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IMPROVEMENT IN THE QUALITY OF LIFE IN WOMEN WITH STRESS URINARY INCONTINENCE AFTER SURGERY FOR PELVIC ORGAN PROLAPSE

POBOLJŠANJE KVALITETA ŽIVOTA KOD ŽENA SA STRESNOM URINARNOM INKONTINENCIJOM NAKON OPERACIJE SPADA GENITALNIH ORGANA

Ljiljana MLADENOVIĆ SEGEDI

Summary

Introduction. Pelvic organ prolapse is commonly associated with symptomatic stress urinary incontinence, in up to 50% of patients. The aim of our research was to examine the quality of life of women with urinary incontinence and pelvic organ prolapse after conventional surgical treatment. **Material and Methods.** The research included 50 patients with stress urinary incontinence and pelvic organ prolapse that underwent vaginal hysterectomy with anterior and posterior colporrhaphy. The pelvic organ prolapse-quantification system was used to determine the degree of genital prolapse. All patients completed a questionnaire to determine the "stress and urge" score preoperatively, as well as the Urinary Distress Inventory-6 and Urinary Impact Questionnaire-7 during the follow-up examination, a year after the surgery. **Results**. One year after surgery, 20 patients (40%) presented with a recurrence of cystocele. The average value of the Urinary Distress Inventory-6 questionnaire a year after surgery was 29.0 ± 10.8, while the average value of the Urinary Impact Questionnaire-7 questionnaire was 3.7 ± 16.3. After the surgery, 6 patients (12%) had persistent stress urinary incontinence and 4 patients (8%) had urge urinary incontinence. Among patients with persistent stress urinary incontinence, two patients reported pronounced symptoms of stress urinary incontinence and reoperation was performed. **Conclusion.** The classical surgical treatment of pelvic organ prolapse with anterior and posterior colporrhaphy leads to improvement in the quality of life of patients with pelvic organ prolapse and stress urinary incontinence. If the symptoms of stress urinary incontinence persist after classical surgical treatment, other anti-incontinence surgical modalities should be considered.

Key words: Quality of Life; Women; Urinary Incontinence, Stress; Pelvic Organ Prolapse; Gynecologic Surgical Procedures; Treatment Outcome

Sažetak

Uvod. Spad genitalnih organa je često kod oko 50% slučajeva udružen sa stresnom urinarnom inkontinencijom. Cilj našeg istraživanja bio je da se ispita kvalitet života žena sa stresnom urinarnom inkontinencijom nakon klasičnog operativnog lečenja genitalnog spada. **Materijal i metode.** Kod 50 žena sa stresnom urinarnom inkontinencijom i genitalnim spadom urađena je vaginalna histerektomija sa prednjom i zadnjom kolporafijom. Stepen spada genitanih organa određivan je prema *Pelvic organ prolapse-quantification* sistemu. Sve pacijentkinje su preoperativno popunile *stress and urge* upitnik, dok su godinu dana nakon operacije popunile the *Urinary distress inventory-6* i *Urinary Impact Questionnaire-7* upitnike. **Rezultati.** Godinu dana posle operacije 20 pacijentkinja (40%) imalo je rekurentni spad prednjeg zida vagine. Srednja vrednost *Urinary distress inventory*-6 upitnika, nakon operacije, iznosila je 29 ± 10,8, dok je srednja vrednost *Urinary Impact Questionnaire*-7 upitnika iznosila 3,7 ± 16,3. Nakon operacije, šest pacijentkinja (12%) imalo je perzistentnu stresnu inkontinenciju dok su četiri pacijentkinje (8%) imale urgentnu inkontinenciju. Dve pacijentkinje sa perzistentnom stresnom inkontinencijom imale su izražene simptome i one su ponovo operisane. **Zaključak.** Kod pacijentkinja sa koegzistentnom stresnom urinarnom inkontinencijom i genitalnim spadom, nakon klasične vaginalne histerektomije sa prednjom i zadnjom kolporafijom dolazi do poboljšanja kvaliteta života. Ukoliko tegobe stresne urinarne inkontinencije i dalje perzistiraju potrebno je razmotriti druge operativne metode lečenja.

Ključne reči: kvalitet života; žena; stres urinarna inkontinencija; prolaps genitalnih organa; ginekološke hirurške procedure; ishod lečenja

Introduction

According to the definition of the International Continence Society, urinary incontinence (UI) represents any complaint of involuntary loss of urine [1]. This is a very common complaint in the female population, with the prevalence varying between 8 – 45% which increases with the age [2–5].

The most common types of UI in women are stress urinary incontinence (SUI) ("complaint of in-

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Abbreviations

UI – urinary incontinence
POP – pelvic organ prolapse
UDI – urinary distress inventory
UIQ – Urinary Impact Questionnaire
SUI – stress urinary incontinence
UUI – urge urinary incontinence

voluntary loss of urine on effort or physical exertion, or on sneezing or coughing"), urge urinary incontinence (UUI) ("complaint of involuntary loss of urine associated with urgency"), and mixed urinary incontinence ("complaint of involuntary loss of urine associated with urgency and also with effort or physical exertion, or on sneezing or coughing") [1, 6].

Pelvic organ prolapse (POP), defined as "the descent of one or more: the anterior vaginal wall, the posterior vaginal wall, the uterus (cervix), or the apex of the vagina (vaginal vault or cuff scar after hysterectomy), is a condition which is frequently associated with UI, probably due to similar risk factors and causes of the occurrence [1, 3, 4, 6–11]. It is considered that up to 50% of women with POP also have symptomatic SIU [9]. Putra et al. have determined that the prevalence of urinary incontinence in women with POP is 37.32% (in I - II grade: 22%, and in III - IV grade: even 82.35%) [3].

The prevalence is probably higher, because a lot of women do not report UI and POP problems, for various reasons: they consider it to be an integral part of life rather than a disease that should be treated; they tolerate symptoms because they do not know that they need to seek medical help, or they have a fear of hospitals. In addition, the financial aspect of treatment cannot be disregarded either. Only when the symptoms become more pronounced and start to disturb their daily, primarily social aspect of life, women decide to seek medical help [3, 9, 12].

Although POP and SUI are not life-threatening diseases, they have a negative impact on the quality of women's lives, primarily on their social, psychological and sexual aspects, due to the feelings of shame, stigmatization and negative body image self-perception [3, 13, 14].

The aim of our research was to examine the quality of life of women with UI and POP after conventional surgical treatment for POP.

Material and Methods

The research was conducted at the Clinic of Gynecology and Obstetrics, after the approval of the Ethics Committee of the Clinical Center of Vojvodina.

Table 1. Determination of stress and urgency score
Tabela 1. *Određivanje stress/urgency skora*

	SS	US
I'm losing urine during laughing, coughing and sneezing/*Mokraću gubim pri smehu, kašljanju i kijanju.*	YES/*DA*	NO/*NE*
Involuntary urine leakage is not followed by a urinary urgency *Nevoljno umokravanje nije praćeno nagonom na mokrenje.*	YES *DA*	NO *NE*
Starting urination is difficult/*Početak mokrenja je težak.*	YES/*DA*	NO/*NE*
I have a chronic cough (bronchitis) or constipation *Imam hroničan kašalj (bronhitis) ili zatvor (opstipaciju).*	YES *DA*	NO *NE*
My uterus and/or the walls of the vagina fall out/*Ispada mi materica i/ili zidovi vagine.*	YES/*DA*	NO/*NE*
I do hard physical work (I used to do)/*Obavljam teške fizičke poslove (obavljala sam).*	YES/*DA*	NO/*NE*
I had more than three abortions/*Imala sam više od tri pobačaja.*	YES/*DA*	NO/*NE*
I lose urine bit by bit (a few drops)/*Mokraću gubim po malo (nekoliko kapi).*	YES/*DA*	NO/*NE*
Leakage of urine is not affected by changes in the weather nor the seasons *Na gubitak mokraće ne utiču promena vremena i godišnja doba.*	YES *DA*	NO *NE*
I had my kidneys, urinary bladder and urinary tract operated *Operisala sam bubrege, mokraćnu bešiku, mokraćovode.*	NO *NE*	YES *DA*
I have a spinal column injury, a severe head injury or previous spine surgery or head surgery *Imam oštećenje kičmenog stuba, težu povredu glave ili prethodne operacije na kičmi ili glavi.*	NO *NE*	YES *DA*
I had frequent urinary tract inflammations/*Imala sam česte upale mokraćnih puteva.*	NO/*NE*	YES/*DA*
I have diabetes, I was treated for alcoholism/*Imam šećernu bolest, lečila sam se od alkoholizma.*	NO/*NE*	YES/*DA*
I had gynecological surgeries (removal of the uterus, plastics of the vagina) *Imala sam ginekološke operacije (vađenje materice, plastika vagine).*	NO *NE*	YES *DA*
I had/have urine leakage during sleep/*Mokraću sam gubila ili sada gubim u snu.*	NO/*NE*	YES/*DA*
I have urine leakage or have a strong urinary urgency when I wash my hands *Umokrim se ili imam jak nagon na mokrenje kada perem ruke u vodi.*	NO *NE*	YES *DA*
I urinate more than 10 times during 24 hours/*Mokrim više od 10 puta u toku 24 sata.*	NO/*NE*	YES/*DA*
It often happens that I have urine leakage by the time I get to the toilet *Često mi se dešava da se umokrim pre nego što stignem do toaleta.*	NO *NE*	YES *DA*

Legend: SS - stress score, US - urgency score/*Legenda: SS - stres skor, US - urgency score*

It included patients who sought surgical treatment for POP grade 2 to 4 and coexisting symptomatic SUI. Patients with POP grade 1, patients with urgent or mixed incontinence, as well as patients with previous small pelvic surgeries were excluded from the research. Following a verbal explanation, detailed gynecological, obstetrical and social medical data were taken, and physical examination was performed. The Pelvic Organ Prolapse-Quantification (POP-Q) system was used to determine the degree of genital prolapse [15].

All patients completed a questionnaire to determine the "stress and urge" score, which has been used at our Clinic for many years, including 18 specific questions related to the etiology and symptoms of involuntary urinary leakage **(Table 1)**. The first nine questions are related to stress, while the other nine are related to the urgency urinary incontinence. The questionnaire was a closed one where patients answered the questions with YES or NO. The score for stress and UUI cannot be higher than nine. If the stress score equals or is higher than 4 and the urge score is less than 4, the findings are in favor of stress incontinence. Tests for objectification of UI were performed as well. All patients underwent vaginal hysterectomy with anterior and posterior colporrhaphy.

Patients also completed the Urinary Distress Inventory-6 (UDI-6) and Urinary Impact Questionnaire-7 (UIQ-7) during the follow-up examination, a year after the surgery. The UDI-6 assesses the lower urinary tract dysfunctions. It contains six questions intended to measure the severity of symptoms of UI grade 1 (not at all) to 4 (quite a bit). The UIQ-7 contains 7 questions intended to investigate the impact of UI on all social spheres in women: household and leisure activities, physical recreation, bus or car travel lasting longer than 30 minutes, taking part in social events, emotional health and feeling of frustration. The answers also ranged from 0 (not at all) to 3 (severe). The score of both questionnaires was calculated by applying the appropriate formula. Percentage, mean value and standard deviation were used in data processing.

Results

A total of 50 patients were included in the study. The general characteristics of patients are present-

Table 2. Characteristics of the study sample
Tabela 2. *Karakteristike ispitane grupe*

Age (mean ± standard deviation - SD)/*Godine (srednja vrednost ± standardna devijacija)*	**61.08±7.87**
< 50 years (*godina)*	6%
50 - 70	80%
> 70	14%
Number of childbirths/*Broj porođaja*	
1	18%
2	58%
3	14%
= > 4	10%
Infant birth weight (grams) (mean ± SD):	**3672.6 ± 5613.96**
Težina dece na rođenju (g) (srednja vrednost ± standardna devijacija)	
< 2500 g	1.92%
2500 - 3499 g	37.50%
3500 - 4499 g	58.66%
> 4500 g	1.92%
Body Mass Index (mean ± SD)/*Indeks telesne mase (srednja vrednost ± standardna devijacija)*	**27.15 ± 2.77**
18.5 - 24.9	22%
25 - 29.9	52%
>30	26%
Hormonal status/*Hormonski status*	
Premenopausal/*Premenopauza*	12%
Postmenopausal/*Postmenopauza*	88%
History of chronic cough (Yes)/*Hronični kašalj u anamnezi (Da)*	28%
Pelvic organ prolapse preoperatively/*Stepen genitalnog spada preoperativno*	
Grade 2/*Stepen 2*	38%
Grade 3/*Stepen 3*	40%
Grade 4/*Stepen 4*	22%
Anatomical recurrence at 1-year (POP-Q > grade 1)	**30%**
Recidiv spada godinu dana posle operacije (POP-Q> stepen 1)	
Anatomical recurrence in anterior compartment at 1 year (POP-Q > grade 1)	**40%**
Recidiv spada prednjeg zida vagine godinu dana posle operacije (POP-Q> 1)	
UDI-6 at 1 year postoperatively/*UDI-6 godinu dana posle operacije*	**29.0 ± 10.8**
UIQ-7 at 1 year postoperatively/*UIQ-7 godinu dana posle operacije*	**3.7 ± 13.6**

Legenda: UDI-6 – *Urinary distress inventory, UIQ-7 – Urinary Impact Questionnaire, POP-Q – Pelvic organ prolapse-quantification*

ed in **Table 2**. The average age of the examinees was 61 years. The patients' age of 50 – 70 years accounted for 80% of the sample. On average, they gave birth to two children, whose mean birth weight was 3.672 grams. The patients' body weight ranged from 59 to 90 kg (mean - 71.4 kg). The average body mass index was 27.15, with 52% of overweight and 26% of obese patients. Eighty-eight percent of patients were postmenopausal; the average duration of menopause was 9.58 years.

