMNE, age 5 to 17 years, 2) completed 24-h urine collection, 3) normal renal function and 4) normal serum electrolytes including calcium level. Exclusion criteria were as follows: (1) urinary tract infections in anamnesis, (2) signs of any acute infection before examination, (3) secondary nocturnal enuresis, and NMNE, (4) no idiopathic hypercalciuria, (5) metabolic diseases, (6) renal stone diseases, (7) impaired kidney function, (8) kidney and urinary tract anomalies, (9) and any pharmacological treatment or diet supplementation in past 6 months (calcium, Vitamin D).

The clinical work up were done in all patients consisting of collecting data to determine age, gender, present and past medical history, daytime and nighttime voiding patterns, bowel emptying habits, family history for nocturnal enuresis and renal stone diseases, and complete physical examination. Laboratory analyzes that included serum urea, creatinine, complete blood count, fasting blood sugar and electrolytes, urinary electrolytes and creatinine levels were tested in all patients. Kidney and bladder ultrasound were also done. Twenty-four hour urine samples were collected for each patient to measure calcium (UCa) and creatinine (UCr). To prevent urine loss the enuretic children were waking up at least two times during night. The completeness of the 24-h urine collections was estimated via measuring 24h-urine creatinine of 0.1–0.2 mmol/kg/24h (14). Urine calcium from 24 h urine was expressed in mmol/kg body weight (BW) and in mmol/l per kg BW. UCa and UCr were determined also in spot urine from second urine sample. Urinary tract infections were excluded on the basis of urinary testing.

PMNE was defined as involuntary nocturnal bedwetting ≥ twice a week for ≥ 3 consecutive months in children of ≥ 5 years of age who have never gained control over night time voiding, but without any low urinary tract problems during the daytime. Idiopathic hypercalciuria (IH) was diagnosed if urine calcium excretion was ≥ 0.1 mmol kg/day in the 24 h urine or urine calcium to creatinine ratio of more than 0.6 mmol/mmol in urine samples in children aged > 7 years and > 0.8 mmol/mmol in those aged 5-7 years (10). Patients were divided into two groups, the first (I) consisted of normocalciuric children with PMNE and the second one (II) included hypercalciuric children with PMNE. The demographic data, urine calcium level as well as family history for nocturnal enuresis and renal stone diseases were compared between groups. Data analysis was performed using SPSS version 21 software. Normal distribution of data was tested with the Shapiro–Wilk W test. Quantitative variables were provided as median and interquartile (IQR) range, while qualitative ones were presented as a percentage. The variables were compared using Student's *"t"* test, Mann-Whitney U-test and chi-square test, where it was appropriate. A p value < 0.05 was considered statistically significant.

Written informed consent was obtained from all the enrolled subjects, subsequent to receive full information about the study. The study was approved by the Ethics Committee of General Hospital Novi Pazar in accordance with the Declaration of Helsinki.

RESULTS

Sixty patients with PMNE, 32 males and 28 girls, median age of 9 (IQR 7.0-12.7) years were enrolled in the study. Only 25 (41.66%) patients successfully completed 24 h urine collection with median 24-h UCr of 0.16 (IQR 0.12-0.18). Hypercalciuria, defined for all ages as 24-h Ucr > 0.1 mmol/kg body weight, was diagnosed in three patients (12%). Clinical characteris-

Table 1. *Clinical sharacteristics of the patients with PMNE who successfully completed 24h-urine collections*

Parameters	All patients n = 25	*Group I n = 3	Group II n = 22	Comparisons between groups I and II
Gender, Males (%)	15 (60.0)	2 (66.7)	13(59.1)	ns
Age in years, Median (IQR)	8.00 (7.00-10.50)	8 (7.00-8.00)	8.00 (7.00-10.25)	ns
Body height (cm), Median (IQR)	125.00 (121.30-141.65)	123.60 (121.50-123.60)	125.15 (118.97-140.12)	ns
Body weight (kg), Median (IQR)	29.00 (21.70-36.00)	26.00 (22.90-26.00)	19.50 (21.37-35.50)	ns
Body mass index (kg/m^2), Median (IQR)	18.47 (15.47-19.45)	17.30 (15.57-17.30)	18.48 (15,28-19.37)	ns
UCa in 24 h urine (mmol/kg), Median (IQR)	0.06 (0.01-0.05)	0.13 (0.12-0.13)	0.01 (0.01-0.05)	p = 0.001
UCa (mmol/l)/kg BW	0.05 (004-0.08)	0.12 (0.07-0.12)	0.04 (0.04-0.06)	p = 0.027
UCr in 24 h urine (mmol/kg), Median (IQR)	0.16 (0.12-0.18)	0.17 (0.11-0,17)	0.15 (0.012-0.18)	ns
UCa/UCr in 24 h urine (mmol/mmol), Median (IQR)	0.33 (0.29-0.43)	0.59 (0.40-0.59)	0.31 (0.28-0.040)	p = 0.014
Ca/Cr spot urine (mmol/mmol), Median (IQR)	0.29 (0.17-0.38)	0.52 (0.16-0.52)	0.28 (0.17-0.35)	ns
Hipercalciuria according to UCa/UCr in 24 h urine (mmol/mmol) (%)	1 (4.0%)	1 (33.33)	0 (0)	p = 0.006
Hipercalciuria according UCa/UCr spot urine (mmol/mmol) (%)	1 (4.0%)	1 (33.33)	0 (0)	p = 0.006
Positive family history for nocturnal enuresis (%)	14 (56.0%)	2 (66.70)	12 (54.50)	ns
Positive family for nephrolithiasis (%)	1 (4%)	0 (0)	1 (4.50%)	ns

PMNE = Primary monosymptomatice nocturnal enuresis; IQR = interquartile range (25-75 percentile), * For group I IQR was presented only as 25 and 50 percentile due to small number of the patients; UCa = Calcium in urine; UCr = creatinine in urine; UCa/UCr = ratio of urinary calcium and creatinine; ns = not significant

Table 2. *Comparative analysis between patients with and without hypercalciuria based on UCa / UCr from 24h urine or spot urine*

Parameters, Median (IQR)	Group 1 Patients with increased UCr/UCa in 24 h urine, n = 5	Group 2 Patients with normal UCr/UCa in 24 h urine n = 55	Group 3 Patients with increased UCr/UCa in spot urine, n = 4	Group 4 Patients with normal UCr/UCa in spot urine n = 56	Comparisons	
					Group 1 vs Group 2	Group 3 vs Group 4
Gender, Males (%)	3 (60%)	29 (52.7 %)	1 (25)	31 (55.4)	ns	ns
Age in years,	7 (6.0-10.50)	10 (7.0-13.0)	5.75 (5.50-11.25)	9.5 (7.00-12.75)	ns	ns
Body height (cm)	117.6 (111.50-137.15)	132.6 (115.30-150.20)	107.80 (103.75-139.07)	131.60 117.60-149.95)	ns	ns
Body weight (kg)	31.0 (22.5-41.0)	33.0 (22.90-42.60)	21.35 (19.17-42.50)	33.00 (23.25-43.57)	ns	ns
Body mass index (kg/m^2)	19.4 (18.0-23.1)	18.8 (17.30-20.00)	18.40 (17.87 -21.40)	18.93 (17.35-20.00)	ns	ns
UCa in 24 h urine (mmol/kg), Median (IQR))	0.06 (0.05-0.10)	0.01 (0.01-0.03)	0.03 (0.02-0.10)	0.10 (0.001-0.045)	p = 0.003	ns
UCa (mmol/l)/kgBW	0.07 (0.06-0.10)	0.03 (0.02-0.03)	0.04 (0.02-0.10)	0.06 (0.02-0.06)	p = 0.007	ns
UCr in 24 h urine (mmol/kg)	0.09 (0.08-0.10)	0.09 (0.07-0.15)	0.06 (0.05-0.10)	0.10 (0.07-0,15)	ns	ns
UCa/Ucr in 24 h urine (mmol/mmol)	0.7 (0.66-0.94)	0.33 (0.25-0.40)	0.53 (0.04-0.99)	0.33 (0.25-0.41)	p = 0.000	p = 0.012
UCa/UCr in spot urine (mmol/mmol) Median (IQR)	0.54 (0.24-0.65)	0.29 (0.18-0.41)	0.69 (0.62-0.94)	0.29 (0.17-0.39)	ns	0.000
UCa in 24 h urine > 0.1 mmol/kg/24 h	1 (20)	3 (5.45)	2 (50)	3 (5.36)	p = 0.027	ns
UCa/UCr in spot urine > 0.6 (mmol/mmol)	2 (40.0)	2 (3.64)	4 (100)	0 (0)	ns	p = 0.000
Positive family history for nocturnal enuresis (%)	2 (40.0)	24 (43.6)	3 (75)	23 (41.1)	ns	ns
Positive family for nephrolithiasis (%)	0 (0)	7 (12.7)	1 (25)	6 (10.7)	ns	ns

IQR = interquartile range (25-75 percentile); UCa = Calcium in urine; UCr = creatinine in urine; UCa/UCr = ratio of urinary calcium and creatinine; ns = not significant

tics of the patients with (group I) and without (group II) hypercalciuria are presented in Table 1. There were no statistically significant differences between these groups neither in age, gender, body height (BH), body weight (BW), body mass index (BMI), nor in family history for NE and renal stone diseases. As expected the patients with IH had significantly higher UCa and UCa/UCr in 24h- urine. In addition, the median 24 h urine calcium (mmol/l)/body weight (kg) ratio was also higher in the group I than in the group II.

Urine calcium/creatinine ratio in spot urine was higher in group I than in group II, but the difference did not reach statistical significance. Only one patient, who belongs to group I had increased ratio of urinary Ca and creatinine from 24h-urine as well as from spot urine.

Hypercalciuria may be diagnosed also according to UCa/UCr ratio when it is > 0.8 mmol/mmol in children aged 5-7 years and > 0.6 mmol/mmol in those aged > 7 years. Using these criteria for 24h- urine and for spot urine hypercalciuria was found in 8.33% and 6.67% of all patients with PMNE, respectively (See Table 2). In addition, the median 24 h urine calcium expressed in mmol/l and body weight ratio was higher in the group with hypercalciuria (group 1) than in the group with normal calciuria (group 2).

A positive family history of nocturnal enuresis was found in 40 to 60.7% of patients, depending on how they were classified. In contrast, a positive history of nephrolithiasis was found in a significantly smaller number (0% to 12%) of patients.

DISCUSSION

Idiopathic hypercalciuria (IH) is defined by hypercalciuria, normocalcemia, and the absence of diseases known to cause increased urine calcium excretion (15). Pathogenesis of IH is very complex and many potential factors can be involved, such as polymorphisms of the gene coding for proteins regulating tubular phosphate and calcium reabsorption and those responsible for proteins preventing calcium salt precipitation or gene coding for a water channel in the proximal tubule (16). Furthermore, in families with an autosomal dominant mode of IH, inheritance connection between IH and loci on chromosome 1q23.3-q24, which contains the human soluble adenylyl cyclase gene, chromosome 12q12-q14, which contains the VDR gene and chromosome 9q33.2-q34.2, were established (17). Environmental factors may also significantly affect renal stone formation. Nutrient intake may change urine composition, but may also influence gene expression by epigenetic mechanisms.

The idea that IH may be an important pathogenic factor of nocturnal enuresis was first proposed by Pace et al. (18) who noted that a proportion of enuretic children had absorptive hypercalciuria. Since that time some strategies were made to measure urinary calcium excretion in the evaluation of nocturnal enuresis (19, 20). It has come so far that the therapeutic response of desmopressin link to the reduction of hypercalciuria as has been demonstrated in some Italian studies (21, 22). However, there are opposing opinions about the possible relationship between hypercalciuria and enuresis. Neveus et al. in their study concluded that the urinary calcium excretion does not differ between enuretic and dry children (23). Kamperis et al. in another study observed no significant difference among calcium excretion of children with or without nocturnal enuresis (24). Different data on the frequency of IH in children with nocturnal enuresis can be explained by heterogeneity in its etiopatogenesis as well as by differences in the methodology of testing or measurement of calcium in the urine.

It is well known that hypercalciuria can be presented with different symptoms associated with urinary symptoms (25, 26). Recently, Esteghamati et al found the prevalence of idiopathic hypercalciuria is 48.3% in children with urinary tract infection, 54.9% and 53.6% in children with microscopic and macroscopic hematuria respectively, 52.1% and 51.8% in children with dysuria and in children with frequency respectively, 49.1% in children with kidney stone, and 28.6% and 37.5% in children with nocturnal and daily urinary incontinency respectively (27). There is insufficient data about IH in monosymptomatic enuresis.