According to the POP-Q classification, 38% of patients had POP grade 2, 40% had POP grade 3, while 22% had POP grade 4. One year after surgery, 40% of patients presented with a recurrence of the cystocele: 15 patients (30%) had cystocele stage 2, two patients (4%) had a cystocele stage 3 and one patient had cystocele stage 4.

A year after the surgery, the average value of UDI-6 questionnaire was 29.0 +/- 10.8, while the average value of UIQ-7 questionnaire was 3.7 +/- 16.3. After the surgery, 6 patients (12%) had persistent SUI and 4 patients (8%) had UUI. Among patients with persistent SUI, 4 patients reported recurrent symptoms and two patients reported pronounced symptoms of SUI and reoperation was required **(Table 2).**

Discussion

The treatment of SUI and POP may be conservative (behavior and lifestyle modifications, pelvic floor muscle exercises, bladder training techniques and use of pessary and medications) and surgical [16, 17]. The treatment depends on the severity of the symptoms and the grade of genital descent. If the symptoms are less pronounced, it is recommended to start with conservative methods. However, the choice of the therapeutic method depends on what the patient wants and expects from the treatment, her commitment to carrying out the prescribed therapy, accepting the risk of side effects and complications of therapy, as well as her financial situation. If a woman has followed all the conservative treatment methods, but still has symptomatic SUI and POP, in case of a higher grade of POP or if a woman does not want to apply the recommended conservative treatment methods, surgical treatment is proposed [16]. Surgical treatment of POP and SUI can be vaginal or abdominal. Vaginal operations are preferred at our Clinic.

Some authors recommend that if the SUI and POP problem is treated vaginally, fascial repair or mesh reinforcement should be combined with a midurethral sling, because the SUI persistence rate is lower than when only the prolapse operation is performed [9, 12]. If only prolapse surgery without continence surgery is performed in women with SUI and POP, the persistent urinary incontinence rate is 36 – 71%, on average 63% [9]. In his study, Borstad et al. found that 27% of women recover from SUI after just a prolapse operation [18]. Lensen found that 38% of women with symptomatic SUI are cured after just a prolapse surgery [19]. If a woman has both a prolapse surgery and continence surgery, then the percentage of postoperative SUI is up to 40%, on average 11% [9]. However, the fact which cannot be ignored is that after the combination of prolapse and incontinence surgery, negative effects such as overactive bladder symptoms, obstructive voiding and complications, are more common, can call into question the outcome of this surgical procedure [12].

Our research has shown that the quality of life improves after the surgical treatment of POP and SUI, which is in accordance with the results of other authors [12]. Anatomical recurrence at one year after vaginal hysterectomy was 30%, while anatomical recurrence in anterior compartment was 40%, which is in line with the results of other authors [20, 21]. According to Lensen's research, anatomical recurrence in the anterior compartment protects women against SUI postoperatively [19].

In our research, 20% of women had a UI problem a year after the surgery, 12% had a persistent SUI, while 8% of patients developed urgent incontinence. However, this problem was pronounced and affecting the quality of life only in three patients. In two patients with SUI the condition required a new incontinence surgery. According to the research of Harvie et al., for women with POP, coexisting UUI and fecal incontinence have a greater impact on the quality of life than coexisting SUI [22].

Our results may be explained by the fact that our patients think of SUI problem as an integral part of life and tolerate symptoms due to the fear of reoperation, but also because of a poor financial situation. We are a poor society and, in most cases, in women with genital descent and SUI, we try to solve the problem with a classical operation. In case of SUI persistence after the surgery, we recommend corrective continence surgery.

Conclusion

This research has shown that the classical surgical treatment of genital organ descent leads to improvement in the quality of life of patients with pelvic organ prolapse and stress urinary incontinence. In societies with lower standard of living, like ours, classic vaginal hysterectomy with anterior colporrhaphy is still the treatment of choice for patients with pelvic organ prolapse and stress urinary incontinence. More expensive methods for pelvic organ prolapse and stress urinary incontinence correction are considered in patients where the desired results were not achieved by the primary operation.

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EFFECTS OF CATARACT SURGERY ON SHORT-TERM AND LONG-TERM INTRAOCULAR PRESSURE FLUCTUATIONS IN NON-GLAUCOMATOUS AND MEDICALLY CONTROLLED PRIMARY OPEN-ANGLE GLAUCOMA PATIENTS

UTICAJ OPERACIJE KATARAKTE NA KRATKOROČNE I DUGOROČNE FLUKTUACIJE INTRAOKULARNOG PRITISKA KOD NEGLAUKOMSKIH PACIJENATA I KOD MEDIKAMENTNO LEČENIH PACIJENATA OBOLELIH OD PRIMARNOG GLAUKOMA OTVORENOG UGLA

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Summary

Introduction. It has been recognized that cataract surgery leads to a reduction of intraocular pressure, both in healthy and in glaucoma patients. This prospective interventional clinical study aimed to investigate the effects of cataract surgery on intraocular pressure and its short- and long-term fluctuations in medically controlled primary open-angle glaucoma patients and non-glaucomatous patients. **Material and Methods.** Two groups of 31 patients (31 eyes) were studied. The observed group included patients with glaucoma and cataract, and the control group included patients with senile cataract only. The intraocular pressure was measured three times daily pre- and at 1, 3 and 6 months postoperatively. **Results.** In both groups, a significant postoperative reduction in both mean and maximum intraocular pressure. Six months after surgery, in the observed group the average and maximum intraocular pressure reduction levels were -2.73 ± 1.91 mmHg and -3.16 ± 2.19 mmHg, and -2.26 ± 1.71 mmHg and -2.53 ± 1.70 mmHg in the control group. In the observed group, at 3 and 6 months after surgery, a significant reduction in short-term fluctuations was observed. Six months after surgery, short-term fluctuations decreased by -1.04 ± 2.20 mmHg compared to preoperative. Postoperatively, in the observed group, long-term fluctuations of average and maximum intraocular pressure were 2.69 ± 2.15 mmHg and 2.88 ± 2.22 mmHg, respectively, and in the controls they were 2.02 ± 1.28 mmHg and 2.42 ± 1.47 mmHg, showing no significant differences between groups. **Conclusion.** In patients with primary open-angle glaucoma, cataract surgery results in a statistically significant reduction in both average and maximum intraocular pressure as well as of short-term fluctuations.

Key words: Phacoemulsification; Cataract; Intraocular Pressure; Glaucoma, Open-Angle; Time Factors

Sažetak

Uvod. Poznato je da se operacijom katarakte postiže sniženje intraokularnog pritiska, kako kod zdravih tako i kod obolelih od različitih oblika glaukoma. Cilj ove prospektivne intervencijske kliničke studije bio je da ispitamo uticaj operacije katarakte na intraokularni pritisak i njegove kratkoročne i dugoročne fluktuacije kod medikamentno lečenih obolelih od primarnog glaukoma otvorenog ugla i kod pacijenata bez glaukoma. **Materijal i metode.** Formirane su dve grupe od po 31 pacijenta (31 oko). Posmatranu grupu činili su oboleli od glaukoma i sa kataraktom, a kontrolnu, pacijenti samo sa senilnom kataraktom. Intraokularni pritisak je meren tri puta dnevno preoperativno, kao i postoperativno prvi, treći i šesti mesec. **Rezultati.** Postoperativno, u obe grupe je nastupilo statistički značajno sniženje i prosečnog i maksimalnog intraokularnog pritiska. U šestom mesecu, redukcija prosečnog i maksimalnog intraokularnog pritiska u posmatranoj grupi iznosila je -2,73 ± 1,91 mmHg i -3,16 ± 2,19 mmHg, a u kontrolnoj grupi, -2.26 ± 1,71 mmHg i -2,53 ± 1,70 mmHg, redom. U posmatranoj grupi, u toku trećeg i šestog meseca, nastupila je statistički značajna redukcija i u kratkoročnim fluktuacijama. U šestom mesecu, kratkoročne fluktuacije bile su niže za -1,04 ± 2,20 mmHg u poređenju sa preoperativnim. Dugoročne fluktuacije prosečnog i maksimalnog intraokularnog pritiska u posmatranoj grupi, postoperativno, iznosile su 2,69 ± 2,15 mmHg i 2,88 ± 2,22 mmHg, redom, a u kontrolnoj, 2,02 ± 1,28 mmHg i 2,42 ± 1,47 mmHg, redom, bez statistički značajne razlike između grupa. **Zaključak.** Kod osoba obolelih od primarnog glaukoma otvorenog ugla operacija katarakte dovodi do statistički značajnog sniženja i prosečnog i maksimalnog intraokularnog pritiska kao i kratkoročnih fluktuacija.

Ključne reči: fakoemulzifikacija; katarakta; intraokularni pritisak; glaukom otvorenog ugla; vremenski faktori

Introduction

Primary open-angle glaucoma (POAG) is the most common type of glaucoma, accounting for 74% of all patients with glaucoma [1]. Elevated intraocular pressure (IOP) is considered to be the most important risk factor for the development and progression of glaucomatous optic neuropathy, and

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Abbreviations

POAG – primary open-angle glaucoma
IOP – intraocular pressure
PHACO – phacoemulsification
BCVA – best corrected visual acuity
WDT – water drinking test
Max.IOP – maximum intraocular pressure
Min.IOP – minimum intraocular pressure
Av.IOP – average intraocular pressure

reduction of IOP is the only proven approach to prevent or slow down the progression of the disease [2, 3]. In addition to elevated IOP, wide short-term and long-term IOP fluctuations have been recognized as an independent risk factor for the development and progression of the disease [4, 5].

The IOP can be lowered by medications, laser or filtering surgery. In recent years, it has been recognized that ultrasound cataract surgery, phacoemulsification (PHACO), leads to IOP reduction, both in healthy and in patients with various types of glaucoma [6–9]. It was found that preoperative IOP was directly associated with postoperative IOP reduction. A higher preoperative IOP is associated with a greater IOP decrease after surgery [10, 11]. There is strong evidence to indicate PHACO as the first line treatment for patients with primary angle-closure glaucoma [12, 13]. A significant postoperative IOP reduction is also achieved in patients with pseudoexfoliation glaucoma [9]. However, there is still insufficient evidence to suggest cataract surgery as a treatment option for POAG patients [14, 15]. These conclusions were drawn from the results of numerous retrospective studies investigating the preoperative and postoperative IOP values obtained most commonly by one measurement during patients' visits in different post-operative follow-ups [9]. Inspired by this knowledge, we performed a diurnal IOP curve, and examined the effects of cataract surgery on the IOP and its short-term and long-term fluctuations in medically controlled POAG patients, with the hypothesis that cataract surgery will lead to reduction of IOP and its fluctuations, and as such, could be considered as an adjuvant therapy for POAG patients.

Material and Methods

From December 2016 to December 2018, 62 patients were included in a prospective interventional clinical study conducted at the Eye Clinic of the University Clinical Center of the Republic of Srpska, Bosnia and Herzegovina. The study was approved by the institutional Ethics Committee and carried out in accordance with the Helsinki Declaration. Two groups of 31 patients (31 eyes) were made. An experimental group, named *POAG + Cataract*, included medically treated patients with clinically significant cataract and earlier detected structural and functional changes defined by POAG. A control group, named *Cataract*, included patients referred for elective senile cataract surgery without any other ophthalmic disorder, who underwent bilateral gonioscopy to determine angle openness and were classified as Shaffer's grade 3 or 4 and with bilateral IOP ≤ 21 mmHg [16].

General inclusion criteria: a signed Informed Consent Form, operative and postoperative course without complications, and participation until the end of the study.

Exclusion criteria: ocular trauma, inflammation, retinal disorder, non-glaucomatous optic neuropathy, long-term use of corticosteroids (systemic or topical), prevous intraocular surgery or laser intervention; suffering from normal tension glaucoma, POAG subtype.

The patient's name, surname, age, gender, best corrected visual acuity (BCVA) measured by using Snellen optotype (value in decimal), goniscopic grading system (Shaffer grade in scale), openness grade, IOP measured with Goldmann applanation tonometer, and diurnal IOP curve test (IOP measurement at 07:30, 13:30 and 19:30), and the number and type of glaucoma therapy were reported.

The maximum (Max.IOP) and minimum IOP (Min.IOP) were determined from the daily IOP curve. The following formulas were used:

Average IOP (AVIOP) = $(IOP_{07:30} + IOP_{13:30} + IOP_{19:30})/3$

Short-term IOP fluctuation = Max.IOP – Min.IOP

The long-term fluctuation (5-month period) of the average and maximum IOP was calculated as the difference between the highest and the lowest mean of three measurements obtained at 1, 3 and 6 months after surgery.

Phacoemulsification (in-the-bag, phaco chop) technique was performed in one eye of all patients under topical anesthesia, using the Stellaris Vision Enhancement System (Bausch & Lomb) and intraocular lens (Akreos Adapt AO, Bausch & Lomb) was implanted. Eye selection was based on the worse BCVA. Phacoemulsification parameter Absolute phaco time were noted at the end of surgery and evaluated.

In order to avoid potential effects of altered topical antiglaucoma therapy on postoperative IOP, all POAG patients postoperatively continued using their preoperatively used antiglaucoma therapy.

Clinical examinations, diagnostic measurements and all surgeries were performed by the same surgeon (B.M.)

Statistical analysis was performed using IBM SPSS Statistics 21.0 software. The Pearson's chi-square test, Student's t-test, Mann-Whitney U test, Wilcoxon signed-rank test and Pearson's correlation coefficient test were used. Data were statistically processed and $p < 0.05$ was considered statistically significant.

Results

The study included 62 patients, of which 30 (48.39%) women and 32 (51.61%) men. The mean age for the *POAG + Cataract* group was 74.35 ±

9.75 (range 44.0 - 88.0) and for the *Cataract* group 71.90 ± 7.10 (range 54.0 - 83.0), without a significant difference between the groups (p = 0.059, Mann-Whitney U test).

There were no significant differences between the groups in preoperative BCVA, as well as at 1, 3 and 6 months after surgery (p = 0.117; *P* = 0.170; p = 0.508; p = 0.232, respectively; Mann-Whitney U

Table 1. The average IOP, the maximal IOP and the short-term IOP fluctuations according to the diurnal IOP curve before surgery and during the post-operative monitoring period
Tabela 1. *Prosečni intraokularni pritisak, maksimalni intraokularni pritisak i kratkoročne fluktuacije intraokularnog pritiska na osnovu dnevne krive pre operacije i u postoperativnom periodu praćenja*

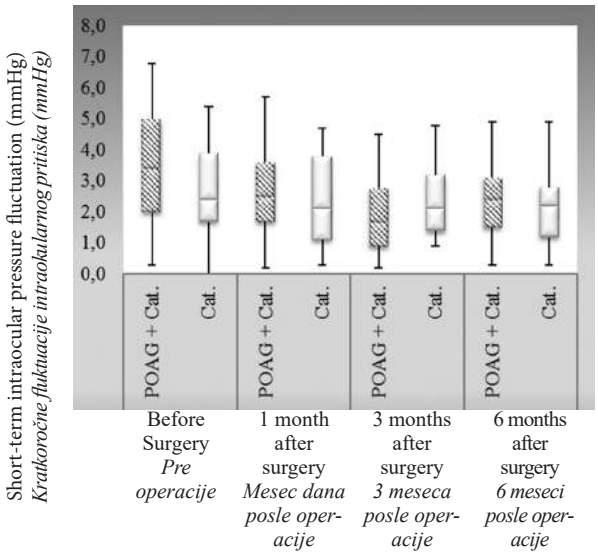
Group Grupa (n)	Av. IOP (mmHg) Mean ± SD (range) *Prosečni IOP (mmHg) prosek ± SD (raspon)*	p *	Max. IOP (mmHg) Mean ± SD (range) *Maksimalni IOP (mmHg) prosek ± SD (raspon)*	p *	Short-term IOP fluctuation (mmHg) Mean ± SD (range) *Kratkoročna fluktuacija IOP (mmHg) prosek ± SD (raspon)*	p *
Before surgery/*pre operacije*						
POAG +Cataract (n=31)	17.19 ± 1.81 (13.7 - 21.1)	< 0.001	18.80 ± 2.21 (14.0 - 25.0)	< 0.001	3.35 ± 1.68 (0.3 - 6.8)	0.160
Cataract (n=31)	14.53 ± 2.04 (10.7 - 19.7)		15.96 ± 2.19 (12.1 - 20.3)		2.79 ± 1.46 (0.0 - 5.4)	
1 month after surgery/*1 mesec nakon operacije*						
POAG+Cataract (n=31)	16.08 ± 2.47 (10.2 - 21.4)	< 0.001	17.36 ± 2.77 (11.7 - 23.8)	< 0.001	2.66 ± 1.37 (0.2 - 5.7)	0.468
Cataract (n=31)	13.53 ± 2.22 (9.6 - 17.6)		14.76 ± 2.43 (10.1 - 19.6)		2.41 ± 1.34 (0.3 - 4.7)	
3 months after surgery/*3 meseca nakon operacije*						
POAG+Cataract (n=31)	14.79 ± 2.35 (9.3 - 18.9)	< 0.001	15.71 ± 2.45 (9.8 - 19.5)	< 0.001	1.96 ± 1.22 (0.2 - 4.5)	0.152
Cataract (n=31)	12.09 ± 2.03 (7.7 - 15.6)		13.29 ± 2.45 (8.1 - 17.9)		2.39 ± 1.08 (0.9 - 4.8)	
6 months after surgery/*6 meseci nakon operacije*						
POAG+Cataract (n=31)	14.47 ± 2.06 (10.1 - 18.9)	< 0.001	15.64 ± 2.12 (9.8 - 19.5)	< 0.001	2.32 ± 1.07 (0.3 - 4.9)	0.786
Cataract (n=31)	12.27 ± 1.89 (9.4 - 15.8)		13.43 ± 2.04 (10.2 - 16.6)		2.24 ± 1.17 (0.3 - 4.9)	

Legend: POAG – primary open-angle glaucoma; Av. – average; IOP – intraocular pressure; Max. – maximal; SD – standard deviation; * - Student's t–test
Legenda: POAG – primarni glaukom otvorenog ugla; Av.- prosek; IOP – intraokularni pritisak; Max. – maksimalan; SD – standardna devijacija; - Studentov t-test*

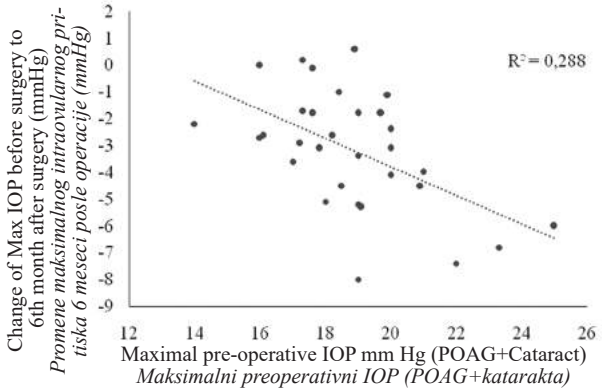
Table 2. Results of Student's t-test for statistical reduction of the average IOP, maximal IOP and short-term IOP fluctuations in the postoperative follow-up period in relation to pre-operative values
Tabela 2. *Rezultati Studentovog t-testa za statističko sniženje prosečnog intraokularnog pritiska, maksimalnog intraokularnog pritiska i kratkoročnih fluktuacija intraokularnog pritiska u postoperativnom periodu praćenja u odnosu na preoperativne vrednosti*

p (Student's t-test)/p (Student-ov t-test)					
Average IOP *Prosečni IOP*		Maximal IOP *Maksimalni IOP*		Short-term IOP fluctuation *Kratkoročna fluktuacija IOP*	
POAG + Cat.	Cataract	POAG + Cat.	Cataract	POAG + Cat.	Cataract
Before surgery - 1 month after surgery/*Pre operacije - 1 mesec nakon operacije*					
0.041	0.003	0.024	0.001	0.122	0.212
Before surgery - 3 months after surgery/*Pre operacije - 3 meseca nakon operacije*					
< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	0.194
Before surgery – 6 months after surgery/*Pre operacije - 6 meseci nakon operacije*					
< 0.001	< 0.001	< 0.001	< 0.001	0.014	0.088

Legend: POAG – Primary open angle glaucoma; Cat. – Cataract; IOP – intraocular pressure
Legenda: POAG – primarni glaukom otvorenog ugla; Cat. – katarakta; IOP – intraokularni pritisak



Graph 1. Short-term intraocular pressure fluctuations before surgery and during the monitoring period
Grafikon 1. *Kratkoročne fluktuacije intraokularnog pritiska pre operacije i u periodu praćenja*
Legend: POAG - Primary open angle glaucoma; Cat. – Cataract
Legend: POAG – primarni glaukom otvorenog ugla; Cat.- katarakta



Graph 2. Relationship between IOP level 6 months after surgery and preoperative maximum IOP in the POAG + Cataract group
Grafikon 2. *Odnos promene intraokularnog pritiska šest meseci nakon operacije i preoperativnog maksimalnog intraokularnog pritiska u grupi POAG+Cataract*
Legend: POAG – primary open angle glaucoma; Cat. – cataract; Max. – maximum; IOP – intraocular pressure;
Legenda: POAG – primarni glaukom otvorenog ugla; Cat. – katarakta; Max. – maksimalan; IOP – intraokularni pritisak;

test). In both groups, a significant increase in mean BCVA was observed postoperatively compared to baseline ($p < 0.001$; Wilcoxon's test). Mean preoperative BCVA in *POAG + Cataract* group was 0.22 ± 0.15 (range 0.0 - 0.5) and in *Cataract* group 0.16 ± 0.15 (range 0.0 - 0.6). Mean postoperative BCVA at the 6th month in *POAG + Cataract* group was 0.93 ± 0.13 (range 0.5 - 1.0) and in *Cataract* group 0.97 ± 0.06 (range 0.8 - 1.0).

The mean values of the Av.IOP as well as Max. IOP were significantly higher in the *POAG + Cataract* group preoperatively, as well as on each postoperative measurement. A significant reduction in the mean Av.IOP and mean Max.IOP was observed in both groups during the postoperative follow-up compared to baseline.

There was no significant difference in the mean short-term IOP fluctuation between the examined groups neither pre- nor post-surgery. A significant reduction in mean short-term IOP fluctuations at 3 and 6 months after surgery was observed in the *POAG + Cataract* group, compared to baseline. The above results are shown in **Table 1**, **Table 2** and **Graph 1**.

The correlation between preoperative Max.IOP and IOP was investigated 6 months after surgery. The Pearson's coefficient showed a moderate negative correlation (r1 = - 0.54) in the *POAG + Cataract* group, and a relatively weak negative correlation (r2 = - 0.44) in the *Cataract* group. **Graph 2** shows the linear regression analysis for the *POAG + Cataract* group.

Table 3. Long-term fluctuations of the average and maximum IOP during the postoperative period
Tabela 3. *Dugoročne fluktuacije prosečnog i maksimalnog intraokularnog pritiska u postoperativnom periodu*

Group *Grupa*	Mean ± Standard Deviation *prosek ± standardna devijacija*	Median (interquartile range) *Medijana (interkvantilni raspon)*	Minimum – Maximum *Minimum - maksimum*	Mann-Whitney U test p-value *Man-Vitnijev U test p-vrednost*
Long-term fluctuations of the Av.IOP in the postoperative period (mmHg) *Dugoročna fluktuacija Av.IOP-a u postoperativnom periodu (mmHg)*				
POAG + Cat.	2.69 ± 2.15	2.5 (1.0, 3.3)	0.3 - 11.4	0.218
Cataract	2.02 ± 1.28	1.9 (1.1, 3.0)	0.1 - 4.7	
Long-term fluctuations of the Max.IOP in the postoperative period (mmHg) *Dugoročna fluktuacija Max.IOP-a u postoperativnom periodu (mmHg)*				
POAG + Cat.	2.88 ± 2.22	2.3 (1.7, 3.5)	0.5 - 12.7	0.499
Cataract	2.42 ± 1.47	2.1 (1.1, 3.4)	0.1 - 6.3	

Legend: POAG – primary open angle glaucoma; Cat. – cataract; Av. – average; IOP – intraocular pressure; Max. – maximum
Legenda: POAG – primarni glaukom otvorenog ugla; Cat. – katarakta; Av. – prosečni; IOP - intraokularni pritisak; Max. – maksimalan

Discussion

In recent years, positive effects of cataract surgery on IOP reduction in both glaucoma and non-glaucomatous patients have been established. Since the goal of glaucoma treatment is to achieve target IOP, low enough to stop the progression of glaucoma, there is a growing interest in studies on the effects of cataract surgery on IOP. This is understandable, bearing in mind that antihypertensive drugs often cause numerous and serious systemic and/or local side effects, that the effect of laser trabeculoplasty is diminished in time, and that filtration surgeries carry an increased risk of intraoperative and postoperative complications such as early and late hypotension, hypertension, bleeding, inflammation, accelerated cataract formation, and need for reoperation.