In the present study we found hypercalciuria in 12% of the patients with PMNE when calcium in urine was determined in properly collected 24 h urine, but only in 8% and in 6.7% of the patients when it was estimated on the basis of calcium and creatinine ratio in 24 h and spot urine, respectively. The prevalence of IH in the healthy pediatric population is considerable, and the authors have reported rates between 3.0% and 7.0% among children (26, 28). Our data confirmed the greater sensitivity of calciuria from 24 h urine compared to spot urine calciuria. Although the determination of calciuria is much more reliable at 24 h urine, proper urine collection for 24 h is very difficult to perform in children with bedwetting. Only 41.7% of our patients managed to properly collect the urine for 24 h. Like other authors (29) we found a strong family history of bedwetting in children and adolescents with PMNE.

Our study has some limitations. One of the limitations in this study was the difficulty of 24-hour urine collection, and, therefore a relatively small number of patients with PMNE who succeed urine collection. Another limitation of the study is the lack of a control group. We suggest that IH in children with PMNE should be examined from 24 h urine in a larger group of children.

CONCLUSION

Children and adolescents with primary monosymptomatic nocturnal enuresis are in risk of hypercalciuria. It is therefore useful to examine 24 hours of urine calcium excretion in these patients.

Abbreviations

PMNE — Primary monosymptomatic nocturnal enuresis

IQR — interquartile range (25-75 percentile)

* For group I IQR was presented only as 25 and 50 percentile due to small number of the patients

UCa — Calcium in urine

UCr — creatinine in urine

UCa/UCr — ratio of urinary calcium and creatinine

ns — not significant

DECLARATION OF INTEREST

The authors declare that there are no conflicts of interests.

Licensing

Sažetak

KALCIURIJA KOD DECE SA PRIMARNOM MONOSIMPTOMATSKOM NOĆNOM ENUREZOM

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Uvod/Cilj: Prevalencija idiopatske hiperkalciurije (IH) se u zdravoj pedijatrijskoj populaciji kreće od 3.0% do 7.0%. Nema dovoljno podataka o IH u dece sa monosimptomatskom enurezom. Cilj studije je bio da ispita izlučivanje kalcijuma u urinu (UCa) kod dece sa primarnom monosimptomatskom noćnom enurezom (PMNE). **Materijal i metode:** IH je ispitana kod dece sa PMNE, uzrasta 5 do 17 godina, iz urina skupljenog za 24 časa (h) i iz drugog jutarnjeg uzorka urina. Kompletnost skupljanja 24 h urina je procenjena na osnovu izlučivanja kreatinina u urinu (UCr) od 0.1 do 0.2 mmol/kg/24h. **Rezultati:** Šezdeset pacijenata sa PMNE, 32 dečaka i 28 devojčica prosečnog uzrasta 9 godina je ispitano u studiji. Samo 41.7% bolesnika uspešno je skupilo 24 h urin. IH, definisana kao UCa > 0.1 mmol/kg telesne težine/ 24-h, dijagnostikovana je kod 12% pacijenata, dok IH definisana kao UCa/UCr > 0.8 mmol/mmol kod dece 5-7 godina i > 0.6 mmol/mmol kod onih > 7 godina, IH je bila 8.3% i 6.7% izmerena u 24h- urinu i jutarnjem uzorku urina. **Zaključak:** Deca i adolescenti sa PMNE su u riziku za hiperkalciuriju. Stoga je korisno kod njih ispitati izlučivanje kalcijuma u urinu.

Ključne reči: Idiopatska hiperkalciurija, skupljanje 24 časovnog urina, umokravanje.

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Original article

RARE MALIGNANT SKIN TUMOURS OF THE HEAD AND NECK

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Abstract: **Introduction:** Malignant skin tumors in the majority of cases arise from the squamous epithelium, although they may occur in other accompanying skin structures, such as skin adnexa (hair follicle, sweat and sebaceous glands), as well as soft tissues participating in the building of skin structure, such as muscles, fibrous, fatty tissue and cartilagå. Those tumors may also have a neuroendocrine origin or may arise from a premalignant lesion (solar keratosis and lentigo maligna). Regardless of their origin, they usually present as a nodule or longstanding, non-healing ulceration. Their early recognition enhances the treatment results and decreases the possibility of complications (invasion of deeper tissue structures and occurrence of regional and distant metastases).

Material and methods: Our retrospective study included 100 patients of both sexes surgically treated for skin malignancy in the Department for Otorhinolaryngology and Maxillofacial surgery of the Clinical Hospital Centre "Zemun" , Belgrade, Serbia.

The goal of this paper is to highlight the frequency of rare malignant tumors compared to the more frequent ones and consider the most appropriate clinical-diagnostic approach as well as the treatment modality for the patient.

Conclusion: Our study has shown that the most frequent tumor of the head and neck skin is basal cell carcinoma.

Key words: rare malignant skin tumor, skin tumor frequency, metastases, surgery, therapy.

INTRODUCTION

Malignant skin tumors are the most frequent tumors in humans, with the constant tendency of increase in number. Their incidence is higher than other groups of tumors altogether, such as lung, breast, large bowel and prostate malignancy (1). It is estimated that more than 80% of all skin tumors is the result of excessive skin exposure to ultraviolet (UV) effect of sunlight which contribute to oncogenesis, DNA impairment, usually with in individuals with fair tan as well as the people with professional sunlight exposure, such as farmers, construction workers, fishermen, etc., although some other factors may contribute significantly to occurrence of this tumor (ionization, chemical agents, immunodeficiency, genetic factors) (2).

It was noticed that in individuals with acquired immunodeficiency, those at immunosuppressive therapy as well as patients with lymphoma, the incidence of skin cancer, especially melanoma, is increased (3). Malignant tumor classification is nowadays a generally accepted principle and it is based on histogenesis, i.e. type of tissue that it is developed from (4, 5, 6).

The most frequent malignant tumors are basal cell carcinomas, squamous cell carcinoma (which are frequently called non-melanoma skin tumors), melanomas, somewhat less frequent neuroendocrine tumor Merkel cell carcinoma as well as apocrine tumors of sweat and sebaceous glands, which occur considerably less frequently (7).

However, basal cell carcinoma (BCC) is a malignant epithelial neoplasm that originates from the pluripotential cells in the epidermis and hair follicles and it represents 50 –75% (according to some authors, even more than 80%) of all skin tumors (Figure 1) (8). It is the most common skin cancer seen in human population (9). It is often slow growing and may take years to enlarge signiWcantly (10), but it can cause extensive local tissue destruction and death if inadequately treated or left untreated (Figure 1). The mortality rates associated with this cancer are low. However, it causes considerable functional and cosmetic deformity and

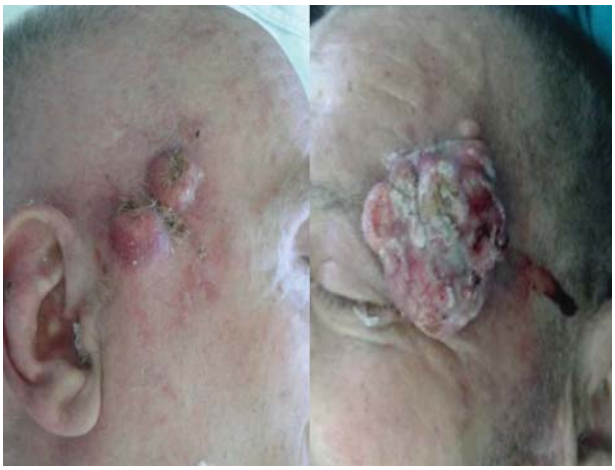

Figure 1. *Nodular basocellular carcinoma localized on the right side of forehead and on the right supraorbital region*

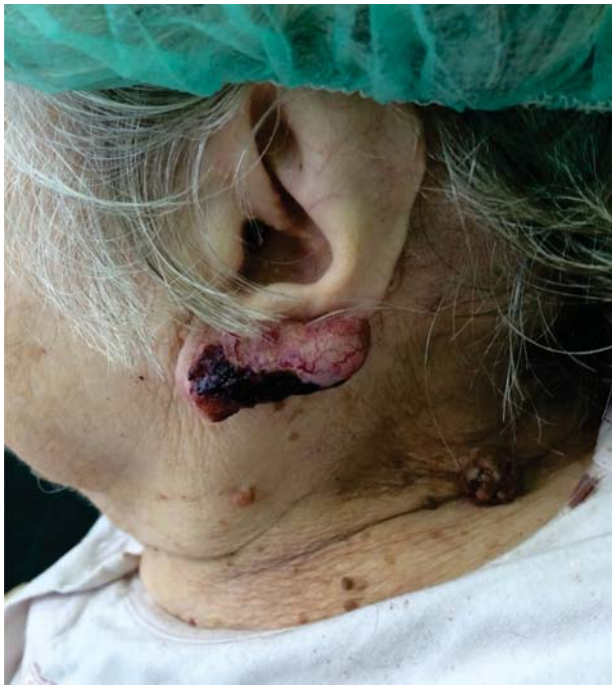

Figure 2. *Squamous cellcarcinoma of earlobe*

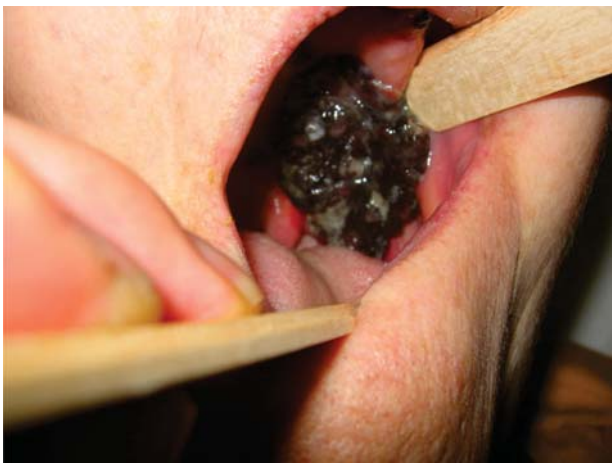

Figure 3. *Melanoma of oral cavity*

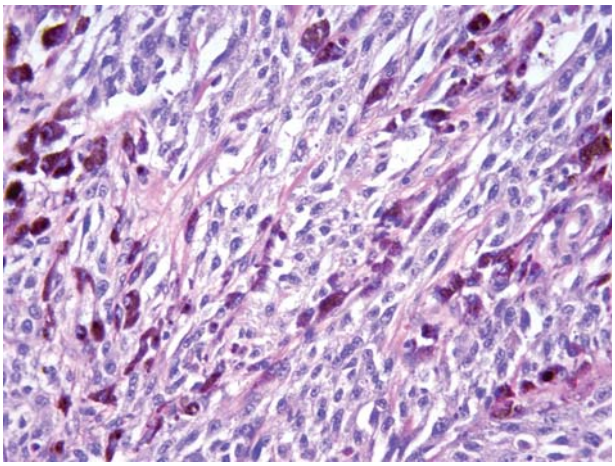

Figure 4. *Histopathological features of melanoma (H&E, x200)*

cost of treatment is signiWcant. In aggressive forms such as *Ulcusrodens* or *Ulcus terebrans*, there is severe mutilation and extensive destruction of adjacent soft tissues and underlying bone (11).

Squamous cell carcinoma (SCC) is an invasive epidermal tumor occurring on skin and on mucous membrane. It is composed of a modified spinous layer of epidermis which infiltrates the surrounding structures. In more than 90% cases, it develops at sun-exposed skin, at first like unobtrusive node or lightly infiltrated lesion, with rapid growth and signs of infiltration into the surrounding tissue. Regardless of its appearance SCC is prone to metastases, considering the fact that SCC at actinic keratosis metastasize more slowly and in a smaller percent than SCC at the scars (2, 12). More than 70% of these tumors occur in the auricle and in the lower third of the face (12).

Melanoma usually arises from melanocytes at the dermoepidermal junction. Beside the skin type and exposure to sunlight, preexisting dysplastic nevus, family history and immunologic dysfunction increase the risk of melanoma (13). Almost half of all melanoma arise from normal skin, and the remaining ones come from pre-existing nevus. Change of size or appearance of the existing nevus, itchiness, ulceration and bleeding require urgent examination and excision sample biopsy (Figure 2). Melanomas are typically present as irregular pigmented lesions with macular or papular appearance, usually pigmented, but can also be amelanotic (14, 15) (Figure 3, 4).

MATERIAL AND METHODS

Our retrospective study included 100 patients of both sexes surgically treated for skin malignancy in the Department for Otorhinolaryngology and Maxillofacial surgery of the Clinical Hospital Centre “Zemun” from May 2015 to May 2017. Before hospitalization,

all patients had a presumptive diagnosis of skin malignancy based on clinical examination performed by an experienced maxillofacial surgeon, otolaryngologist or dermatologist. Criteria for participation in the study were: age of 18 or older and postoperatively histopathological verified malignant lesion of head, face, and jaw and neck skin. The patients who did not respond to follow up were excluded from the study.