As a biological phenomenon, intraocular pressure is not a fixed value, but fluctuates over a 24-hour cycle and from one visit to another [17]. Parameters such as average and maximum IOP (peak) show significant short-term and long-term fluctuations, and therefore single IOP measurement during so-called office hours is insufficient to characterize the IOP profile of patients with glaucoma [18].

Various extraocular and intraocular devices with integrated pressure sensors are designed in order to gather data on IOP fluctuations as accurate as possible. Due to the number of shortcomings, such as impracticality, discomfort, data presentation as well as high cost, these devices are not applicable in daily clinical practice and at preset they remain only a research tool.

Some of the studies have found a strong correlation between IOP peaks in provocative water drinking test (WDT) and IOP diurnal peaks, suggesting WDT as a suitable alternative to 24-hour measurements of IOP [19, 20].

Diurnal IOP curve test is reliable when performed by an trained examiner, relatively inexpensive, but also impractical both for the examiner and the patient (several visits during the day or hospital admission) so it is rarely applied in everyday clinical practice [21].

There are still controversial data whether Av. IOP, Max.IOP, short-term or long-term IOP fluctuations, are the most reliable and consistent predictors of glaucoma. Different sample sizes, inclusion-exclusion criteria, lack of a standard IOP fluctuation definition, IOP measurement time, study design, and duration of study are just some of the reasons for the controversies.

Our research examined the effect of PHACO on the abovementioned IOP parameters.

We found that cataract surgery resulted in a significant decrease in both MeanIOP and Max.IOP in both groups in the first month following surgery, with a further downward trend **(Tables 1 and 2)**. Six moths after surgery, in the POAG patients , the mean Av.IOP value was lower by -2.73 ± 1.91 mmHg (-15.82%) compared to the same preoperative parameter, and in the control group it decreased by-2.26 ± 1.71 mmHg (- 15.55%) **(Table 1)**.

At 6 months postoperatively, the mean value of Max.IOP in POAG patients was reduced by -3.16 ± 2.19 mmHg (- 16.81%) compared to baseline, and in the control group by -2.53 ± 1.70 mmHg (- 15.83%) **(Table 1)**. The obtained postoperative reductions are consistent with the results of other studies. Chen et al. found a postoperative IOP drop by -2.3 mmHg (range -1.1 mmHg to - 4.0 mmHg), that is, -13% (range -7% to -22%) [9]. The study by Armstrong et al. found postoperative IOP drops by 12%, 14%, 15% and 9% after 6, 12, 24 and 36 months of follow-up, respectively [22].

According to our knowledge, previous studies on this issue analyzed the preoperative and postoperative IOP readings recorded on the basis of one measurement during the visit and values of the Av.IOP and Max.IOP, considering the fact that derivatives of the IOP daily curve were not available. Therefore, according to our knowledge, there are no available data to be compared with our research results, making this research unique.

Studies have found that the range of postoperative IOP reduction in non-glaucomatous subjects ranged from 1.5 mmHg to 3.5 mmHg, which is consistent with our results **(Table 1)** [7, 11].

The significance of large daily fluctuations and the determination of IOP peaks as factors associated with the glaucoma progression were also indicated by Asrani et al. who, with seemingly compensated 105 POAG eyes with an average IOP of 17.6 ± 3.2 mmHg, found a fluctuation of 10.0 ± 2.9 mm Hg when IOP was measured 5 times daily [23]. Barkana et al., in a 24-hour study including 32 patients, demonstrated that peak IOP was recorded outside of office hours in at least 1 eye in 69% of patients with POAG, resulting in immediate treatment change in 36% of eyes [24]. Jiang et al. investigated Max.IOP, standard deviation of IOP, range of IOP and mean IOP as predictors of glaucoma in 3.666 subjects during a 4-year follow up and identified Max.IOP as the most consistent parameter [25].

We also found Max.IOP to be a more clinically important parameter than Av.IOP, whereas the postoperative Max.IOP reduction was in correlation with preoperative IOP, concluding that patients with a higher baseline IOP experienced greater postoperative IOP reduction **(Graph 1)**, which is in line with other studies that investigated the correlation between preoperative and postoperative IOP reduction [10, 11, 15].

In the *POAG + Cataract* group, the greatest reduction of -8 mmHg (-42.11%), with a preoperative Max. IOP of 19 mmHg, was observed in one patient **(Graph 2)**. Based on this data, there is a need for additional research on the identification of patients with a high response, where there is a chance to achieve an adequate IOP reduction by PHACO.

In our study, POAG patients had the greatest short-term fluctuations preoperatively, 3.35 ± 1.68 mmHg

(Table 1) and a significant IOP reduction in relation to baseline occurred at the 3rd and 6th postoperative months **(Table 2)**.

The goals of our study are similar to the study of Saccà et al., who analyzed diurnal IOP curve data preoperatively and at the 1st and 6th months postoperatively in 57 non-glaucomatous and 51 POAG patients. Phacoemulsification was performed in 13 non-glaucomatous and 15 POAG patients. The rest of the patients were operated by other techniques. Six months after PHACO, IOP has reduced by – 3.03 mmHg in non-glaucomatous patients, and by – 4.39 mmHg in POAG patients. In POAG group, postoperative reduction by -3.33 mmHg in daily fluctuation occurred 6 months after surgery in comparison to preoperative values [26].

Reduction of short-term IOP fluctuations by -1.04 ± 2.20 mmHg (-30.74%) after 6 months in relation to the baseline, that we found, is not in agreement with Saccà's result, and one of the possible explanations is the sample size, our sample being larger by 51.61% (16 patients).

In order to assess effects of cataract surgery on long-term (monthly) fluctuations of IOP, preoperative data on long-term (monthly) fluctuations are needed as well. Lacking this information, our results on postoperative long-term fluctuations showed that they are uniform among the groups and relatively at low-range for the Av.IOP and Max.IOP **(Table 3)**. We also noted that in the *POAG + Cataract* group there were individuals with long-term fluctuations exceeding the desired low ranges and reaching 11.4 mmHg for Av.IOP and 12.7 mmHg for Max.IOP. This was not the case in the *Cataract* group in which the highest value of long-term fluctuation was 6.3 mmHg for the Max.IOP.

There are some limitations to this research: patients were not divided into groups according to preoperative IOP (e. g.: 9 – 14; 15 – 20; ≥ 21 mmHg) in order to examine the relation with postoperative reduction of IOP more accurately; no groups were formed based on glaucoma stage to determine the correlation between postoperative IOP reduction and stage of the disease; we did not have data on preoperative long-term IOP fluctuations.

Conclusion

Cataract surgery statistically significantly reduces both average and maximum intraocular pressure in patients with primary open-angle glaucoma and in non-glaucomatous patients. In primary open-angle glaucoma patients, a significant reduction in short-term intraocular pressure fluctuations was found three months after surgery and it retained six months after surgery. Long-term postoperative intraocular pressure fluctuations are short on average in primary open-angle glaucoma and in non-glaucomatous patients. The diurnal intraocular pressure curve is impractical to perform, but thanks to that procedure it is possible to identify patients in whom a clinically significant intraocular pressure reduction was achieved after surgery, which can lead to a reduction in the number of antiglaucoma medications or to exclude further filtration surgery if previously considered.

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ACUTE POISONING IN CHILDREN AND ADOLESCENTS HOSPITALIZED AT THE INSTITUTE OF CHILD AND YOUTH HEALTH CARE OF VOJVODINA BETWEEN 2015–2017

AKUTNO TROVANJE DECE I ADOLESCENATA HOSPITALIZOVANIH NA INSTITUTU ZA ZDRAVSTVENU ZAŠTITU DECE I OMLADINE VOJVODINE U PERIODU 2015–2017. GODINE

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Summary

Introduction. Acute pediatric poisoning has become an increasingly important medical emergency. This study was aimed at determining characteristics of acute poisoning in children and adolescents hospitalized at the Institute of Child and Youth Health Care of Vojvodina from 2015 to 2017. **Material and Methods**. Data were collected from medical records of all patients hospitalized for suspected acute intoxication at the Institute of Child and Youth Health Care of Vojvodina during the observed time. **Results.** This study included 519 patients hospitalized for suspected exposure to toxic substances. There were 49% male and 51% female patients. The intoxications had no seasonal features. The toxic substances were commonly taken orally. Medications were the most frequent cause of all poisonings, among which the most commonly reported were drugs for central nervous system disorders. Medications were the most frequent cause of poisoning in children and adolescents, as well as in children up to 10 years of age. In adolescents, the most prevalent cause of intoxication was alcohol abuse. Poisoning with suicidal intent and intentional self-poisoning without suicidal attempt were considerably more frequent in girls than in boys. There were no fatalities. **Conclusion.** It is of great importance to be familiar with the characteristics and circumstances of acute poisoning to plan and implement adequate preventive measures.

Key words: Poisoning; Acute Disease; Child; Adolescent; Risk Factors; Hospitalization; Accident Prevention; Alcohol Drinking; Drug-Related Side Effects and Adverse Reactions

Sažetak

Uvod. Akutna trovanja predstavljaju jedno od čestih urgentnih stanja u pedijatriji. Cilj ovog istraživanja bio je da se odrede karakterisike akutnih trovanja kod pacijenata hospitalizovanih u Institutu za zdravstvenu zaštitu dece i omladine Vojvodine u periodu od 2015. do 2017. godine. **Materijal i metode.** Podaci za istraživanje prikupljeni su iz medicinske dokumentacije pacijenata koji su zbog sumnje na akutnu intoksikaciju ksenobioticima bili hospitalizovani u Institutu za zdravsvenu zaštitu dece i omladine Vojvodine tokom posmatranog perioda. **Rezultati.** Ovom studijom obuhvaćeno je 519 pacijenata koji su hospitalizovani zbog izloženosti toksičnim materijama. Bilo je 49% pacijenata muškog i 51% pacijenata ženskog pola. Učestalost trovanja nije imala sezonski karakter. Dominantni put unosa ksenobiotika je peroralni. Najčešći etiološki činilac ukupnih trovanja su lekovi, među kojima su najčešći uzročnici trovanja bili lekovi za lečenje bolesti centralnog nervnog sistema. Najčešći uzročnik trovanja kod dece i adolescenata su lekovi, kao i kod dece uzrasta do 10 godina. Kod adolescenata najčešći uzrok trovanja je alkohol, unet u svrhu uživanja, koji su više konzumirali mladići nego devojke. Trovanja sa suicidalnom namerom i namerna samotrovanja bez suicidalne namere bila su značajno češća kod devojaka nego kod mladića. Nije bilo smrtnih slučajeva. **Zaključak.** Poznavanje karakteristika i okolnosti akutnih trovanja je značajno kako bi se mogle planirati i sprovoditi adekvatne preventivne mere.

Ključne reči: trovanje; akutna oboljenja; dete; adolescent; faktori rizika; hospitalizacija; prevencija nezgoda; konzumiranje alkohola; lekovima izazvani nus efekti i neželjene reakcije

Introduction

Acute poisoning accounts for a significant proportion of morbidity and mortality in children and adolescents and it is one of the most common medical emergencies in pediatrics [1–5]. Poisoning in children is always an emergency, regardless of the clinical signs and symptoms. The diagnosis is based on anamnestic and heteroanamnestic data, physical examination of the patient, as well as various laboratory and toxicological test results [6].

Poisonings are either intentional or accidental. Unintentional poisoning is rather common in childhood, and it is mainly caused by the drugs used by parents or caregivers, as well as by household chemicals [7–11]. Infants are at risk of accidental overdose due to miscalculation of drug dosage or parental drug misuse [10]. Pediatric poisoning is most common between 1 and

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5 years of age, when children are very active and curious, so they examine the world around them, and they can walk but their physical abilities are limited, and they are inexperienced [11]. The incidence of accidental poisonings decreases gradually with the age and cognitive development of the child, being considerably less frequent in adolescents [12]. Poisonings in adolescents are most commonly induced by substance abuse or as intentional self-poisonings (with or without suicidal intent), taken as a form of mechanism of overcoming a problem the adolescents face during the process of maturation [13]. Cases of intentional self-poisoning are usually non-fatal; however, those who survive the suicidal attempt may encounter severe health consequences which require long-term medical help and psycho-social support [14, 15].

This study was aimed at determining the age and gender distribution of patients, mode of poisonous substance intake, circumstances under which poisoning occurred, as well as groups of poisonous substances causing acute poisoning in children and adolescents hospitalized at the Institute of Child and Youth Health Care of Vojvodina.

Material and Methods

This retrospective study included data from medical records of all patients hospitalized for suspected acute substance-induced intoxication at the Institute of Child and Youth Health Care of Vojvodina in the period from January 1, 2015, to December 31, 2017.

The study data were taken from the medical records of the study sample, including the doctors' reports, medical histories, laboratory test results and other examinations. The following data were analyzed: number of patients exposed to toxic substances hospitalized in the study period, gender and age of patients, symptoms of poisoning on admission, month or period of the year when the patients were hospitalized, medical data on the type of consumed poisonous substance/s, mode and circumstances of intake, and treatment outcome. If a patient was admitted several times for suspected acute poisoning, each admission was considered as an individual case.

Microsoft Office Excel 2010 program was used to process the collected data statistically as mean values, standard deviations and percentage relations among groups. Statistical significance was determined by χ^2-test and $p \leq 0.05$ was considered statistically significant. The results are shown in graphs and tables.

Results

There were 540 patients (100%) hospitalized at the Institute of Child and Youth Health Care of Vojvodina for exposure to toxic substances in the period from 2015 to 2017. The highest number of poisoning cases was recorded in 2015 (199 cases), and then in 2016 (194), whereas in 2017 it was statistically significantly lower (147 cases of poisoning) (χ^2, $p \leq 0.05$). Out of 540 patients, 21 were hospitalized for suspected gas poisoning, what turned out to be a mass psychogenic reaction, so they were left out of the analysis and 519 patients were analyzed.

There were 259 male patients (49.90%) and 260 female patients (50.01%) during the observed time.

Gender and age distribution of patients is represented in **Graph 1**. The highest number of patients was between 14 and 16 years of age – 183 (33.33%). Chi-square test was performed to determine gender differences, and the difference was found to be statistically significant in the age group from 4 – 6 ($p \leq 0.01$), the boys having been affected by poisoning much more frequently, whereas the girls outnumbered boys in the age group from 14 – 16 ($p \leq 0.05$). During the observed period, no cases of poisoning were found in the newborns.

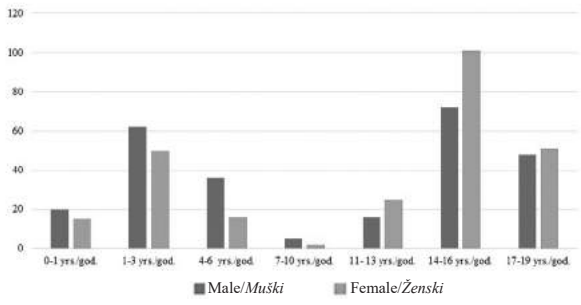
On admission, 323 patients (62.23%) had symptoms of poisoning and 196 patients (37.77%) were without symptoms, so the discharge diagnosis was non-toxic exposure. There were no available data regarding the period between the toxic substance exposure and hospital admission for all patients. Therefore, we cannot determine with certainty the patients who had non-toxic exposure in regard to those who received appropriate aid before and on admission.

The number of children and adolescents hospitalized for suspected acute poisoning was found to be similar when analyzed by months.

The majority of patients ingested toxic substances (483 - 93.06%), 20 patients (3.85%) inhaled them, while 11 (2.12%) patients combined oral and inhalation. In 4 patients (0.77%) the route of toxic substance intake was ingestion and skin absorption, and 1 patient (0.19%) subcutaneously injected the substance **(Graph 2)**.

Medications were the most common cause of poisoning, of which the following groups were most frequent: medications for the treatment of central nervous, cardiovascular, and musculoskeletal systems **(Graph 3)**.

Medications and household chemicals were the dominant etiological agents for poisoning during the first ten years of life, which were all accidental **(Table 1)**.



Graph 1. Age and gender structure of patients
Grafikon 1. *Struktura pacijenata prema polu i stawsnoj dobi*

Table 1. Age distribution of patients and etiological agents reported in medical history data
Tabela 1. *Struktura pacijenata prema uzrastu i etiološkim činiocima prijavljenim u anamnezi*

Age (yrs.)/*Uzrast (god.)*	0 - 1	1 - 3	4 - 6	7 - 10	11 - 13	14 - 16	17 - 19	Total/*Ukupno*
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Etiological agents/*Etiološki činioci*								
Medications/*Lekovi*	14 (40)	67 (59.82)	26 (50)	2 (28. 57)	23 (44.23)	69 (34.85)	21 (20.59)	222 (39.78)
Alcohol/*Alkohol*	/	/	1 (1.92)	2 (28. 57)	13 (25)	100 (50.50)	71 (69.61)	187 (33.51)
Household chemicals *Sredstva koja se koriste u domaćinstvu*	12 (34.28)	30 (26.78)	13 (25)	1 (14.29)	2 (3.85)	5 (2.52)	1 (0.98)	64 (11.47)
Toxic gases/*Štetni gasovi*	/	2 (1.79)	/	2 (28. 57)	13 (25)	11 (5.56)	2 (1.96)	30 (5.38)
Pesticides/*Pesticidi*	7 (20)	7 (6.25)	3 (5.77)	/	/	/	/	17 (3.05)
Psychoactive substances/*Psihoaktivne supstancije*	/	1 (0.89)	/	/	/	13 (6.57)	4 (3.92)	18 (3.23)
Poisonous plants and mushrooms *Otrovne biljke i gljive*	1 (2.86)	3 (2.68)	8 (15. 39)	/	1 (1.92)	/	1 (0.98)	14 (2.51)
Other/*Ostalo*	1 (2.86)	2 (1.79)	1 (1. 92)	/	/	/	2 (1.96)	6 (1.07)
Total/*Ukupno*	35 (100.00)	112 (100.00)	52 (100.00)	7 (100.00)	52 (100.00)	198 (100.00)	109 (100.00)	558 (100.00)

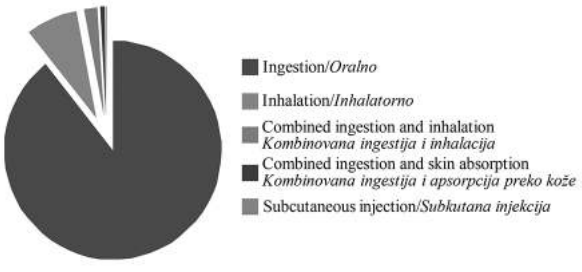
In adolescents, poisoning was most frequently caused by abuse of toxic substances including psychoactive substances (60.38%). Intentional self-poisoning was the second most frequent type of poisoning, in 32.91% of cases, whereas in 6.71% of cases poisoning was unintentional.

Circumstances of poisoning in adolescents, gender distribution, and causes were very specific and therefore they were analyzed separately **(Table 2)**. Due to acute poisoning by abuse of psychoactive substances, 110 male adolescents (58.1%) and 79 female adolescents (41.8%) were admitted, and the gender distribution was statistically significant (χ^2, $p \leq 0.05$). Intentional self-poisoning was the reason for admission of 87 female adolescents (84.47%) and 16 male adolescents (15.53%), the difference being statistically significant (χ^2, $p \leq 0.01$). There was no difference between genders in cases of accidental poisoning – 10 male adolescents (47.62%) and 11 female adolescents (52.38%).

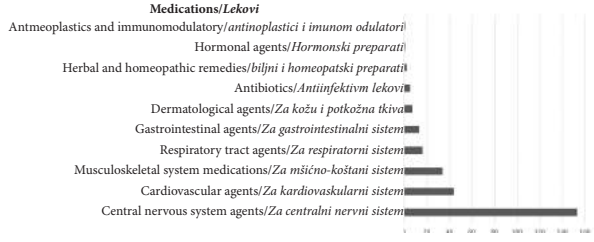
The most frequent causative agents of poisoning in adolescents were alcohol (168 cases, i.e. 53.67%) and medications (99 cases, i.e. 31.63%), and drug abuse was recorded in 21 patients (6.71%). Of all psychoactive substances, alcohol abuse was most frequent (168 cases, i.e. 88.89%), while medications were most common in intentional self-poisoning (89 cases, i.e. 86.41%).

Acute alcohol intoxication was the reason for admission of 96 male (57.14%) and 72 female adolescents (42.86%), and the gender difference was statistically insignificant (χ^2, $p = 0.06$). Acute poisoning caused by medications was recorded in 81 female adolescents (81.82%) and 18 male adolescents (18.18%), and the gender difference was statistically significant (χ^2, $p \leq 0.01$). Fifteen male and six female adolescents were hospitalized because of drug abuse, and the difference between male and female adolescents was statistically significant (χ^2, $p \leq 0.05$).

Out of 103 adolescents (100%) who reported that the reason of poisoning was their intent to commit



Graph 2. Route of xenobiotic intake
Grafikon 2. *Put unosa ksenobiotika*



Graph 3. Medication groups reported as the most frequent causes of acute poisoning according to anamnestic data
Grafikon 3. *Grupe lekova koji su najčešći uzročnici akutnih trovanja prema anamnestičkim podacima*

Table 2. Gender, causative agents and poisoning circumstances in adolescents according to medical history data
Tabela 2. *Struktura adolescenata prema etiološkim činiocima prijavljenim u anamnezi, polu i okolnostima trovanja*

Poisoning circumstances *Okolnosti trovanja*	Abuse psychoactive substances/*Unošenje psihoaktivnih supstancija u svrhu uživanja*		Intentional self-poisoning *Namerno samotrovanje*		Accidental poisoning *Nenamerno trovanje*		Total *Ukupno*
Gender/*Pol*	Male *Muški*	Female *Ženski*	Male *Muški*	Female *Ženski*	Male *Muški*	Female *Ženski*	
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	N (%)
Etiological agents *Etiološki činioci*							
Alcohol/*Alkohol*	96 (87.27)	72 (91.14)	/	/	/	/	168 (50.30)
Medications/*Lekovi*	1 (0.91)	0 (0.00)	12 (75)	77 (88.51)	5* (27.77)	4* (16.67)	99 (29.64)
Toxic gases/*Štetni gasovi*	/	/	/	/	11 (61.11)	15 (62.5)	26 (7.79)
Psychoactive substances (PAS) *Psihoaktivne supstance* (PAS)**	12 (10.91)	6 (7.59)	3 (18.75)	/	/	/	21 (6.29)
Alcohol and medications *Alkohol i lekovi*	/	1 (1.27)	1 (6.25)	6 (6.89)	/	1* (4.16)	9 (2.69)
Household chemicals *Sredstva koja se koriste u domaćinstvu*	/	/	/	4 (4.60)	1 (5.56)	4 (16.67)	9 (2.69)
Other/*Ostalo*	1 (0.91)	/	/	/	1 (5.56)	/	1 (0.60)
Total/*Ukupno*	110 (100.00)	79 (100.00)	16 (100.00)	87 (100.00)	18 (100.00)	24 (100.00)	334 (100.00)

* Ten adolescents reported having accidentally taken the medication. Two girls took more than 1 tablet of ibuprofen for severe headache and toothache, one girl reported side effects within therapeutic dose of metoclopramide and yet another one consumed a medication by mistake thinking it was of a candy. Another girl said someone had put a medication into her drink. A boy had side effects of a medication given within the therapy for epilepsy and another one after consuming an energetic supplement. Two boys said they had taken by mistake a medication prescribed to somebody else, which aroused suspicion of intentional self-poisoning/*Deset adolescenata je prijavilo da je nenamerno unelo lek. Dve devojke su uzele više od 1 tablete ibuprofena zbog glavobolje i zubobolje, jedna devojka je imala nuspojave u okviru terapijske doze metoklopramida, jedna devojka je uzela lek misleći da je bombona. Jedna devojka je izjavila da joj je neko sipao lek u piće. Jedan mladić je imao nuspojave u okviru doze lekova u terapiji epilepsije, jedan mladić je imao neželjenu reakciju nakon uzimanja energetskog suplementa. Dva mladića su navela da su greškom uzeli lek drugog ukućanina, što pobuđuje sumnju na namerno samotrovanje.*

** Separately or in combination with medications/*Samostalno ili u kombinaciji sa lekovima*

suicide or intentional self-poisoning, fifty-eight adolescents (56.31%) were referred to the Department of Psychiatry for further treatment.

Regarding the treatment outcome, all poisoned patients were successfully treated and there were no fatalities.

Eight patients were admitted due to repeated acute poisoning, among which there were seven adolescents and one toddler.

A female toddler was hospitalized because she accidentally ingested a rodenticide, and a year later she had taken clonazepam, a drug used by her grandmother.