All patients gave a written consent for surgery as the most optimal treatment modality. Based on clinical finding and local tumor extent, complete tumor removal using wide surgical excision was performed in all patients. The resulting defects were closed by means of direct suture, local flaps or free skin grafts, depending on the tumor size and extent of resection. All of the pathology specimens were examined and reported by the Department of Pathology at our center. Patients were regularly checked by attending surgeon on a monthly basis during at least 12 months. Patients with verified lymphomas were treated by the hematologists.

Diagnostics

Although histopathological analysis of the removed lesion is a golden standard for setting the diagnosis of each lesion individually, nowadays dermatoscopy as the auxiliary diagnostic method is used -it is a non-invasive technique, simple to perform and significantly improves the precision during differentiation of various pigmented skin lesions (16).

Generally, it is considered that the risk for malignant alteration with melanocytic nevus is very low, compared to atypical and gigantic congenital nevus, which are recommended to be monitored regularly. Preventive surgical removal for large congenital lesions and avoidance of exposure to UV radiation (photo protection) are the most significant preventive ways to lower the risk factors for melanoma occurrence (17).

RESULTS

In the period from May 2015 until May 2017, 100 patients with head and neck skin malignancy were analyzed. The study included 64 men and 36 women. The average age of the patients was 60 years (59.80), and average age by category was 61.57 years (men) and 52.96 (women). The youngest patient was 20 years old, and the oldest patient was 92 years old. No patient had intraoperative and postoperative complications (allergy to anesthetic, heavy bleeding, wound infection, cardiological intraoperative complications). Malignant tumours had the following distribution: 80 basal cell

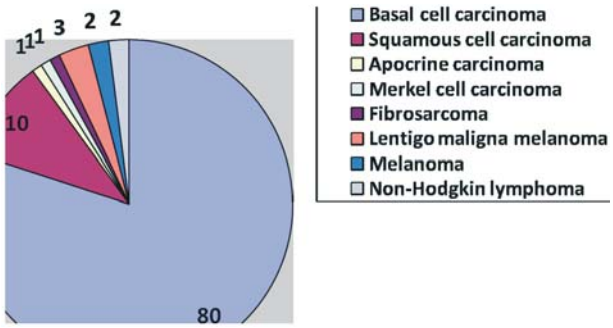

Figure 5. *Distribution of patients by pathology finding expressed in percentage*

Table 1. *Distribution of patients surgically treated for skin malignancy at Department of Otorhinolaryngology with Maxillofacial Surgery of CHC "Zemun" from May 2015 to May 2017*

	Total cases by PH type	Gender		Primary location									
		M	F	Scalp	Forehead	Temple	Eyelid	Cheek	Nose	Lips	Chin	Neck	Ear
Basal cell carcinoma	80	50	30	5	7	10	6	16	12	6	4	9	5
Squamous cell carcinoma	10	6	4	1	/	2	1	1	1	3	/	/	1
Apocrine carcinoma	1	1	/	/	/	/	/	/	/	/	/	1	/
Merkel cell carcinoma	1	1	/	/	/	/	/	/	/	/	/	1	/
Fibrosarcoma	1	1	/	/	/	/	/	/	1	/	/	/	/
Lentigo maligna melanoma	3	2	1	1	/	/	/	2	/	/	/	/	/
Melanoma	2	1	1	/	/	/	/	/	/	/	/	2	/
Non-Hodgkin lymphoma	2	2	/	/	/	1	/	/	/	/	/	1	/

carcinomas, 10 squamous cell carcinomas, 3 lentigo maligna melanomas, 2 melanomas, 2 non-Hodgkin lymphomas, 1 apocrine carcinoma, 1 Merkel cell carcinoma and 1 fibrosarcoma each (Figure 5, Table 1).

DISCUSSION

The majority of all malignant tumor of face, neck, jaw belonged to BCCs and occur mostly in men. It is accordance with previous data that BCC is the most common tumor in this part (18) (Figure 1). The higher incidence in men is probably due to increased recreational and occupational exposure to the sun. However, the incidence in women is increasing because of changing fashions in lifestyle. The likelihood of developing BCC increases with age, and it is rarely found in patients younger than 40 years (18). The mean age of our patients is 65.6. In our study, there are no significant difference between sex in BCC; even men had 1,7 times more incidence of BCC. The exact cause of BCC is unknown. Several factors are believed to predispose the patient to basal cell carcinoma. Exposure to sunlight is the most frequent association. Cumulative exposure to sunlight over years is necessary for tumor development (17, 18). There are three types of UV radiation: UV-A (320–400 nm), UV-B (290–320 nm), and UV-C (200–280 nm). UV-B rays are the most carcinogenic, triggering skin cancer via photochemical damage to DNA, injury to DNA repair mechanisms, and partial suppression of cell-mediated immunity (15, 16, 17). Patients often have a history of chronic sun exposure. Excisional biopsy is the biopsy type that we usually prefer. We advise excisional biopsy for small lesions that enable primary closure afterwards that does not cause distortion of the environmental tissues. Otherwise, an incisional biopsy may be done before the definitive treatment. Once the pathologic diagnosis of BCC is confirmed, the next step is to plan for tumor eradication by correlating tumor characteristics with patient's age, skin history, medical history, social history, and cosmetic expectations. Treatment options include standard surgical excision, Mohs micrographic surgery, nonsurgical ablation, and topical chemotherapy. Surgical excision is the preferred method in our center. We generally perform excision under local anesthesia or in the outpatient surgery settings.

In our study, the second frequent tumor was squamous cell carcinoma. More than 70% of SCC occur in the ear lobe area (Figure 2) and in the lower third of the face (15, 18). Our study partially confirmed that finding, but is should take into account that we found only 10 SCC for two years of follow up (small sample).

The other malignant tumor of the head and neck were sporadic, and we could call them rare tumors (Figures 6, 7, 8). We came to the very interesting finding

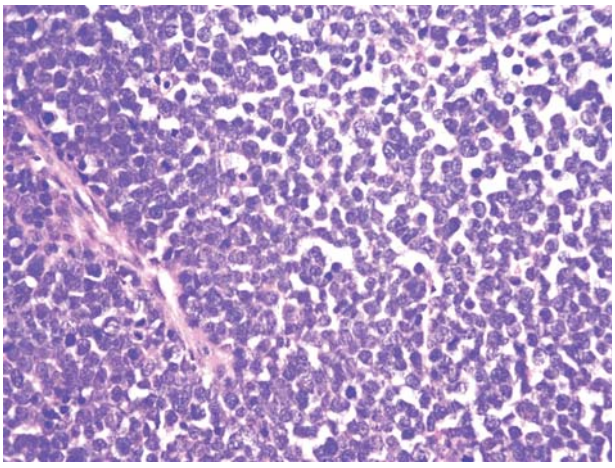

Figure 6. *Histopathological features of Merkel cell carcinoma (H&E, x200)*

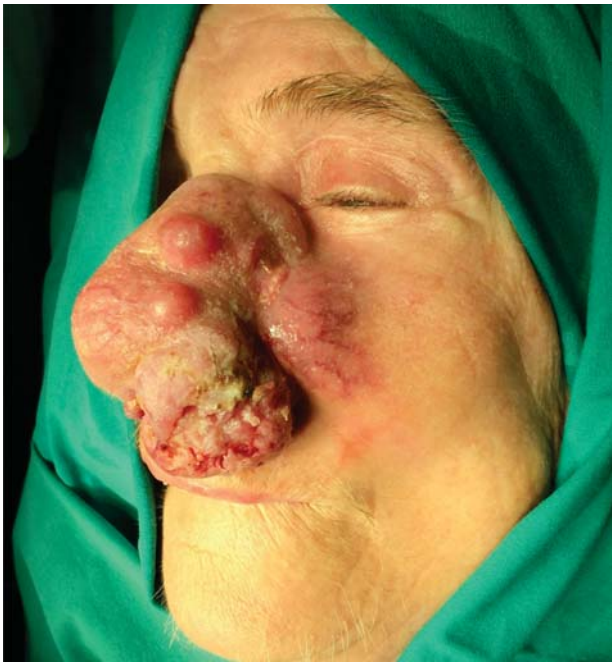

Figure 7. *Dermatofibrosarcoma localized in the nasal region of an elderly patient*

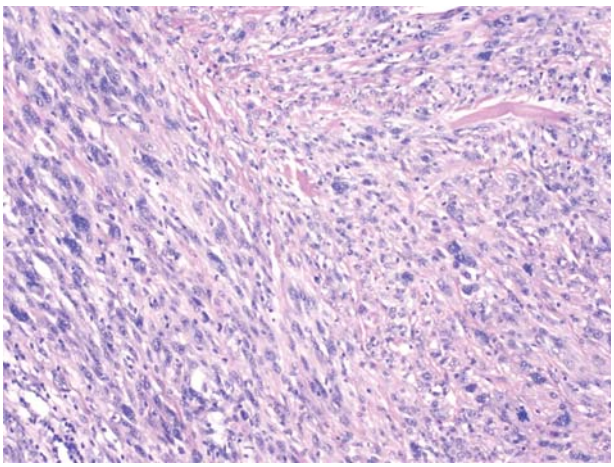

Figure 8. *Histopathological pattern of leiomyosarcoma (H&E, x100)*

of only two melanomas for 2 years of following. Rare tumors were one up to three in the observed period. Three lentigo maligna melanoma and two non-Hodgkin lymphomas were observed, while Merkel cell carcinoma, apocrine carcinoma and fibrosarcoma were found only in one patient each.

CONCLUSION

Our study has shown that the most frequent tumor of the head and neck skin is basal cell carcinoma, while the second one was squamous cell carcinoma. All the patients were surgically treated and are still alive, with no signs of recurrence and are regularly seen by attending physician. Although there is relatively low attributable mortality, the morbidity and cost of treatment are significant. A large body of information serves as a foundation for oncologic principles, diagnosis methods, surgical excisions, follow-up protocols, and reconstructive methodologies that are currently in use.

Abbreviations

BCC — basal cell carcinoma
SCC — squamous cell carcinoma
UV — ultraviolet

DECLARATION OF INTEREST

The autors declare that there are no conflicts of interests.

Licensing

Sažetak

RETKI MALIGNI TUMORI KOŽE GLAVE I VRATA

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Uvod: Maligni tumori kože u većini slučajeva potiču od skvamoznog epitela, mada se mogu javiti u drugim strukturama pridruženim koži, poput adneksa (folikuli dlake, znojne i lojne žlezde), kao i drugih tkiva koja učestvuju u izgradnji kože, poput mišićnog, fiboznog i masnog tkiva i hrskavice. Ovi tumori mogu imati i neuroendokrino poreklo, a mogu poticati i od premalignih dermatoza (solarna keratoza, lentigo maligna). Bez obzira na poreklo, uglavnom se javljaju u vidu nodulusa ili dugotrajnih ulceracija koje ne zarastaju. Njihovo rano prepoznavanje svakako poboljšava rezultate lečenja i smanjuje mogućnost komlikacija (infiltracija dubljih struktura, regionalne i udaljene metastaze).

Materijal i metode: Naša retrospektivna studija je uključila 100 pacijenata oba pola hirurški lečenih od kutanih maligniteta u Službi za otorinolaringologiju sa maksilofacijalnom hirurgijom Kliničko-bolničkog centra „Zemun“ u Beogradu, Srbija.

Cilj ovog rada je da prikaže učestalost retkih maligniteta kože u poređenju sa nešto češćima, kao i da razmotri za pacijenta najoptimalniji kliničko-dijagnostički i terapijski pristup.

Zaključak: Naša studija je pokazala da je najčešći tumor kože glave i vrata bazocelularni karcinom.

Ključne reči: retki maligni tumori kože, učestalost tumora kože, metastaze, hirurgija, terapija.

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EVALUATION OF A PROGRAM OF PHYSICAL ACTIVITIES ADAPTED TO THE MORPHOLOGICAL, PHYSIOLOGICAL AND BODY COMPOSITION PARAMETERS OF OVERWEIGHT AND OBESE ADOLESCENTS OF THE LUKUNGA SPORTS CLUB OF KINSHASA, DEMOCRATIC REPUBLIC OF CONGO

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Abstract: **Objective.** To study the effects of regular physical activity on the morphological, physiological and body composition parameters of overweight and obese adolescents.

Methods. We conducted an experimental study with30 adolescents divided in two according to their body mass index. The group 1 was composed of overweight subjects with a body mass index between 25-29.9 kg/m^2, and group 2 obese subjects with a body mass index ≥ 30 kg/m^2 subjected to a program of adapted physical activity associated with a low-calorie nutrition education low in cholesterol and in saturated fatty acids (bad fats), low-fat rich in vegetables, fruits and vitamins for a period of six months.