Among adolescents, there were five female and two male patients hospitalized due to repeated self-poisoning.

Four female adolescents were previously treated by a psychiatrist. Three of them had repeatedly taken a great amount of drugs they used in regular therapy, and one of them had taken a drug used by her mother for treatment of epilepsy. After receiving appropriate aid, these patients were referred to the Department of Psychiatry for further treatment. One female adolescent took a large amount of sedatives due to a family conflict. After detoxication she was discharged with an advice to visit a child psychiatrist. Two months later, this girl was admitted because of the same reason. After stabilization, she left the treatment and there is no further data about this case.

One of the two male adolescents took several medications (sedatives and analgesics) on two occasions, first due to a family conflict, and next time the intent of poisoning was unclear. After treatment, he was also referred to the Department of Psychiatry. Another male patient had symptoms of poisoning due to inadequate compliance of drugs used in the therapy of epilepsy. The next time he was hospitalized for alcohol abuse.

A group of 21 adolescents attending the same school were hospitalized for suspected exposure to a toxic gas on the same day. Toxicological test results showed no substance of any toxicological importance. Teachers, who were with the patients on

the same premises that day, did not have any symptoms. Therefore, it was concluded that it was a case of mass psychogenic reaction.

Discussion

The study included 519 patients with suspected acute poisoning who were admitted at the Institute of Child and Youth Health Care of Vojvodina in the period from 2015 to 2017.

Of the patients hospitalized for acute poisoning, 51% were females and 49% were males, so the difference between genders was not statistically significant. Similar results were obtained by studies performed throughout the world [3, 12, 16].

In this study, acute poisoning was most frequent in patients between 14 and 16 years of age, and then in those aged 1 to 3. These results are in accordance with those obtained by Even et al., who reported the majority of acute poisoning in patients below 3 and above 13 years of age [2], whereas Oliveira et al. showed that acute poisoning was most common in children up to 4 years of age [13], thus confirming that children at this age are at risk because of being more active and curious. As for the gender, females prevailed in the age group between 11 and 18 years, and males in the group up to 11 years of age that is in accordance with the research of Lee et al. [16].

Zakharov et al. have reported that the number of non-fatal self-poisoning attempts is highest in the spring (31.3%) [14, 15]. A similar study conducted in Turkey showed that the highest number of intoxications occurred in the autumn and summer [3]. Our study showed no seasonal differences in the frequency of poisoning, and monthly variations were random. For example, in February 2015, there was a rise in the number of patients hospitalized at the Institute of Child and Youth Health Care of Vojvodina for suspected accidental exposure to poisonous gas, which was later ruled out.

In our study, 62% of patients had symptoms of poisoning, while 38% were without symptoms and it is also in accordance with other researches [14 - 16]. If patients arrived within an hour after the exposure, adequate measures to prevent the absorption of poisonous substance were undertaken. As a result, patients did not develop symptoms of poisoning. Also, some of them had non-toxic exposure to harmful substances.

In our study, ingestion of toxic substances was most common (89%), as well as in many other similar studies [3, 17–21].

In this study, medications were the most frequent etiological agents in all age groups, which is in accordance with other previous researches [16, 19]. The second most common cause of poisoning was alcohol, followed by household chemicals which are somewhat less frequent, and it is in accordance with the results obtained in Croatia [20].

Medications used in the therapy of central nervous system disorders were the most frequent causes of intoxication, which is in accordance with other authors' findings [16, 19, 22–24]. The second and third place in our study was taken by medications used in the therapy of cardiovascular and musculoskeletal system diseases, which is in agreement with the most frequently consumed medications in general population of the Republic of Serbia [25].

Regarding the circumstances of poisoning, accidental poisonings were the most common in this study, as well as in other studies [2, 26]. In children up to 10 years of age, all poisonings were accidental, whereas in adolescents 6.7% of poisonings were unintentional. Due to acute poisoning by abuse of psychoactive substances, 60.38% of adolescents were hospitalized. The percentage of intentional self-poisonings in adolescents was 32.9% of cases in our study, and it was similar to the study done by Liisanantti et al. [22].

The most common etiological agent of poisoning in adolescents in this study was alcohol (50.3%) followed by medications (29.64%). Almost identical results were obtained in Croatia (alcohol – 55.7%, medications – 28.89%) [17]. Alcohol was also the most frequent agent of poisoning followed by medications, according to a Finnish study [18]. In this study, 6.29% of adolescents consumed psychoactive substances (sometimes combined with alcohol) and 2.6% of adolescents combined medications with alcohol, that is in accordance with several researches [14, 15, 21].

Alcohol abuse is the most common cause of acute poisoning in individuals aged between 10 and 18 years in the most developed European countries as well [27–29]. Young people may consider consumption of alcohol a part of growing up and imitation of adult drinking habits [28]. In our study sample, there were more male patients hospitalized for acute alcohol intoxication, which complies with the results of other studies, but the gender difference was not significant, which implies that female adolescents use alcohol almost as often as male adolescents [17, 21, 30]. The most common etiological agents of intoxication in male and female adolescents were alcohol and medications, respectively. Intentional self-poisoning caused by medications was more frequent in female patients, and that is in accordance with other studies [17, 18, 21]. Araújo Veras et al. explained this phenomenon by the fact that male adolescents tend to express their aggressiveness towards their environment in circumstances causing frustration in young people, whereas girls are self-aggressive, they are prone to self-infliction [18].

Among the adolescents who were admitted due to intentional self-poisoning or intended suicide, 56.31% were referred to the Department of Psychiatry for further treatment. According to the literature data, the mortality rate due to acute intoxication ranges between 0.4% and 7.6% [19, 22, 29, 30]. The treatment outcome was good in all the patients included in our study and there were no fatalities.

A group of 25 adolescents attending the same school, who were hospitalized for suspected exposure to harmful gas on the same day, is interesting because it suggests a possibility of a phenomenon of mass panic disorder in adolescents, which is important to be recognized and managed at institutions dealing with treatment of poisoning in children and adolescents.

Conclusion

This study included 519 patients hospitalized at the Institute of Child and Youth Health Care of Vojvodina in Novi Sad in the period from January 1, 2015, to December 31, 2017. There were no gender differences in admitted patients. Intoxications were without a seasonal pattern. The poisonous substances were most commonly taken orally.

Medications were the most frequent cause of poisoning in children and adolescents. Medications and household chemicals were the most frequent causes of poisoning in children up to 10 years of age, whereas in adolescents (more often males than females) it was alcohol abuse. Poisoning with suicidal intent, and intentional self-poisonings without attempted suicide, were considerably more frequent in girls than in boys. Medications were the most common etiological agents in intentional self-poisoning.

Acute poisoning is a serious health problem and therefore it is of utmost importance to take necessary preventive measures against it.

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SEXUAL DIMORPHISM IN BODY COMPOSITION OF CHILDREN IN THE NORTH BAČKA REGION

POLNI DIMORFIZAM TELESNE KOMPOZICIJE KOD DECE U SEVERNOBAČKOM REGIONU

Valerija P. PUŠKAŠ, Tatjana M. PAVLICA and Rada S. RAKIĆ

Summary

Introduction. Anthropometric measurements are widely used in the assessment of growth, nutritional status and body composition in children. The objective of the study was to describe growth and body composition of children using simple anthropometric measures. **Material and Methods.** The investigation was performed in 13 primary schools in the territory of North Bačka during 2017 and at the beginning of 2018. A total of 593 schoolchildren aged 6.50 - 10.49 years (in decimals) were included in the study. The following parameters were measured: height, weight, upper arm circumference and triceps skinfold thickness. These measurements were used to calculate the body mass index, total upper arm area, upper-arm muscle area, upper-arm fat area, and the arm fat mass percentage for each individual. **Results.** The study results show that children's growth is almost linear over the first decade of life and the lean body mass increases at similar rates in boys and girls. However, girls show higher percentage of body fat and higher triceps skinfold thickness, while the body mass index is not significantly different. The secular trends in height are slowing down or have already ceased, but the weight generally continues increasing. **Conclusion.** Although sexual differences in anthropological measures are insignificant, the differences in body composition are evident before puberty.

Key words: Growth; Puberty; Body Composition; Child Development; Obesity; Adipose Tissue; Anthropometry; Child; Serbia; Sex Characteristics

Sažetak

Uvod. Antropometrijske mere se često koriste za procenu rasta, stanja uhranjenosti i telesne kompozicije kod dece. Cilj ovog istraživanja bio je da se analiziraju rast i telesna kompozicija kod dece pretpubertetskog uzrasta. **Materijal i metode.** Istraživanje je izvršeno tokom 2017. i početkom 2018. godine u 13 osnovnih škola na teritoriji Severne Bačke, a obuhvatilo je 593 učenika uzrasta od 6,50 do 10,49 decimalnih godina. Izmerene su: visina, masa tela, obim relaksirane nadlaktice i debljina kožnog nabora nad tricepsom. Iz ovih mera za svakog ispitanika izračunati su: indeks telesne mase, ukupna površina nadlaktice, mišićna masa nadlaktice, masna masa nadlaktice i procenat masne mase ruke. **Rezultati.** Tokom prve decenije rast dece je skoro linearan, a nemasna masa tela se povećava sličnim intenzitetom kod pripadnika oba pola. Međutim, devojčice pokazuju veći procenat telesne masti i veću debljinu kožnog nabora na tricepsu, dok se indeks telesne mase ne razlikuje značajno. Sekularni trend u visini se usporava, ali masa tela pokazuje i dalje trend porasta. **Zaključak.** Iako polne razlike u antropološkim merama nisu izražene, razlike u sastavu tela su uočljive pre puberteta.

Ključne reči: rast; pubertet; telesni sastav; razvoj deteta; gojaznost; masno tkivo; antropometrija; dete; Srbija; polne karakteristike

Introduction

The growth and development of children is regulated by a complex interaction between internal (biological) and external factors. Complex interaction of hormonal influences, tissue responsiveness and nutrition affect the growth and development of children, whereas metabolic and genetic signals modulate these responses [1]. Some authors reported that genetic factors, more than environmental, determine anthropometric features and these characteristics are highly heritable components, with heritability range from 40 – 91% [2]. Anthropometric characteristics, such as height and weight, are widely used to estimate the growth and development, as well as the nutritional status of children, but changes in body composition are also essential elements in growth. Prepubertal growth is relatively stable and remains constant throughout childhood, until the onset of puberty. A general rule is that a child grows 10 cm in the first year of life and later, to the beginning of puberty, the increase is mostly uniform and in most children 5 to 7.5 cm per year, while the increase of body weight is about 2 – 3 kg per year [3]. Before adolescent growth spurt, boys and girls differ only by some 2% in height, and later by about 8%, on average. In adults, the difference in body height between men and women is around 13 cm, of which 2 cm are due to prepubertal growth. Because of small gender differences in anthropometric characteristics, the prepubertal period is often re-

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Abbreviations

BMI – body mass index
TUA – total upper-arm area
UMA – upper-arm muscle area
UFA – upper-arm fat area
FM% – fat mass percentage
MUAC – mid-upper arm circumference
SD – standard deviation
DI – dimorphism index
TSFT – triceps skinfold thickness

ferred to as the period of neutral childhood. Gender differences in body size and shape seen in adults are the result of differential growth patterns at later period of adolescence. Even though no sex differences were expressed in height and weight, there is some evidence to support sexual dimorphism in body composition, but the time of life when sex differences in body composition first occur is currently unknown.

A number of studies conducted over the last few decades have reported an increasing trend of overweight and obesity in children and adolescents worldwide [4, 5]. Today, the most frequently used anthropometric indicator for evaluation of the nutritional status is the body mass index (BMI kg/m^2). However, BMI cannot point to the body composition and distribution of fat tissue. Determination of body composition, i.e. fat and fat-free mass, is of considerable interest for gathering accurate data of a person's nutritional status. Fat component of the human body represents the fat mass or percentage of body fat, while the non-fat component is known as the lean body mass. Excess weight does not necessarily imply excess fat, and being underweight is not necessarily associated with protein energy malnutrition. This is particularly the case when the degree of under- or overweight is moderate [6]. When it comes to body composition assessment, anthropometric measurements have a lot of practical advantages, such as being non-invasive and inexpensive [7]. Arm anthropometry is used for evaluation of body composition in both clinical and field researches [8]. Such evaluation of fat and fat-free mass relies on facts that the arm is cylindrical in form and the subcutaneous fat is evenly distributed around a circular core of muscle [9]. There is a direct correlation between some diseases, biochemical changes and nutritional status and the upper arm composition. This is explained by the fact that arm contains muscles and the subcutaneous fat tissue represents an important parameter in detecting undernutrition, particularly in situations when it is impossible to measure the height and weight [10]. Many investigations have shown that upper arm muscle area (UMA) and upper arm fat area (UFA) are very good indices of growth and nutritional status of children and adolescents [11 - 14]. Nutritional status and muscle mass can be determined by calculating UMA, which is determined based only on two anthropometric measurements, mid-upper arm circumference (MUAC) and triceps skinfold thickness (TSFT). In this study, we aimed to describe the growth and nutritional status in prepubertal children in North Bačka region by height, weight and upper arm anthropometry derived from MUAC and TSFT.