Results. This study reveals that after six months of intervention, overweight subjects significantly decreased waist circumference (82.9 ± 4.2 cm before versus 77.6 ± 4.6 cm after), heart rate (86.8 ± 3.6 beat/min before versus 81.4 ± 3.8 beat/min after), total fat (32.2 ± 1.8% before versus 27.2 ± 1.5% after), visceral fat (16.6 ± 2.3% before versus 11.1 ± 2.5% after), and decreased muscle (15.6 ± 2.7% before versus 19.4 ± 4.1% after), while obese subjects significantly decreased waist circumference (88.9 ± 6.2 cm before versus 85.8 ± 5.9 cm after), visceral fat (17.4 ± 3.2% before versus 14.1 ± 3.1% after), respiratory capacity (61.1 ± 2.7% before versus 65 ± 2.1%). In addition this study reveals that overweight subjects compared to obese subjects more changed their waist circumference (77.6 ± 4.6 cm for overweight versus 85.8 ± 5.9 cm for obese), body mass index (24.9 ± 4.1 kg/m^2 for overweight versus 28.8 ± 1.2 kg/m^2 for obese), heart rate (81.4 ± 3.8 beat/min for overweight versus 28.8 ± 1.2 beat/min for obese), visceral fat (11.1 ± 2.5% for overweight versus 14.1 ± 3.1% for obese), and muscle (19.4 ± 4.1% for overweight versus 17.1 ± 2.1%).

Conclusion. Obese adolescents have by means of regular activity significantly changed their morphological, physiological and body composition parameters of overweight and obese.

Key words: Adolescent, body composition, morphology, physiology, overweight, obesity.

INTRODUCTION

Overweight and obesity are now ranked fifth among global mortality risks. In addition, 44% of the burden of diabetes, 23% of the burden of ischemic heart disease and between 7% and 41% of the burden of some cancers can be attributed to them (1). Obesity has negative health consequences in childhood as well as in the long term.

In addition to a higher risk of obesity and noncommunicable diseases at a later age, children with other adverse effects such as breathing difficulties, increased risk of fractures, hypertension, early markers cardiovascular diseases, insulin resistance and psychological effects (2).

In 2005, noncommunicable diseases were estimated to cause nearly 35 million deaths worldwide, 80% of them in low- and middle-income countries (3).

The progression of childhood obesity over the last decade is catastrophic. Current estimates suggest that the rate of obesity in developed countries is twice that of developing countries, in absolute numbers the prevalence is much higher in developing countries. The number of overweight / obese children in these countries is estimated at 35 million, compared to 8 million in developed countries (4).

In Africa, the number of overweight or obese children has almost doubled since 1990, from 5.4 million to 10.3 million (5).

In the Democratic Republic of Congo (DRC), its prevalence has doubled since 1980, it was estimated at 5.7% by a survey of the Ministry of Health conducted in Kinshasa in 2006. This survey focused on risk factors for noncommunicable diseases in Kinshasa, the World Health Organization (WHO) Ministry of Public Health (6, 7).

To prevent and minimize the complications of overweight and obesity in children and adolescents, the World Health Organization has developed strategies for management including physical activities and a diet.

The practice of physical activities in the Democratic Republic of Congo, tends to be neglected in our schools for pedagogical reasons including the lack of qualified teachers, lack of appropriate program and rigor in the application of the program in basic education, the lack of appropriate infrastructure or their assignment to other more lucrative activities for the school (party room, classroom or lack of awareness of the contribution of sport physical activity (SPA) in the prevention or treatment of obesity).

We have found that few studies conducted in our community (8) have evaluated the effects of physical activity only on psychological parameters.

However, none of these studies evaluated the effects of physicalactivity in adolescent subjects on the morphological, physiological and body composition parameters of obese adolescents. Therefore, with this study we aimed to fill this gap.

MATERIAL AND METHODS

Nature and period of study

We opted for the experimental method and conducted a longitudinal study that consisted in following the evolution of the morphological, physiological (cardiorespiratory) parameters and body composition of overweight and obese adolescents during the period from August 20, 2017 to January 20, 2018.

Framework of the study

The present study took place at the Lukunga Sports Club, CPA district in the city of Mbudi, city Kinshasa province, Democratic Republic of Congo served as a framework for the present study.

Sample of the study

Our target population was all overweight and obese teenagers practicing physical activities at the Lukunga sports club in Kinshasa.

Our study sample consisted of 19 overweight and 11 obese subjects. **Inclusion criteria:** to have freely accepted to participate in our study, being present on the day of the evaluation, tohave 12-17 of age, to be regular in practicing physical activities at the Lukunga sports club, not to have pathologies that are contraindicated for physical activity, and BMI ≥ 25 kg/m^2. **Exclusion criteria:** any overweight or obese teenager who has not met the inclusion criteria above.

Variables of the study

The variables used were the following:

• morphological

- Height (cm): It was assessed using a SECA branded toothy, the teenager in underwear, was measured standing, heel joints, head placed so that the line of vision is perpendicular to the body.

- Weight (kg): It was measured using a weight scale of SECA brand calibrated in kilograms (kg) to 100 g near, the teenager was standing on the scale, head up, look towards the horizon with an undergarment.

The body mass index (BMI) of adolescents was calculated according to the formula: BMI: mass (kg) / Height (m). According to the World Health Organization (WHO) and the international Obesity Task Force (13,14), overweight has been defined for BMI values between 25-29.9 kg/m^2, obesity when it was ≥ 30 kg/m^2.

- Waist circumference (WC) (cm): it was measured using a metric tape.

• Physiological

- Heart rate (HR) (bpm): it was taken using a stethoscope and stopwatch.

- Respiratory frequency (RF) (Cycle / min): it was taken using a stopwatch.

- Forced expiratory volume (FEV)per second (%): It was evaluated using a Piko-6 brand spirometer

• Body composition (%)

The body composition was evaluated using an Omeron BF-511 scale impedance meter, it allowed us to evaluate the percentage of total fat (TF), percentage of visceral fat (VF) and percentage of muscle.

Content of the program

The content of our program was based on aerobic endurance exercises, stretching, coordination, gymnastic balance, and muscle building. This program of intervention in Physical Activities was practiced two ses-

sions per week of 45 minutes at a moderate to severe intensity. To avoid monotony these different exercises were practiced with several variants. Nutritional education was composed of foods, hypocaloric low in cholesterol and saturated fatty acids (bad fats), low sodium rich in vegetables, fruits and vitamins.

Statistical analysis

The data collected was entered using the Microsoft Excel 2013 software and imported into SPSS software version 21.0 (Statiscal Package For Social Sciences). Quantitative variables were presented as mean ± standard deviation and their extremes in the tables.

To verify the effects of exercise on nutritional status, we used we used the analysis of variance (ANOVA) to compare more than two means.The statistical test results used were interpreted at the significance level $p \geq 0.05$ for statistical decision making.

Ethical consideration

All the parents of the children had consented in writing for the participation of their children in the study according to the declarations of Helsinki. The information collected from the children was kept confidential.

RESULTS

The results reported in Table 1 show a significant decrease in waist circumference, heart rate, visceral fat and an increase in muscle mass of overweight or obese subjects after the intervention program. However, these decreases or increases were much more observed in overweight subjects.

DISCUSSION

The aim of this study was to study the effects of aerobic-type regular physical activity and muscle building on the morphological, physiological and body composition of obese adolescents. It appears from this study that before the intervention program, no significant difference was observed between overweight and obese adolescents.

With regard to overweight adolescents taken in an isolated manner, this reveals that the latter have the mean weight, respiratory rate and forced expiratory volume per secondhave not been significantly modified, decreased their waist circumference by -5.3 cm. body mass of -3.2 kg/m^2, heart rate of -5.4 bpm, total fat of -5%, visceral fat -5.5% but their muscle increased statistically significantly by +3 8. That regular physical activity allows obese patients to significantly improve their morphological, physiological and body composition (9, 10, 11). On the other hand, they are superior to those revealed by Bellow et al (10). In his analysis of 46 studies, where the average duration of exercise was 16.3 weeks demonstrated that the practice of physical exercises allows to modify the morphological state of the obese subjects. This is justified by the fact that our duration of study was superior to them.

Our results corroborate that of the literature, which emphasizes that moderate to high exercise for at least 8 weeks in overweight or obese subjects is effective in reducing abdominal fat. Numerous studies have confirmed the existence of an inverse relationship between the level of physical activity and waist circumference, the waist circumference / hip circumference, and the measurement of intra-abdominal adiposity by different techniques. medical imaging (12). These favorable effects and body modifications can occur even in the absence of significant weight loss (12, 13). Indeed, for the same body mass index (BMI), individuals with good physical fitness (fitness) have less subcutaneous abdominal fat and visceral fat than subjects with a low level of fitness (12, 14).

Training reduces resting heart rate (with no increase in maximum heart rate), increases myocardial mass (mainly left ventricle) and stroke volume, decreases cardiac muscle oxygen consumption, and improves ex-

Table 1. Comparison of the morphological, physiological and body composition means of the participants before and after the intervention program

Parameters	Before		After		
	Overweight	Obese	Overweight	Obese	ANOVA
	X ± SD	X ± SD	X ± SD	X ± SD	p value
Weight (kg)	66.6 ± 2.2	66.8 ± 2.3	61.4 ± 2.06	62.7 ± 1.5	0.821
WC (cm)	82.9 ± 4.2*	88.9 ± 6.2*	77.6 ± 4.6*	85.8 ± 5.9*	0.000
BMI (kg/m^2)	28.1 ± 1.2	31.8 ± 1.5	24.9 ± 4.1	28.8 ± 1.2	0.437
HR (beat/min)	86.8 ± 3.6*	89.4 ± 5.1*	81.4 ± 3.8*	85.5 ± 5.6*	0.002
FR (cycle/mn)	21.5 ± 3	21.7 ± 2.4	20 ± 3.5	18.9 ± 2.7	0.063
FEV (%)	61.5 ± 2.8*	61.1 ± 2.7*	64.9 ± 3.1*	65 ± 2.1*	0.000
TF (%)	32.2 ± 1.8	33.2 ± 2.7	27.2 ± 1.5	29.3 ± 2.7	0.079
VF (%)	16.6 ± 2.3*	17.4 ± 3.2*	11.1 ± 2.5*	14.1 ± 3.1*	0.000
Muscle (%)	15.6 ± 2.7*	15.6 ± 3.3*	19.4 ± 4.1*	17.1 ± 2.1*	0.005

WC: waist circumference ; **BMI**: body mass index; **HR**: heart rate; **FR**: frequency respiratory; **FEV**: forced expiratory volume; **TF**: total fat; **VF**: visceral fat; * : $p < 0,05$: significant

traction of oxygen at the muscular level. The muscular architecture is modified with the possibility of significant increase in slow-twitch fibers during a specific endurance training (12, 13).

With respect to obese subjects, we noted that after the intervention program, they significantly modified their waist circumference, respiratory rate, forced expiratory volume per second, visceral fat, while no statistical difference was found for weight, body mass index, heart rate, total fat and muscle.

This study reveals overweight subjects have significantly improved after the program, their waist circumference, body mass index, heart rate, visceral fat, muscle versus obese subjects.

Our results are in line with the literature, which reports that physical activity limits the loss of muscle mass conventionally observed during energy restrictions. Thus, regular physical activity also helps to sustain weight loss achieved during dietary restriction, maintaining muscle mass and increasing daily energy expenditure (15, 16). Our results are superior to the latter because we have associated the practice of physical exercises with nutrition education.

Regular physical activity may help to reduce the pro-inflammatory status frequently encountered in the presence of obesity, especially abdominal, and contribute to accelerate atherosclerosis (17, 18). These findings corroborate our as have also shown a significant reduction in abdominal fat.

CONCLUSION

The results obtained demonstrate that the regular practice of aerobic endurance and muscle building exercises improve body composition in the direction of decrease in fat mass and increase in muscle mass, morphological parameters by a decrease in weight and physiological parameters by decreasing the resting heart and respiratory rate, and an improvement in respiratory capacity. However, these improvements were more noticeable in these overweight subjects than in the obese subjects.

DECLARATION OF INTEREST

The autors declare that there are no conflicts of interests.

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Sažetak

PROCENA PROGRAMA FIZIČKE AKTIVNOSTI ADAPTIRANE PREMA MORFOLOŠKIM, FIZIOLOŠKIM KAO I PARAMETRIMA SASTAVA TELA KOD ADOLESCENATA SA POVEĆANOM TELESNOM MASOM I GOJAZNIH ADOLESCENATA, SPORTSKOG KLUBA „LUKUNG“ KINŠASA, U DEMOKRATSKOJ REPUBLICI KONGO

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Cilj rada bio je da se ispitaju efekti redovne fizičke aktivnosti na morfološke, fiziološke parametre, kao i na telesnu kompoziciju kod gojaznih i adolescenata sa povećanom telesnom masom. **Metode:** Eksperimentalna studija izvedena je na 30 adolescenata koji su razvrstani prema indeksu telesne mase (BMI) u dve grupe. Grupu 1 činili su adolescenti sa povišenom telesnom masom, BMI 25-22,9 kg/m^2 , a grupu 2 činili su gojazni adolescenti sa BMI ≥ 30 kg/m^2 koji su bili podvrgnuti programu adaptirane fizičke aktivnosti koja je povezana sa niskokalorijskom ishranom. Niskokalorijska ishrana podrazumevala je edukaciju o niskom nivou holesterola kao i niskom nivou zasićenih masnih kiselina (loše masne kiseline), ishrane bogate povrćem, voćem i vitaminima. Ovaj režim ishrane trajao je 6 meseci. **Rezultati:** Ova studija je pokazala da se nakon šest meseci ovakvog načina života, kod

adolescenata sa povišenom telesnom, značajno smanjio obim struka (82,9 ± 4,2 cm pre vs. 77,6 ± 4,6 cm nakon), srčana frekvenca (86,8 ± 3,6 srčana ciklusa/min pre vs. 81,4 ± 3,8 srčana ciklusa/min nakon), ukupna masnoća (32,2 ± 1,8% pre vs. 27,2 ± 1,5% nakon), visceralna masnoća (16,6 ± 2,3% pre vs. 11,1 ± 2,5% nakon), i smanjenje mišićne mase (15,6 ± 2,7% pre vs. 19,4 ± 4,1% nakon), dok se u grupi gojaznih adolescenata značajno smanjio obim struka (88,9 ± 6,2 cm pre vs. 85,8 ± 5,9cm nakon), visceralna masnoća (17,4 ± 3,2% pre vs. 14,1 ± 3,1% nakon), respiratorni kapacitet (61.1 ± 2.7% pre vs. 65 ± 2.1% nakon). Štaviše, ova studija je pokazala da adolescenti sa povišenom telesnom masom u poređenju sa gojaznim adolescentima više menjaju sledeće parameter: obim struka (77,6 ± 4,6 cm za osobe sa povećanom telesnom masom prema 85,8 ± 5,9 cm za gojazne), indeks telesne mase (24,9 ± 4,1 kg/m^2 za osobe sa povećanom telesnom masom vs. 28,8 ± 1,2 kg/m^2 za gojazne), srčanu frekvencu (81,4 ± 3,8 beat/min za osobe sa povećanom telesnom masom vs. 28,8 ± 1,2 beat/min za gojazne), visceralnu masnoću (11,1 ± 2,5% za osobe sa povećanom telesnom masom vs. 14,1 ± 3,1% za gojazne) i mišiće (19,4 ± 4,1% za osobe sa povećanom telesnom masom vs. 17,1 ± 2,1% za gojazne). **Zaključak:** Kako gojazni adolescenti, tako i adolescenti sa povišenom telesnom masom nakon primenjenog režima ishrane i fizičke aktivnosti značajno su promenili svoje morfološke, fiziološke parametre kao i parametre telesnog sastava.

Ključne reči: adolescenti, telesni sastav, morfologija, fiziologija, povišena telesna masa, gojaznost.

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COMPARISON OF MOTIVATION FOR PARENTING IN HEALTHY AND DEPRESSED PATIENTS

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Abstract: **Objective:** The aim of present study was to examine whether there is a difference in parenting motives between patients diagnosed with depression and control groups (non-depressed). **Material and Method:** The survey included 66 patients who were treated at the Psychiatric Hospital in Novi Pazar (average age = 44.64, SD = 10.00) and 65 subjects who were not diagnosed with depression (average age = 42, SD = 13.05). Participants volunteered to participate in the research and received no compensation for their participation. Respondents were given a Parent Motivation Scale. **Results:** Results showed that participants in our study are motivated for parenthood mostly by instrumental motivation, altruistic and fatalistic motivations are equally present, and narcissistic motivation is the lowest. Instrumental, fatalistic and altruistic motives for parenting are significantly lower in group consisted of depressed patients. There was no difference in narcissistic motivation between two groups. **Conclusion:** This finding can be seen in the light of the general condition and the characteristic of people suffering from depression. In them, namely, all aspects of motivation are reduced and it is not surprising that this is so with the motives for parenting.

Key words: depression, altruistic, fatalistic, narcissistic, instrumental motivation.

INTRODUCTION

Depression

Depression is the psychological condition in which mood is changed and this impairs the person's basic state of mind, perception, body condition, behaviour and social functioning (1). Depressive mood is characterized by turning the patient to himself, despondency, collapse of the vital dynamism, sleeplessness, appetite loss, pessimism, slow process of thought, hopelessness and helplessness (2, 3, 4).

It is considered that depression is caused by genetic, environmental, psychological, and biochemical factors. Depression usually starts between the ages of 15 and 30, and is much more common in women. Approximately 7% to 12% of men and 20% to 25% of women suffer from depression during lifetime. Women can also get postpartum depression after the birth of a baby. Some people get seasonal affective disorder in the winter. Depression is one part of bipolar disorder (5). Several scientific studies determined statistic correlations between depression and the use of certain agricultural pesticides (6).

Depression is much more than a passing feeling of sadness and fatigue; patients with depression often present complex and overlapping emotional and physical symptoms, including pain complaints. In everyday clinical practice we often see patients with depression co-morbid with physical diseases where depression increases health care costs, leading to lower cooperation in the treatment and clinical outcome is worse. Depression is sometimes not recognized or misdiagnosed, and delaying of the treatment increases the suffering of the patient and his environment. Undiagnosed and untreated severe depression leads to attempted suicide or in some cases murder of family members. Contemporary data show that suicide risk is most common in depressed patients and shows an increasing trend. Number of suicide is higher in men then in women. In recent years we have had intensive research of biology of depression and suicidality. The key is a holistic approach and determination of the mental status of a person, and diagnosis is made on the basis of agreed diagnostic criteria contained in CD- 10 classification (7).

Depressive disorder is a significant problem in the field of mental health worldwide. According to the

World Health Organization, depression is fourth biggest global health problem, by the year 2020. it will become the second global health issue, also it is the largest cause of disability among adults (8).

There are two main groups of theoretical approaches to depression. One group considers depression as a consequence of psychological factors, in Behaviourist theory of learning, Psychodynamic theory- Freud (1917), Cognitive approach- Beck's (1967) theory, Humanist approach- Maslow (1962).

In the second group there are theories that accentuate biological and physiological factors. Current neurobiological theories with the most valid empirical foundation are based on studies investigating psychosocial stress and stress hormones, proinflammatory cytokines, neurotransmitters such as serotonin, norepinephrine, dopamine, glutamate and gamma-aminobutyric acid (GABA), neurocircuitry, neurotrophic factors, and circadian rhythms. According to one model, depression can be considered as a psychoneuroimmune disease in which peripheral immune activation is stimulated by secretion of mediators of the inflammation which is responsible for numerous behavioural, neuroendocrine and neurochemical changes which are related to psychiatric condition (9). Collected data indicate the equal importance of serotonin, norepinephrine and dopamine in the occurrence of depressive mood, and in that relation were synthesized new effective antidepressants (11).

Motivation for parenting

Hoffman and Hoffman (1973) amongst first examined the value which children have for parents. Nine groups of such values have been identified, from economic and practical values (e.g., showing the status of an adult or economic gain) to psychological (e.g., parenting). It seems that with the advancement of society the economic value of the child decreases (for example, the child seen as a work force or as support in old age), and its psychological value increases (mutual love, attachment, sense of fulfilment, etc.) (12).

Research has shown that fertility motivation is influenced by many factors, from the biological, personal meanings for potential parents (psychological needs, attitudes and values), socioeconomic factors (material condition, education, employment, housing issues), to the quality of the partner relationship of potential parents to the historical and social circumstances and internal norms related to the fertility behaviour that the individual adopted during socialization in his family and the wider social environment (13, 14, 15, 16). Also, a parenting motive for those who are already parents can be changed depending on sex, number of children and their order of birth (17, 18).

One of the first responses to the question what parents expect from children and what kind of parent's needs children should fulfil was given by Rabin (19), who grouped the motivation for parenting into four categories. Altruistic motivation involves love for children, a desire to care for them, to give them love and protection, and so on. Fatalistic motivation refers to the belief that reproduction and extension of the species is the meaning of life, human destiny or God's will; it's something that is predetermined and inevitable. When a child is seen as a means by which some specific parent goals can be achieved (e.g. material profits, old age support, etc.), this is an instrumental motivation. Finally, the narcissistic motivation for parenting relates to the expectation that a child will increase the value of parents, that it will be evidence of his sexual capacity and masculinity, or femininity.

It is obvious that for the same persons, motivation for parenting can be conditioned by multiple and different reasons. We can differentiate the reasons by their strength, their focus on themselves and other features. But, as one could expect, the greatest correlation was between instrumental and narcissistic motivation, because in both types of motivation, the child serves to achieve a parental goal, whether it is continuation of a family line, transfer of a family name, insurance in old age or even proving of their own value (20).

The unselfish altruistic motivation, expressed in the desire to have a child for love, the joy that it provides and the desire to care for the child, separates this type of motivation from other categories of motivation for parenting. It is therefore not surprising that its connection with narcissistic motivation was the weakest and, in general, its connection with other categories of motivation was lower than the interconnectedness of the other three categories of motivation for parenting (20). Of course, these motives are not mutually exclusive, they can also be found in a variety of combinations.

Parenthood that begins with one type of motive (for example, fatalist) can later be enriched with other types (for example, altruistic motifs). Belsky has dealt with parental behaviour issues and has come up with three main groups of factors that influence parental behaviour, such as: the individual characteristics of parents, the characteristics of the child and contextual factors (21). Individual characteristics of parents that influence parental behaviour are age, sex, behaviour of their parents towards them, knowledge and beliefs about child development and satisfaction with marriage (12). On the other hand, there are also the characteristics of the child that will direct parental behaviour, and this includes child's gender, age, temperament and abilities. Then, contextual factors have a major impact on the interaction and relationship of the child and par-

ents, because parental behaviour does not take place in social isolation, but in interaction, socialization and communication with the child. That is why we include factors such as: parent's social networks, workplace, marital relations etc. (21). All the factors that we listed could cause stress, but also support. For example, stress at work that can affect and change behaviour towards a child, as much as the perception of marital relationships affects parental behaviour, so if a woman feels the support from her husband, she is more likely to deal more easily with her children (21).

OBJECTIVE

The aim of present study was to examine whether there is a difference in parenting motives between patients diagnosed with depression and control groups (non-depressed).

MATERIAL AND METHOD

The survey included 66 patients who were treated at the Psychiatric Hospital in Novi Pazar (average age = 44.64, SD = 10.00) and 65 subjects who were not diagnosed with depression (average age = 42, SD = 13.05). Participants volunteered to participate in the research and received no compensation for their participation.

Respondents were given a Parent Motivation Scale (22). The scale consists of 52 claims where respondents mark the number (0 "I do not agree" to the 4 "I fully agree") to match their agreement with given claim. Scale examines four types of motivation for parenting: altruistic, fatalistic, narcissistic and instrumental. They also received a short questionnaire on socio-demographic characteristics (gender, age, marital status and education level).

Retrospective study has been used. For statistical analysis we used the methods of descriptive statistics, t test and Spearman's correlation coefficient. Data processing was performed using SPSS 20.

RESULTS

We first checked the ratio of presence of four types of parenting motives among respondents. That is, we wanted to see which motive is the most represented, and whether some of the motives are present to the same extent within same respondent.

As we can see from Table 1 instrumental motivation is the strongest, altruistic motivation and fatalistic motivation are nearly equal, and altruistic motivation is the lowest.

A repeated measures ANOVA with a Greenhouse-Geisser correction because of the violated assumption of sphericity, determined that there is statistically significant difference in the presence of each of the four parenting motives in the individual respondent ($F(1.456, 189.266) = 947.736$, $p < 0.01$).

Post hoc pairwise comparisons using the Bonferroni correction (Table 2.) revealed that there is statistically significant difference between pairs of participant's scores on altruistic, narcissistic, instrumental motivation ($p < 0.01$), and as it could be expected from Table 1 there is no significant difference between scores on altruistic and fatalistic motivation.