Material and Methods

Anthropological examination was carried out in 2017 and at the beginning of 2018, in 13 primary schools in the North Bačka region. A cross-sectional sample of 593 schoolboys and girls (N = 302; N = 291, respectively) aged from 7 to 10 years were measured for height, weight, upper arm circumference and TSFT using standard techniques given by Tanner et al. [15]. Age was calculated as the difference between the date of birth and the date of data collection. Age groups were categorized by the midpoint of an age range. For example, the group of participants aged 7 years included all participants between 6.50 and 7.49 years. The subjects were grouped into four age categories (6.50 – 10.49). A formal consent was obtained from participants and their parents before data collection and participation was on voluntary basis. The research protocol was approved by the Provincial Secretariat for Education, Regulations, Administration and National Minorities – National Communities, Scientific Committee of the Department of Biology and Ecology, University of Novi Sad and primary school regulations.

Anthropometric measurements were taken using standard techniques in standing participants wearing light clothing and without shoes. Height was measured using an anthropometer (± 1 mm; Sieber Hegner Maschinen AG Zürich, Switzerland) with the head positioned in the Frankfurt plane (position in which the lower margins of the orbits, the orbitales, and the upper margins of the ear canals, the poria, all lie in the same horizontal plane), and a portable electronic digital scale was used to measure weight with accuracy of ± 0.1 kg. Mid upper arm circumference was measured with a plastic tape with the right arm hanging relaxed at side, and the measurement was done at the mid-point between the tip of the shoulder and the tip of the elbow (olecranon process and the acromion). The TSFT was measured to the nearest 0.1 mm with a Holtain skinfold caliper, at the midpoint between the elbow and the acromion process of the scapula. Three measurements were taken, and the mean was recorded. The BMI was calculated from the ratio of weight/height^2 (kg/m^2). The subjects were classified into underweight, normal weight, overweight and obese, according to age- and sex specific cut-off points proposed by the International Obesity Task Force (IOTF) [16]. Overweight and obesity were defined as having a BMI above the age- and sex-specific thresholds, respectively (equivalent of BMI > 25 kg/m^2 and the equivalent of BMI > 30 kg/m^2). Nutritional status was also assessed by indirect anthropometric measurements

Table 1. Mean, standard deviation and dimorphism index in body height, body weight, mid-upper arm circumference and triceps skinfold thickness in boys and girls
Tabela 1*. Prosečne vrednosti, standardna devijacija i polni dimorfizam visine tela, mase tela, obima relaksirane nadlaktice i debljine kožnog nabora na tricepsu kod dečaka i devojčica*

Anthropometric characteristics *Antropometrijske karakteristike*	Age *God.*	Boys *Dečaci*			Girls *Devojčice*				
		N *Br.*	Mean *Srednja*	SD *Stand. devij.*	N *Br.*	Mean *Srednja*	SD *Stand. devij.*	p	DI % *Polni dimorfizam %*
Body height (cm)‡ *Visina tela (cm)‡*	7	42	125.62	5.70	41	123.98	4.74	0.157	0.43
	8	91	129.04b	5.65	86	129.97c	5.04	0.255	
	9	91	135.13c	6.03	92	134.02c	6.48	0.232	
	10	78	142.03c	7.24	72	141.61c	6.78	0.719	
Body weight (kg)‡ *Telesna masa (kg)‡*	7	42	28.55	7.95	41	25.76	5.32	0.064	5.25
	8	91	28.96	5.53	86	28.85a	4.85	0.891	
	9	91	32.94b	6.58	92	32.53c	7.70	0.699	
	10	78	40.72c	12.57	72	36.90c	8.89	**0.035**	
Mid-upper arm circumference (cm)‡ *Obim relaksirane nadlaktice (cm)‡*	7	42	18.95	3.32	41	18.41	2.82	0.429	0.35
	8	91	18.76	2.65	86	19.12	2.50	0.357	
	9	91	19.37	2.89	92	19.84	3.11	0.297	
	10	78	21.87c	4.30	72	21.29b	3.24	0.350	
Triceps skinfold thickness (mm)† *Debljina kožnog nabora na tricepsu (mm)†*	7	42	12.10	5.96	41	12.73	4.54	0.065	-9.36
	8	91	12.10	4.32	86	14.26	5.20	**0.003**	
	9	91	12.66	5.14	92	15.12	5.33	**0.001**	
	10	78	16.13c	7.59	72	16.31	5.88	0.369	

Legend: ‡ t – One-Way ANOVA for Independent Samples (LSD Post Hoc); † Mann-Whitney U test and Kruskal Wallis test; a, b, c – statistically significant increase in relation to the previous year: [a] $p < 0.05$, [b] $p < 0.01$, [c] $p < 0.001$; Bold values are statistically significant
Legenda: *‡ t – jednosmerna ANOVA za nezavisne uzorke (LSD Post Hoc); † Man-Vitnijev U test i Kruskal Valisov test; a, b, c – statistički značajno povećanje u odnosu na prethodnu godinu: a p < 0,05, b p < 0,01, c p < 0,001; Boldovane vrednosti su statistički značajne*

– total upper-arm area (TUA), UMA, UFA and arm fat mass percentage (FM %). Substituting C for MUAC, and measurements made in centimeters, the following formulas according to Fricancho [6]) were used:

$TUA = C^2/(4 \times \pi) = cm^2$

$UMA = [C – (TSF \times \pi)]^2/(4 \times \pi) = cm^2$

$UFA = TUA – UMA = cm^2$

$FM\% = (UFA \times 100)/UFA + UMA$

The dimorphism index (DI) was calculated based on the equation by Borgognini et al., [17], based on sample means:

$DI = ((Mean_m – Mean_f)/Mean_f)) *100$

where $Mean_m$ stands for males and $Mean_f$ for females.

Data were analyzed with SPSS software for Windows, version 20 (Incorporation, Chicago, USA). Height, weight, MUAC, TSFT, BMI, TUA, UMA, UFA and FM% were expressed as mean ± standard deviation (SD). The Mann-Whitney U test and Independent Sample t-test were used to identify the statistical difference of anthropometric indicators in boys and girls, depending on the normality of the distribution determined by the Shapiro-Wilks test. The difference between the number of boys and girls was determined using the Chi-square test. The age difference was determined using One-Way ANOVA for Independent Samples (LSD Post Hoc) or Kruskal-Wallis test. The overall significance level was set at $p < 0.05$.

Results

There were no statistically significant differences between the mean values of body height and body weight in boys and girls (**Table 1**). Although boys showed slightly higher values of these characteristics, no statistical differences were detected, except for the weight values recorded at the age of ten. The mean DI of height was somewhat lower (0.43%) in comparison with the weight DI (5.25%). The MUAC did not differ significantly (DI = 0.35%), but the mean TSFT was greater in girls of all ages, with significant differences recorded at the ages of eight ($p < 0.001$) and nine ($p < 0.001$). Triceps skinfold thickness values were, on the whole, by 9.36% greater in girls than in boys.

With regard to the BMI (**Table 2**), no significant differences were found between boys and girls. The boys showed slightly higher values at the age of seven, eight and ten, but significant differences were only recorded in the oldest age group. On average, boys showed greater BMI by 4.39%. The TUA values did not point to a notable difference between boys and girls, while the UMA results were higher in boys of all ages, but without statistical significance. On average, the UMA values were by 6.78% higher in boys than in girls. The opposite trend, however, was evident in case of UFA and

Table 2. Mean, standard deviation and DI of BMI, TUA, UMA, UFA and FM in boys and girls
Tabela 2*. Prosečne vrednosti, standardna devijacija i polni dimorfizam (DI) indeksa BMI, TUA, UMA, UFA i FM kod dečaka i devojčica*

Anthropometric indices *Antropometrijske karakteristike*	Age *God.*	Boys *Dečaci*			Girls *Devojčice*				
		N *Br.*	Mean *Srednje*	SD *Stand. devij.*	N *Br.*	Mean *Srednje*	SD *Stand. devij.*	p	DI % *Polni dimorfizam %*
BMI (kg/m^2)‡ *Indeks telesne mase (kg/m^2)‡*	7	42	17.89	3.74	41	16.67	2.78	0.097	4.40
	8	91	17.29	2.48	86	17.06	2.50	0.535	
	9	91	17.94	2.76	92	17.98[a]	3.31	0.934	
	10	78	19.94[c]	5.05	72	18.27	3.53	0.020	
TUA (cm^2)† *Ukupni obim nadlaktice (cm^2)†*	7	42	29.45	11.17	41	27.62	8.85	0.498	1.48
	8	91	28.57	8.16	86	29.59	8.07	0.395	
	9	91	30.54	9.45	92	32.09	10.27	0.377	
	10	78	39.54[c]	16.31	72	36.92[c]	11.84	0.920	
UMA (cm^2)† *Mišićna masa nadlaktice (cm^2)†*	7	42	18.54	4.56	41	16.81	4.44	0.084	6.79
	8	91	18.06	4.08	86	17.22	3.37	0.138	
	9	91	19.09	4.17	92	18.40	4.62	0.289	
	10	78	22.91[c]	6.57	72	21.17[c]	5.70	0.086	
UFA (cm^2) † *Masna komponenta nadlaktice (cm^2) †*	7	42	10.91	7.34	41	10.80	5.26	0.937	-5.85
	8	91	10.54	4.88	86	12.37	5.82	**0.025**	
	9	91	11.45	6.04	92	13.69	6.50	**0.017**	
	10	78	16.63[c]	10.69	72	15.75[a]	7.61	0.566	
% FM ‡ *Procenat telesne masnoće ruku*	7	42	34.48	9.51	41	37.84	7.86	0.084	-9.87
	8	91	35.47	7.73	86	40.25	8.90	**0.000**	
	9	91	35.58	8.66	92	41.04	8.12	**0.000**	
	10	78	39.05[b]	10.00	72	41.28	8.90	0.152	

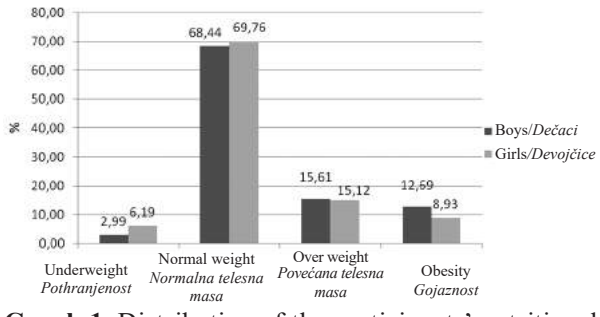
Legend: ‡ t- One-Way ANOVA for Independent Samples (LSD Post Hoc); † Mann-Whitney U test and Kruskal Wallis test; a, b, c – statistically significant increase in relation to the previous year: [a] $p < 0.05$, [b] $p < 0.01$, [c] $p < 0.001$; Bold values are statistically significant
Legenda: *‡ t - jednosmerna ANOVA za nezavisne uzorke (LSD Post Hoc); † Man-Vitnijev U test i Kruskal Valisov test; a, b, c – statistički značajno povećanje u odnosu na prethodnu godinu: a $p < 0,05$, b $p < 0,01$, c $p < 0,001$; Boldovane vrednosti su statistički značajne*

FM% results, as higher values were found in girls of all ages, with significant differences observed at the age of eight and nine ($p < 0.001$). The FM% was on average by 9.86% greater in girls than in boys.

Most subjects had normal weight (**Graph 1**); 15% of boys and girls were overweight, the number of obese was slightly higher in boys (12.96%) than in girls (8.93%), while the number of underweight children was generally low, with girls showing greater percentage (6.19%) than boys (2.99%).