One way ANOVA was performed in order to see whether depressed patients differ significantly from

Table 1. *Mean and standard deviation of the participants scores on types of motivation for parenting*

	Mean	Std. Deviation	N
Altruistic motivation	37.90	8.144	131
Fatalistic motivation	37.70	8.466	131
Narcissistic motivation	12.95	4.154	131
Instrumental motivation	70.73	19.609	131

Table 2. *Pairwise comparison of the participants scores on types of motivation for parenting*

(I) factor 1	(J) factor 1	Mean Difference (I-J)	Std. Error	Sig.
Altruistic Motivation	Fatalistic m.	.198	.509	1.000
	Narcissistic m.	24.947	.756	0.001
	Instrumental m.	-32.832	1.271	0.001
Fatalistic Motivation	Altruistic m.	-.198	.509	1.000
	Narcissistic m.	24.748	.733	0.001
	Instrumental m.	-33.031	1.195	0.001
Narcissistic motivation	Altruistic m.	-24.947	.756	0.001
	Fatalistic m.	-24.748	.733	0.001
	Instrumental m.	-57.779	1.644	0.001
Instrumental motivation	Altruistic m.	32.832	1.271	0.001
	Fatalistic m.	33.031	1.195	0.001
	Narcissistic m.	57.779	1.644	0.001

Table 3. *Mean value and standard deviation of the four parenting motives in compared groups*

		N	Mean	Std. Deviation
Altruistic motivation	Depressed patients	66	32.41	7.547
	Control group	65	43.48	3.767
	Total	131	37.90	8.144
Fatalistic Motivation	Depressed patients	66	31.67	7.478
	Control group	65	43.83	3.617
	Total	131	37.70	8.466
Narcissistic motivation	Depressed patients	66	12.86	4.121
	Control group	65	13.05	4.218
	Total	131	12.95	4.154
Instrumental Motivation	Depressed patients	66	55.24	15.940
	Control group	65	86.46	4.925
	Total	131	70.73	19.609

Table 4. *Results of the ANOVA used for comparing the groups in strength of their parenting motives*

		Sum of Squares	Df	Mean Square	F	Sig.
Altruistic motivation	Between Groups	4011.540	1	4011.540	112.249	0.001
	Within Groups	4610.170	129	35.738		
	Total	8621.710	130			
Fatalistic motivation	Between Groups	4845.584	1	4845.584	139.783	0.001
	Within Groups	4471.805	129	34.665		
	Total	9317.389	130			
Narcissistic motivation	Between Groups	1.091	1	1.091	.063	0.803
	Within Groups	2242.634	129	17.385		
	Total	2243.725	130			
Instrumental motivation	Between Groups	31917.374	1	31917.374	227.877	0.001
	Within Groups	18068.275	129	140.064		
	Total	49985.649	130			

control group of non-depressed participants in parental motivation. Table 3 shows mean and standard deviation of the scores on four motives for parenting, as it could be seen scores of the control group are higher than in group of depressed patients for all motives except for narcissistic. Results of the ANOVA from Table 4 show that differences seen in Table 3 are statistically significant ($p < 0.01$), except for narcissistic motivation.

DISCUSSION

Results showed that participants in our study are motivated for parenthood mostly by instrumental motivation, altruistic and fatalistic motivations are equally present, and narcissistic motivation is the lowest. It should be noted that the strength of the instrumental motive is almost twice as high as altruistic and fatalistic motivation, and as six times as narcissistic (Table 1). This is a new and interesting finding, somewhat unexpected, since we have shown the results of the research Tucak-Junaković and Ahmeti in which a strong correlation was found between instrumental and narcissistic motivation (20). Someone could have thought that this was a consequence of the fact that half of the sample was consisted of depressed patients in whom narcissism is reduced, but as it could be seen in Table 3, control group also has low narcissistic motivation for parenting not statistically different from depressed participants (Table 4).

Another important finding shows that instrumental, fatalistic and altruistic motives for parenting are significantly lower in group consisted of depressed patients. The individual experiences himself both as the seller and as the commodity to be sold on the market, his self-esteem depending on conditions beyond his control. If he is žsuccessful' he is valuable; if he is not "successful" he is worthless. The degree of insecurity which results from this orientation can hardly be overestimated. If one feels that one's own value is not constituted primarily by the human values one possesses, but by one's success on a competitive market with ever-changing conditions, one's self-esteem, is bound to be shaky

and is in constant need of confirmation by others. Hence one is driven to strive relentlessly for success, and any setback is a severe threat to one's self-esteem; helplessness, insecurity, and inferiority feelings are the result. If the vicissitudes of the market are the judges of one's value, the sense of dignity and pride is destroyed (22).

CONCLUSION

This finding can be seen in the light of the general condition and the characteristic of people suffering from depression. In them, namely, all aspects of motivation are reduced it is not surprising that this is so with the motives for parenting.

DECLARATION OF INTEREST

The autors declare that there are no conflicts of interests.

Sažetak

KOMPARACIJA MOTIVACIJE ZA RODITELJSTVO KOD ZDRAVIH I DEPRESIVNIH PACIJENATA

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Cilj: Svrha ove studije bila je da ispita da li postoji razlika u roditeljskim motivima između roditelja kojima je dijagnostikovana depresija i kontrolne grupe (bez depresije). **Materijal i Metode:** Istraživanje je obuhvatilo 66 pacijenata koji su lečeni u Službi za psihijatriju bolnice u Novom Pazaru (prosečne godine = 44.64, SD = 10.00) i 65 osoba kojima nije dijagnostikovana depresija (prosečne godine = 42, SD = 13.05). Učesnici su svojevoljno učestvovali u istraživanju i za to nisu dobili nikakvu novčanu naknadu. Ispitanicima je data Skala za Roditeljsku Motivaciju. **Rezultati:** Rezultati su pokazali da su učesnici u našem istraživanju motivisani za roditeljstvo najčešće instrumentalnom motivacijom, dok su altruistička i fatalistička motivacija jednako prisutne, a narcistička je na najnižem nivou. Instrumentalni, fatalistički i altruistički motivi za roditeljstvo su značajno niži u grupi ispitanika sa depresijom. Nije bilo razlike među grupama kada se radi o narcističkoj motivaciji. **Zaključak:** Ova otkrića mogu biti viđena u svetlu opšteg stanja i karakteristika ljudi koji pate od depresije. Kod njih su konkretno svi aspekti motivacije smanjeni tako da nije iznenađujuće što je to slučaj i sa motivima za roditeljstvo.

Ključne reči: depresija, altruistička, fatalistička, narcistička, instrumentalna motivacija.

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Case report

HEMOPHILIA PATIENT WITH DIFFICULTY IN BLOOD PRESSURE CONTROL

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Abstract: Hypertension prevalence is increasing in patients with hemophilia. Therefore it is an important complication of hemophilia. We aimed to present a 49-year-old male patient with hemophilia-A who presented with acute hemarthrosis and hypertensive attack. The patient was treated in our internal medicine clinic.

Key words: Hemophilia, hypertension.

INTRODUCTION

Comorbid conditions are more common in hemophilia patients since the life span in hemophilia patients is longer than those of previous years due to improvements in hemophilia care. One of the most common comorbid conditions seen in hemophilia patients is hypertension (1). We aimed to present a hemophilia patient who presented with acute hemarthrosis and hypertensive attack to our internal medicine clinic.

CASE REPORT

A 49-year-old male patient with hemophilia-A was admitted to the emergency room due to swelling in his right knee 2 days before. On physical examination, blood pressure (BP) was 220/110 mmHg, heart rate was 92/min, swelling in the right knee was remarkable. Hemogram and routine biochemical parameters were normal except for prolonged activated prothrombin time (APTT = 115 sec). The recombinant factor eight present in the patient itself was given at a dose of 50 IU/kg. The 30th minute control APTT value was determined to be 38 seconds. He was admitted to our Internal medicine Clinic because of the failure of controling BP in the emergency department and the diagnosis of hemarthrosis and hypertensive attack. After the administration of perindopril-indapamide 5/1.25 mg combination and bisoprolol 5 mg in treatment, BP gradually reached the target values. Because of admission to the hospital with hypertensive attack, we planned the test in order to determine the cause of hypertensive attack. Left ventricular concentric hypertrophy was detected on echocardiography. No pathological findings were observed in abdominal ultrasonography and renal artery doppler ultrasonography. Rheumatological parameters, urine metanephrine and normetanephrine values were in normal range. The patient was evaluated as an essential hypertension. The discharge of the patient was considered due to the regression of hemarthrosis and adequate blood pressure control. It was discharged with a combination of perindopril / indapamide and bisoprolol. The patient was directed to a center where factor 8 and inhibitor tests could be performed.

DISCUSSION AND CONCLUSION

Prevalence of hypertension is increasing in patients with hemophilia (2). Hypertension is thought to be more common in hemophilia patients than nonhemophiliacs (3, 4). The cause of increased prevalence of hypertension in cases with hemophilia is unknown. Sedentary lifestyle due to increased bleeding risk is one of the hypotheses (2). In patients with increased risk of bleeding such as mild and severe hemophilia, hypertension may be affected by the obligatory sedantery lifestyle due to the risk of bleeding. Interaction of hemostatic factors with the vascular wall or reduction in hemostasis is thought to be the effect on vascular tone or endothelial relaxation (5, 6). There are also studies showing that hypertension triggers bleeding episodes. Our patient was admitted together with attacks of bleeding and hypertension. Elderly hemophilia patients should be closely monitored to avoid comorbidities and bleeding episodes. Antihypertensive therapy sho-

uld be considered concurrently with factor 8 replacement in the management of patients with a risk of hypertensive attack and hemophilia. Since pieces of information on the prevalence and severity of hypertension is limited during hemophilia, it is important to investigate the frequency and pathogenesis of hypertension in hemophiliacs.

DECLARATION OF INTEREST

The autors declare that there are no conflicts of interests.

Sažetak

PACIJENT SA HEMOFILIJOM SA POTEŠKOĆAMA U KONTROLI KRVNOG PRITISKA

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Prevalenca hipertenzije kod pacijenata sa hemofilijom je u porastu. Dakle, može se reći da je hipertenzija ozbiljna komplikacija hemofilije. Cilj našeg rada bio je da predstavimo 49-godišnjeg muškog pacijenta koji boluje od hemofilije A, kod kojeg se javila akutna hemartroza i napadi hipertenzivne krize. Pacijent je lečen u našoj Klinici za internu medicinu.

Ključne reči: hemofilija, hipertenzija.

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Case report

SEVERE PNEUMONIA CAUSED BY ANTIPSIHOTIC DRUGS - WHAT DOES NOT SUIT, THE PATIENT OR THE DRUG?

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Abstract: **Introduction:** Antipsychotic drugs are generally categorized as typical antipsychotics (sometimes referred to as first-generation or conventional antipsychotics, or neuroleptics) and atypical antipsychotics; both are approved for the treatment of acute and chronic psychoses (i.e, schizophrenia), mania, agitation, and other psychiatric disorders. In 2005 the US Food and Drug Administration issued a warning about the increased risk of all-cause mortality associated with atypical antipsychotic use in elderly patients with dementia. Community acquired pneumonia (CAP) was one of the most frequently reported causes of death. The same warning was extended to typical antipsychotics in 2008 with extension to people with or without dementia.

Case report: We present a 65-year-old Caucasian woman who was admitted to hospital due to massive pneumonia. She was suffered forschisophrenia 15-years and at moment of admission she was in remission. She had continuously high fever up to 40 degrees. All collected cultures (blood, sputum, urine, smear of aspirating catheter) were negative. She was treated with various antibiotics without improvement. After changing antipsychotic drugs, she showed slow improvement until total recovery after 3 months.

Discussion and conclusion: Antipsychotic-associated CAP seems to be a clinically relevant issue in frail elderly patients, as consistently documented in several epidemiologic investigations. No clear evidence exists for an increased risk of pneumonia in younger patients treated with antipsychotics. In elderly populations, the increase in risk is dose-dependent, and is more pronounced in the early phases of treatment. Future studies should better define the mechanism underlying antipsychotic-induced pneumonia and identify subgroups of antipsychotic users at higher risk of developing pneumonia.

Key words: antipsihotic drugs, schizophrenia, pneumonia, drug toxicity.

INTRODUCTION

Antipsychotics, indicated for acute and chronic psychosis and other psychiatric disorders treatment, are generally distinguished as atypical and typical agents (1). Because pneumonia isone of the most frequently reported death causes in olderpatients, several observational studies have evaluated the association between antipsychotic usage and the risk of fatal/nonfatal community-acquired pneumonia (CAP) recently (2).

CASE REPORT

A 65-year-old Caucasian woman was presented to the Emergency Department, complaining of a 3-day continuous high fever up to 40 degrees associated with a productive cough. The patient had a 15-years schisophrenia history and has achieved full remissionfor two last years, but becauseof new onset of anxiety, psychiatrists changed therapy to Risperidone 2 mg daily, Mirtazapine 15 mg daily, Carbamezepine 200 mg daily and Parohetine 20 mg daily usage, a week before admition to hospital. Her last therapy was clozapine, when she achieved remission for two years. At the Emergency Department, the patient was febrile- 39C, generally weak and with a depressive mood. Her blood pressure was 95/65 mm Hg, while her pulse was 110 beats per minute and regular. Chest examination revealed dullness on the upper right lobe; other breath and heart sounds were normal. There were no signs of hepato-

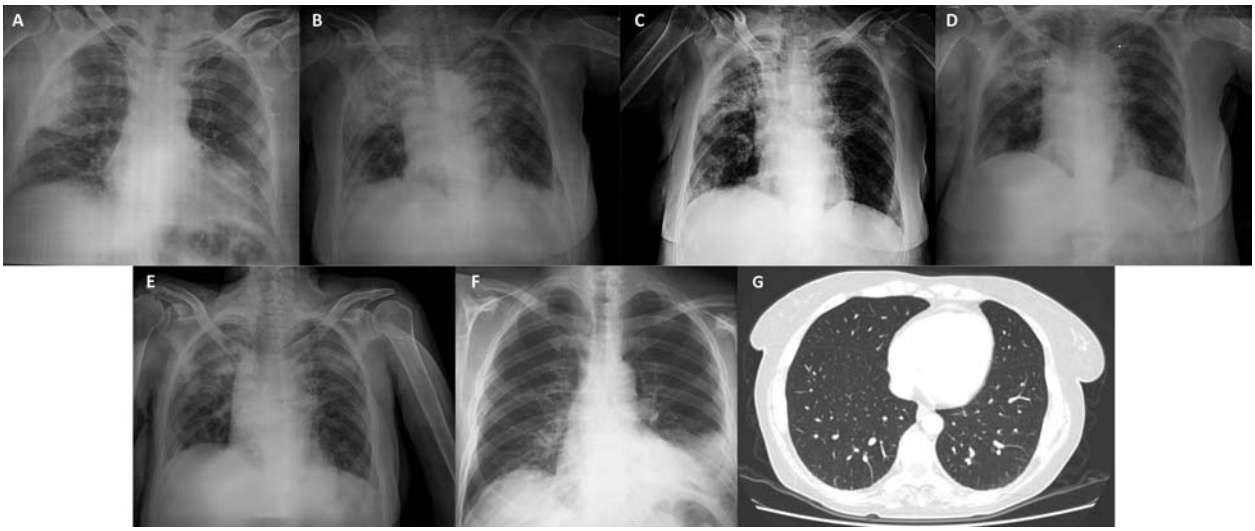

Figure 1. Chest X ray of the antipsychotic-drugs induced severe pneumonia patient
***A**-on admitting; **B**-Chest X ray taken after initiation of antibiotics (ceftriaxone and ciprofloxacin) three days after; **C**-After 3 days of initiation of Vankogal, Metronidazole and Amikacin-showing no improvement; **D**-Atthird dayafter initiation of Levofloxacin and Metronidazole and reducing antipsychotic drugs dosage; **E**-Little regression of inflammation and start with Colistin; **F**- Significant radiological regression of inflammatory process after one month from treatment induction; **G**- complete resolution of inflammatory process after 3 weeks from last chest X ray*

splenomegaly, lymphadenopathy, abdominal tenderness and pathological abdominal masses. The chest radiogram has shown the right-sided upper pneumonia and the patient was admitted to the hospital (Figure 1A). Her laboratory finding were: C-reactive protein (CRP) 500 ng/dl (normal range < 5 ng/dl), presepsin (P-SEP) 780 pg/mL (reference values 55–184 pg/mL), leucocytes number 24 x 10^9 cells/liter, with 95% of neutrophils and normocytic anemia. Biochemical analysis were within normal range. She has initially been treated with antibiotic therapy Ceftriaxone 2 g intravenously and ciprofloxacin 1g intravenously. Cultures of urine, blood and sputum were all sterile, although repeated for several times. The patient body temperature remained high- up to 40 degrees. Clinical pharmacologist was consulted on the third day, suggesting administration of Vancomycin 2 g per day intravenously, Metronidazole 500 mg three times a day and Amikacin 2 g intravenously daily (Figure 1B). Three day after, chest X ray was repeated, showing no regression of inflammation (Figure 1C). Despite antibiotics treatment, the patient was constantly febrile, with slow inflammatory markers regression: 350 ng/dl CRP and Le 11 x 10^9 cells/liter, accounting for neutrophils in 85,5%. Bronchoscopy was performed showing much mucus and pus. Material obtain using bronchoscopy was sent to laboratory for analyses. Arrived cultures for sterile. Infectologist was called in consultation, suggesting Levofloxacin 750 mg daily intravenously with cessation of antipsychotic drugs, which brought the patient's fever down to 38 degrees. We empirically administered 2 millions units of Colistin three times a day intravenously, reaching the normal body temperature for the first time on the third day of treatment (Figure 1D, E). Inflammatory markers decreased as well: 70 ng/dl of CRP, presepsin 100 and leucocytes 7,8 with 72% of neutrophils. After 10 days of Colistin application, the patient was discharged. Since she was in psychiatric remission for a long time, her psychiatrist has decided to reduce her regular antipsychotic drugs dosage for a month due to pneumonia recovery. The patient came back for a regular check-up after a month and herchest X-ray showed regression (Figure F). She continued taking her psychiatric drugs in reduced dose. After three weeks CT scan was performed showing complete regression of inflammatory changes (Figure G). Psychiatrist switched her therapy to clozapine. After three months, she came to pulmonology check up because she was afraid to acquired pneumonia again. She felt well with one antipsychotic drug and her physical examination was within normal range, as well as chest X-ray.

DISCUSSION AND CONCLUSION

Here, we have presented a case of antipsychotic drugs-induced severe pneumonia in a patient with schizophrenia who was treated with one antipsychotic drugs for 15 years, but due to new symptoms psychiatrist changed her therapy into four drugs. Until antipsychotic agents were excluded, the patient was continuously febrile. Although discontinuation of APs drugs is frequently associated with exacerbation of

psychotic symptoms in clinical practice, that was not the case with our patient, preserving his previous mental state, functional state and quality of life. However, consultation of an experienced psychiatric should be recommended in those situations in order to avoid the ceased-therapy caused adverse events, out of which suicide could be the most serious one. Therefore, it would be essential to have a written expert opinion about down-titrating or cessation of psychiatric therapy in those cases signed by an experienced psychiatrist.

The biological pathways underlying antipsychotic-induced pneumonia are not fully understood, although several plausible hypotheses have been postulated (3). Further understanding of drugs that are associated with higher risk of pneumonia and application of this knowledge in practice would enable prescription of non-pneumonia risk drugs in patients with predisposition risks for infectious respiratory diseases, such are: bedridden state, chronic respiratory diseases and/or sedative drugs usage. Observational data studies suggest a different safety profile for individual antipsychotics (AP) by class (4, 5). The review from the literature has identified several biological mechanisms that could lead to pneumonia accompanied by AP use. Pharmacology data in vitro have confirmed receptor affinities identified in the literature. Two targets, thromboxane A2 receptor (TBXA2R) and platelet activating factor receptor (PTAFR) were found to be the novel AP target receptors, potentially associated with pneumonia.

Biological pathways constructed using Cytoscape have identified biological links that could lead to pneumonia: downstream of TBXA2R and PTAFR innovative approaches for biological substantiation of drug-adverse event associations may strengthen evidence on drug safety profiles and help tailoring pharmacological therapies (5).

Complete Declarations:

• Ethics approval: The protocol of the study was approved by Medical School, University of Belgrade. All procedures were performed in accordance with the Declaration of Helsinki.

• Every patient who was admitted to our hospital had previously given written consent that his/her data could be used in scientific purposes and that their results could be published but not using their names or anything which could reveal their identity.

DECLARATION OF INTEREST

The authors declare that there are no conflicts of interests.

Sažetak

TEŠKA PNEUMONIJA IZAZVANA ANTIPSIHOTIČNIM LEKOVIMA - ŠTA NE ODGOVARA, PACIJENT ILI LEK?

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Uvod: Antipsihotični lekovi se načelno dele na tipične antipsihotike (ponekad se na njih odnosi termin „konvencionalni" ili „antipsihotici prve generacije" ili neuroleptici) i na atipične antipsihotike; obe grupe su pogodne za lečenje akutne i hronične psihoze (na primer shizofrenija), manije, agitacije i drugih psihijatrijskih poremećaja. 2005. godine Američko udruženje za hranu i lekove je izdalo upozorenje o povećanom riziku opšte stope mortaliteta udružene sa atipičnim antipshoticima koji se koriste u starijoj populaciji pri lečenju demencije. Nebolnička pneumonija (CAP) bila je jedna od najčešće navođeniih uzroka smrti. Isto upozorenje bilo je prošireno i uključivalo je tipične antipsihotike 2008. godine, koje je sada uključivalo i ljude sa ili bez demencije.

Prikaz slučaja: Predstavljamo 65-godišnju ženu, bele rase, koja je hospitalizovana zbog masivne pneumonije. Ona je bolovala od shizofrenije unazad 15 godina i u momentu prijema u bolnicu bila je u remisiji. Imala je konstantnu temperaturu od 40 stepeni Celzijuseve skale. Sve učinjene mikrobiološke analize bile su negativne (hemokultura, sputum, urino kultura, bris aspiriranog sadržaja uzetog kateterom). Bila je lečena različitim antibioticima bez napretka. Nakon promene antipsihotičnih lekova, pacijentkinja je pokazala spori napredak do potpunog ozdravljenja koje je usledilo nakon 3 meseca od početka terapije.

Diskusija i zaključak: Pneumonija povezana sa antipsihoticima je zapravo klinički vrlo značajan problem kod starih pacijenata, koji je zapažen u nekoliko epidemioloških studija. Ne postoji jasan dokaz koji govori u prilog postojanju povišenog rizika od pneumo-

nije kod mlađih pacijenata koji su lečeni antipsihoticima. U populaciji starih, povećan rizik je dozno-zavisan i više je naglašena u ranijim fazama bolesti. Dalje studije treba da bolje definišu mehanizme koji se nalaze u osnovi pneumonije koju indukuju antipsihotici i koji treba da identifikuju podtipove korisnika antipsihotičnih lekova, koji su u povećanom riziku od razvoja pneumonije.

Ključne reči: antipsihotični lekovi, shizofrenija, pneumonija, toksičnost lekovima.

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Case report

TREATMENT OF SUBLUXATION INjURY CONCOMITANT WITH CORONAL FRACTURE: A CASE REPORT

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Abstract: Traumatic dental injuries are not only a serious public health problem, but they are also the most common injuries among children according to the epidemiological data. Subluxation is defined as the loosening of a tooth without displacement. Coronal fractures are the most common injuries. Considering the treatment options, which are suitable for the concomitant occurrence of these two traumatic injuries, there are only limited number of studies in the literature. In the concomitant occurrence of these two trauma types, like in other traumatic injuries, if the treatment is not implemented timely, long-term problems may develop. The objective of this case report was to describe the therapeutic approach to the subluxation concomitant with a coronal fracture.

Key words: Composite restoration, Crown fracture, Dental trauma, Luxation injury, Paediatric dentistry, Subluxation.

INTRODUCTION

Subluxation is defined as the loosening of the tooth without displacement (1, 2). The intraoral examination of the subluxated teeth may reveal increased mobility and sensitivity to percussion. Bleeding in the gingival sulcus may accompany this clinical condition. Radiological examination shows that the tooth is in its socket and in its normal position (1). In subluxated teeth, the periodontal ligament is not completely torn but the neurovascular support of the pulp is damaged. Electrical pulp testing may provide negative results until the blood perfusion to the pulp is restored (1). Therefore, in respect of the prognosis, colour change and the emergence of the periapical radiolucent lesions are more acceptable diagnostic criteria (1, 3). Therapeutic choices in the subluxation vary from the follow-up without any invasive intervention to the tooth extraction (2, 4). Crown fracture is a type of injury, in which a part of the enamel is lost due to the impact of a vertical or oblique force on the incisal region of the tooth. Regarding the possible complications and the development of the sequelae, the clinical progress is milder compared to the luxation injuries (5).

Traumas may cause also several other injuries along with the hard tissue injuries. Although there are several guidelines for the coronal fractures and luxation injuries treatmen (5, 6). There are only limited investigations focused on the subluxation injuries concomitant with coronal fractures (5, 7). In this case report presented the one-session treatment of the coronal fracture concomitant with the luxation injury.

CASE REPORT

A 12-year old girl, who applied to the clinic with the complaint of fractures in the teeth 11 and 12. The initial examination showed that she fell in the school just 10 minutes before her admission to the clinic and had an uncomplicated coronal fracture and subluxation injury, which was determined with the presence of the bleeding in the sulcus and sensitivity to percussion (Figure 1). We did not observe any increase in the mobility and any other pathological finding in the radiological examination. As the control, which was done with the electric pulp testing, (Parkell Gentle Pulse, Parkell Electronics, USA) showed that the teeth

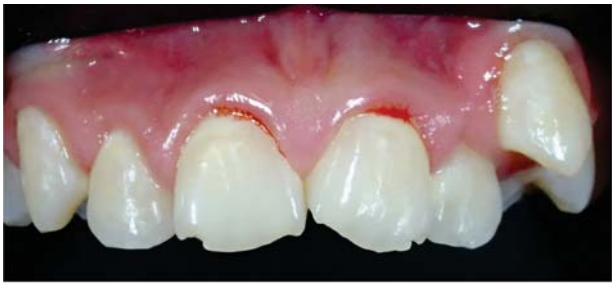

Figure 1. *Initial appearances*

were vital and had a response within the normal limits, we decided for a composite resin restoration in one session. The tooth colour was determined with the colour scale of the Style Italiano My Shade Guide (SmileLine, CH). CE enamel (Estelite Sigma Quick, Tokuyama Dental, Japan) and OA2 and OA3 dentine (Estelite Sigma Quick, Tokuyama Dental, Japan) composite materials, which will compose the decided colour, were placed on the teeth with a thickness less than 0.5 mm and polymerized with light for 10 seconds (Figure 2a). The colour of the dentine and enamel layers were determined with the help of the picture taken with Cross Polarizer Filter (Smile Lite MDP, SmileLine, CH) (Figure 2b). After the enamel and dentine colours to be used were determined, the composite residues on the buccal surface of the teeth were removed. The teeth were cleaned with a 2% chlorhexidine gluconate solution (Klorhex, Drogsan, Turkey) and the maxillary teeth were recorded without pressure application. Following the mock-up, silicon matrix was formed with Type C silicon (Zetaplus, Zhermack, Germany) (Figure 3).

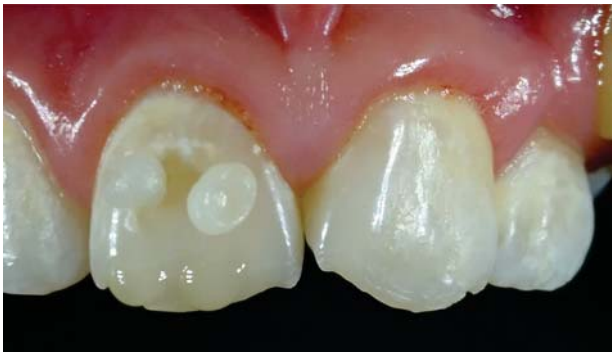

Figure 2a. *After placing composite parts*

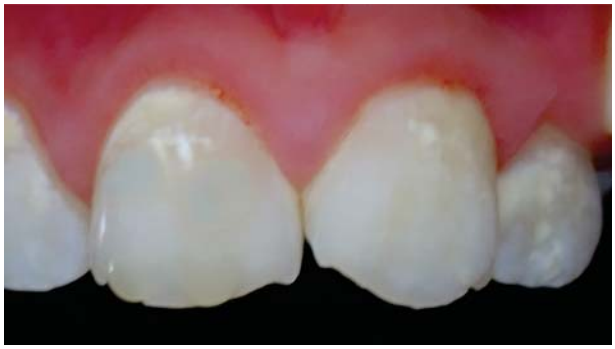

Figure 2b. *Appearance with cross polarizer filter*

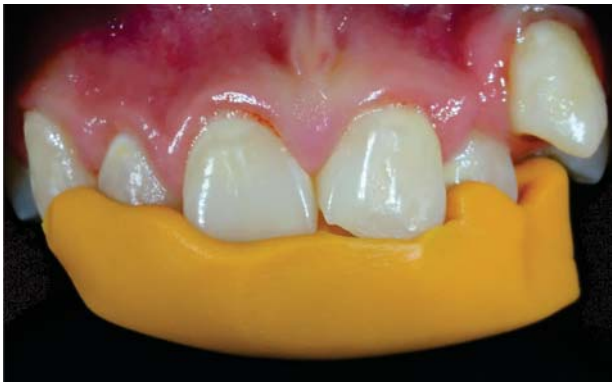

Figure 3. *Silicon matrix*

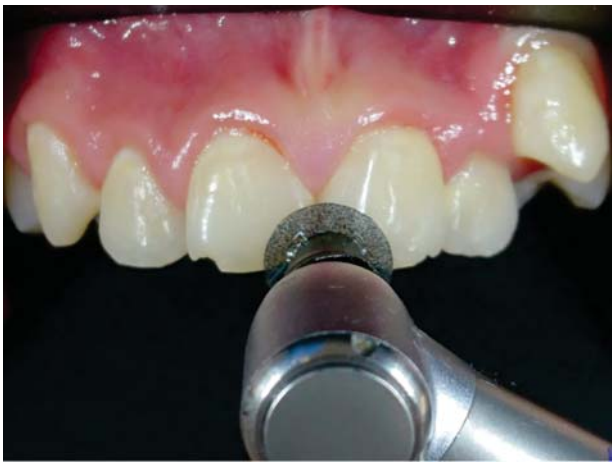

Figure 4. *Roughening the fracture line*

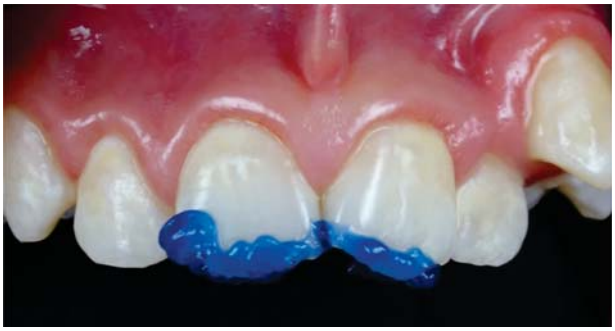

Figure 5a. *Etching*

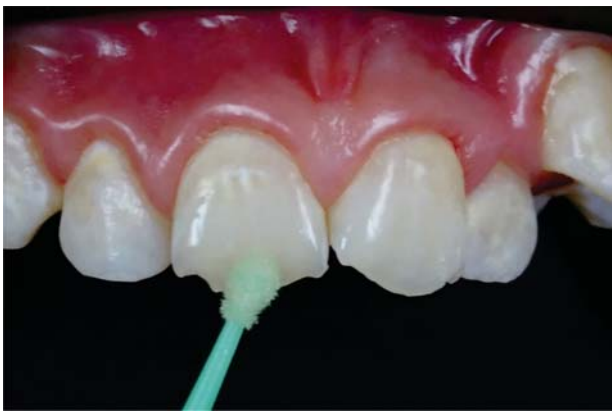

Figure 5b. *Bonding*

After the placement of Optra Gate (Ivoclar Vivadent AG, Liectenstein) for isolation, etching was performed on the buccal enamel surface with the black coloured polishing disc (Rainbow, Shofu Dental, Japan) in order to roughen the fracture line (Figure 4). Following the application of orthophosphoric acid (Scotchbond Universal Etchant, 3M Espe, Germany) and bonding (Single Bond Universal Adhesive, 3MEspe, Germany), (Figure 5a, 5b) the silicon matrix was placed and the

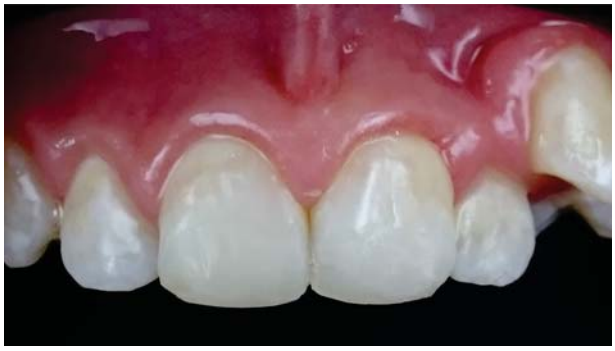

Figure 6. *Final Appearances*

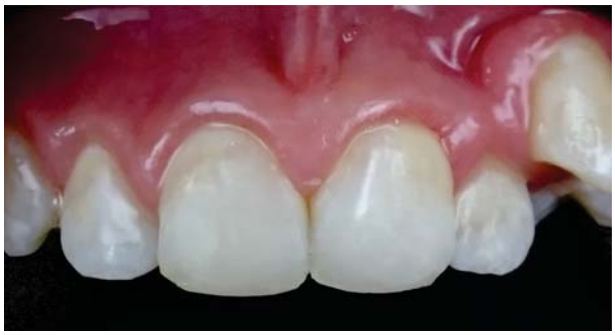

Figure 7. *Follow-up 8th weeks*

enamel and dentine composites were inserted. The surface of the composite was protected with the glycerine gel (Liquid Strip, Ivoclar Vivadent AG, Liectenstein) after the polymerization. The treatment was finalized with finishing and polishing (Rainbow Polishing Disks, Shofu Dental, Japan) (Figure 6).

Soft diet was recommended to the patient for 15 days and a training for the mouth hygiene was provided. In the follow-up controls in the 2nd and 4th weeks, we determined that the teeth were still vital, which continued also in the controls in the 6th and 8th weeks. There were no findings of resorption on the root surface and the patient and her family were satisfied with the cosmetic outcome of the restoration (Figure 7).

DISCUSSION

Regarding the prognosis of the traumatic tooth, a imely and appropriate acute trauma planning and se - lection of the suitable treatment constitute the first step to the success (8). Trauma does not only damage the healthy structure of the tooth but also affects negatively the self-confidence and quality of life of the patient. Dental injuries caused by trauma, have a negative impact on the factors directly related to the quality of life of the patients like the restriction of the school and business life, sleep disturbances, impairment of eating and smiling (9). In addition, it was reported that both the child and his/her parents had more concerns about the cosmetic appearance than the symptomatic findings (10, 11, 12). Therefore, first, the concerns of the parents about the aesthetic outcome should be relieved. The best way for the relieving of the aesthetic concerns of the patient is the implementation of the biomimetic permanent restoration as quickly as possible.

Teeth may be exposed to several different injuries due to the trauma. Studies have shown that pulp necrosis is more common if the luxation injury is accompanied by a complicated or uncomplicated coronal fracture (7).

Nevertheless, if the fracture involves enamel and dentine or enamel, dentine and pulp, the treatment should be initiated without wasting time (5). Depending on the localization of the fracture, dentinal tubules about 15,000 - 45,000/mm^2 are exposed (13). Depending on the low amount of the peritubular dentine, the width of the dentinal tubules, the closeness to the pulp and the high quantity of the dentinal tubules create a path for the bacteria to access the pulp and thus pulpal disorders may emerge (14, 15). The exposed dentine in the uncomplicated fractures or the exposed pulp in complicated fractures should be covered with a suitable material and disconnected from the oral cavity (16). As it is well known that the posttraumatic composite restoration does not have the risk of necrosis, composite restoration can be directly implemented in the uncomplicated cases (8). In untreated patients with the suspicion of the luxation injury, the coverage of the exposed dentine with glass ionomer and the follow-up controls of the pulp is recommended. On the other hand, there is no doubt that if the pulp is intact, the treatment can be performed with the total-etching technique and resin-based composites (17). In this case, we were able to carry out the composite restoration immediately, as the time spent after the trauma was short, the mobility was within the physiological limits, there was no need for a dental splint and pulp responded positively to the vital metric testing.

There is only limited information about the recovery process after the bleeding and oedema in the periodontal ligament (PDL) following small traumas like concussion and subluxation. In a clinical luxation study, after the concussion trauma, the development rate of the surface resorption was higher compared to the subluxation (18). This finding indicates that in the injuries like the concussion, in that the tooth is not mobile within the socket, the pressure, which emerges due to the bleeding in the PDL, may damage the root surface. Considering the subluxation, the posttraumatic force moves the tooth and relieves the pressure (6). The findings of the surface resorption can be observed in the radiological examinations earliest in the 6th week (18). We did not observe any pathological finding in the follow-up controls in the 6th and 8th weeks.

Conclusion

In cases, who have subluxation along with uncomplicated coronal fracture, treatment in one session is possible if the patient has a vital pulp, good cooperation and less concern about aesthetics. However, the long-term outcome should be investigated with further studies.

DECLARATION OF INTEREST

The autors declare that there are no conflicts of interests.

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Sažetak

LEČENJE SUBLUKSACIJSKE POVREDE ISTOVREMENO SA PRELOMOM KRUNICE: PRIKAZ SLUČAJA

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Traumatske povrede zuba nisu samo ozbiljan problem javnog zdravlja, već su i najčešće povrede među decom prema epidemiološkim podacima. Subluksacija se definiše kao otpuštanje zuba bez pomeranja. Prelomi krunica su najčešće povrede. Obzirom na opcije lečenja, koje su pogodne za istovremenu pojavu ove dve traumatske povrede, postoji ograničen broj studija u literaturi. Kod istovremene pojave ova dva tipa trauma, kao i kod drugih traumatskih povreda, ako se tretman ne sprovede blagovremeno, mogu se javiti dugoročni problemi. Cilj ovog izveštaja jeste opisivanje terapeutskog pristupa subluksaciji u kombinaciji sa frakturom krunice zuba.

Ključne reči: Kompozitna obnova, prelom krunice, povreda zuba, luksacijska povreda, pedijatrijska stomatologija, subluksacija.

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