Discussion

This study focuses on the growth, development and nutritional anthropometric status among prepubertal children from North Bačka region using the height, weight and indirect anthropometric measurements of the upper arm. The study shows that in general, at this age, children have similar anthropological characteristics. Over the first decade, the children's growth is almost linear, which is in agreement with other studies [18] and boys and girls accrue lean body mass at similar rates [19]. However, girls show a tendency to get higher percentage of body fat and also show higher TSFT, while BMI is not significantly different, which is in line with other investigations [20, 21]. Compared to previous studies of children of the same age and in the same geographical region, similar values were found for body height, however, the body weight in the studied children shows an upward trend, i.e. the



Graph 1. Distribution of the participants' nutritional status
Grafikon 1*. Struktura ispitivane grupe u odnosu na stepen uhranjenosti*

positive secular trend [22]. In the survey of prepubertal children (8–10 years) from this region conducted 20 years ago, the mean height of boys was 135.25 cm and in girls it was 135.06 cm, which is quite similar to the values recorded in the present survey (135.40 cm and 135.20 cm, respectively). However, the weight values obtained 20 years ago (31.10 and 31.05 kg, respectively) are lower compared with the present results (34.21 and 32.76 kg). The secular trend provides insight into the link between growth and the environment [16] and highlights the complex interplay between genes, physiology and environment in determining the body size and shape of individuals from one generation to the next [23]. This phenomenon is a biological indicator that is used in auxology and for assessing the degree of socio-economic development of a country, which is an important information for public health policies [24]. The positive secular trend has largely been attributed to improved nutrition, health conditions and socio-economic circumstances, while negative secular change in a population's height is a response to environmental deterioration. Many studies of the secular trend have highlighted a progressive decrease of the intensity and speed of growth among the industrialized countries over the last few decades [25], which means that the populations achieved their full genetic potential and/or that their socio-economic conditions had ceased to improve. This investigation shows that the secular trend in height is slowing down or has already ceased. We can assume that this may indicate a stagnation of living standards, and no improvement of environmental conditions in recent decades. The other possible reason is that Serbian population has reached its genetic potential in height and in that case the situation cannot be explained by existing social or economic conditions. In contrast, weight generally continues to increase. The mean BMI is significantly higher today (18.39 kg/m^2 in boys and 17.77 kg/m^2 in girls) than it was 20 years ago (16.82 and 16.71 kg/m^2, respectively). Overall, the prevalence of overweight/obesity in prepubertal children today is 28.57% among boys and 24.05% among girls. The percentage of the underweight is lower, with more girls belonging to this category than boys. According to the data presented in the National Program for Obesity Prevention in Serbian Children and Adults, 70% of children have normal nutritional status, 15% are overweight, 4.9% are obese, and 5% are underweight [26]. In comparison with the findings presented here, the number of overweight children is almost identical, while the number of obese boys and girls is higher in this study. According to the recent investigations in some European countries, the prevalence of overweight and obesity in European children under the age of ten approximately equals 20%, with considerable variations among countries and socio-economic groups [27]. Thus, the prevalence varies from 40% in South Europe to less than 10% in North European countries.

The use of skin-fold thickness in the assessment of nutritional status of children is based on the assumption that increased subcutaneous fat, resulting from high calorie intake or low energy expenditure reflects a greater calorie reserve [28]. This study shows that girls have thicker triceps skinfold than boys, the difference being significant at the age of 8 and 9, while the BMI does not differ, except in 10-year-old children. Compared with previous surveys of children in the same region, when the mean TSFT equaled 10.81 mm in boys and 12.78 mm in girls, the positive secular trend is notable regarding this trait as well [22]. Due to the fact that the thickness of these folds is a measure of the subcutaneous adipose tissue, these data indicate that girls of this age exhibit a significantly higher amount of body fat than their male counterparts. The findings are additionally supported by the FM%, as these values are also higher in girls than in boys of all ages. The results are in line with other studies which show that sex differences in body composition are evident before puberty [29, 30], but opposite to some earlier studies [31] where any sexual dimorphism in body composition was denied up to the onset of puberty. It is well known that adult females have a higher amount of absolute and relative amount of subcutaneous fat tissue, while males have higher amount of fat free mass, i.e. lean body mass, including bone and muscle mass [32]. These differences are mainly due to gender typical secretion of sex hormones. Estrogen has been associated with healthier, peripheral fat distribution in women [33], while testosterone in men has more pronounced effects on visceral adipose tissue and maintains the lean mass [34]. Gender differences in lipid metabolism [35] can also affect differences in body composition. In postnatal life, significant gender differences in sex hormone levels occur not before puberty, and it is considered that gender differences in body composition in prepubertal age are slight [31]. However, some studies have documented that gender differences in body fat and lean body mass are present even at the age between 3 and 10 years [29, 30, 36, 37], and these findings are in line with the results of this survey. Other studies have found statistically significant gender differences in FM% and fat-free mass in full-term newborns, at ~1 month of age, but by 6 months of age, these differences no longer existed [38]. The authors explained that male infants possess less FM% and greater fat-free mass during early development when their testosterone production peaks. When testosterone production decreases at ~3 months of life, body composition between male and female infants no longer differs. Other studies also point out that gender differences appear very early and exist even between newborns, while newborn girls exhibit a significantly higher amount in relative fat mass and a lower amount in lean body mass in comparison to newborn boys [38]. These gender differences in the amount of body fat may also be interpreted as a

result of natural selection, and higher amount of relative fat tissue in prepubertal girls and even during early development, may reflect the preparation of the female body for future reproductive function [30]. According to some authors, gender differences in body fat reflect gender typical energetic demands of reproductive physiology [39, 40]. Sufficient quantities of body fat supply the female body with the energy needed for pregnancy and lactation, while low fat storage has adverse effects on female reproductive success.

Conclusion

The investigation of prepubertal children points to minor differences in anthropological characteristics between boys and girls. Boys show slightly greater height and weight, and the dimorphism index equals 0.43% and 5.25%, respectively. The study shows that the secular trend in height is slowing down or has already ceased. In contrast, weight generally continues to increase resulting in positive secular trends in overweight and obesity. The body mass index shows no significant sex difference, but the findings point to a generally higher percentage of overweight and obese children. Almost 26% of children are overweight. Although boys and girls show no significant differences in anthropological traits and body mass index values, considerable differences are detected in their body composition, thus pointing to the fact that sex differences are present even before the onset of puberty. Considering the present increase in the prevalence of overweight, the assessment and quantification of body composition is extremely important in order to inform the public on possible health risks related to overweight and obesity.

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EFFECTS OF TRAINING AND DETRAINING ON MUSCLE STRENGTH IN ROWERS

UTICAJ TRENINGA I DETRENINGA NA MIŠIĆNU SNAGU VESLAČA

Nebojša JANJIĆ, Mina MARIČIĆ, Andrea ZUBNAR, Vedrana KARAN, Miodrag DRAPŠIN and Aleksandar KLAŠNJA

Summary

Introduction. Annual and periodized training protocols significantly affect the muscle adaptation in rowers. Considering that the main goal of the training period is increasing specific muscle strength and of detraining period increasing general strength and active rest, the aim of this study was to compare the strength of different muscle groups between training and detraining periods. **Material and Methods.** The study was conducted at the Department of Physiology, Faculty of Medicine Novi Sad, and it included 34 male and female rowers, 15 to 18 years of age. The muscle strength was measured using a Concept 2 DYNO dynamometer. The strength of the arm extensors and flexors, as well as the leg extensors was measured twice, at the end of the competition season (peak of performance) and before the beginning of the preparation season (after detraining). **Results.** A statistically significant decrease was found in absolute and relative muscle strength, flexor and arm extensor contraction rate, as well as relative leg extensor strength and contraction rate during the training and detraining periods ($p < 0.05$). No difference was found in the absolute leg extensor power between the two measurements ($p > 0.05$). **Conclusion.** Periodization of the annual training program in rowers has a higher impact on differences in the upper limb muscle adaptation, compared to lower limb muscles in terms of absolute strength.

Key words: Adaptation, Physiological; Muscle Strength; Water Sports; Athletic Performance; Muscle Strength Dynamometer; Resistance Training

Sažetak

Uvod. Periodizovani trenažni protokol značajno utiče na mišićnu adaptaciju veslača. S obzirom na to da je glavni cilj perioda treninga povećanje specifične mišićne snage, a perioda detreninga povećanje opšte snage i aktivan odmor, cilj ovog istraživanja bio je da se snage raznih mišićnih grupa uporede između perioda treninga i detreninga. **Materijal i metode.** Istraživanje je sprovedeno na Zavodu za fiziologiju Medicinskog fakulteta u Novom Sadu. Uključeno je 34 veslača oba pola, starosti između 15 i 18 godina. Mišićna snaga je merena pomoću *Concept2* DYNO dinamometra. Snaga ekstenzora i fleksora ruku i ekstrenzora nogu je merena dva puta, na kraju takmičarske sezone (vrh performansi) i pre početka sledeće takmičarske sezone (nakon detreninga). **Rezultati.** Dokazano je statistički značajno smanjenje apsolutne i relativne mišićne snage, brzine kontrakcije fleksora i ekstenzora ruku, kao i relativne snage i brzine kontrakcije ekstenzora nogu između perioda treninga i detreninga ($p < 0,05$). Nije nađena razlika u apsolutnoj snazi ekstenzora nogu između dva merenja ($p > 0,05$). **Zaključak.** Periodizacija godišnjeg treninga veslanja ima veći uticaj na variranje adaptacije gornjih ekstremiteta u poređenju sa donjim ekstremitetima u smislu apsolutne snage.

Ključne reči: fiziološka adaptacija; mišićna snaga; vodeni sportovi; sportski učinak; dinamometar; trening otpora

Introduction

Rowing was first used as a means of transport in ancient Egypt, Greece and Rome. As a sport, it probably began in England, in the 17th and early 18th centuries, with the Oxford - Cambridge university boat race, which was inaugurated in 1828. Rowing is one of the oldest Olympic sports. Today, there are fourteen boat classes which race at the Olympics [1].

While rowing, the human body works as the engine to propel the rowing boat across the water. During each stroke, the athlete applies the equivalent of a 40 to 45 kg load to the oar handle in each of the 220 to 250 strokes that occur during the race [2]. Rowing is a sport which requires a well conditioned body to operate at a high performance level during periods of training and competition. This sport is one of the few non-weight bearing sports that exercises all the major muscle groups, including quadriceps, biceps, triceps, latissimus dorsi, gluteus and abdominal muscles. The sport also requires strong core balance, physical strength, flexibility and cardiovascular endurance [3, 4]. The general training objectives in rowing are to increase maximum oxygen utilization, increase strength endurance, increase maximum strength, improve the efficiency of rowing technique, and improve flexibility and coordination. Strength training is an integral part of the structured regimen

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Abbreviations
RM – repetition maximum
VO_2 max – maximum rate of oxygen consumption

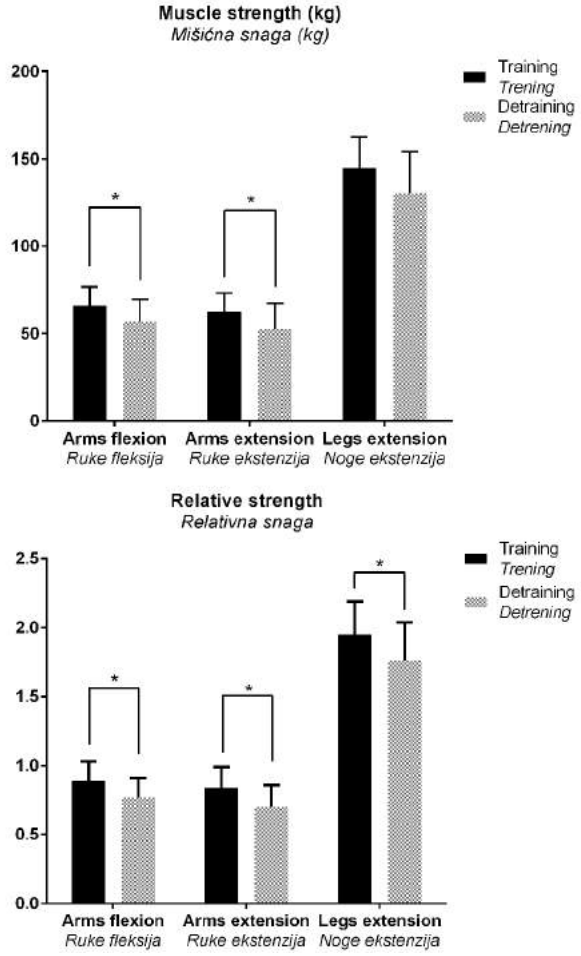
of elite rowers, accounting for 10 – 20% of total training time [5]. During the competitive season, rowers perform strength training with loads between 85 and 95% of their one repetition maximum (1 RM) [6]. Adaptations in strength training are focused on the development and maintenance of the neuromuscular units needed for force production. Neural adaptation dominates in the early phase of neuromuscular development. In the later adaptation phase, muscle protein content increases, and the contractile units begin to contribute the most to the changes in performance capabilities [7, 8].

Detraining has been defined as the partial or complete loss of training-induced adaptations, in response to an insufficient training stimulus. Detraining is closely related to the terms 'reversibility' and 'periodization'. Reversibility is a reduction in the conditioned state of the individual and occurs when the training stimulus is insufficient. Significant conditioning is lost after 2 – 6 weeks of insufficient training. Periodization is a concept which takes into account the fact that it is not possible to train all aspects successfully at once. It also recognizes that cessation or reduction of a training stimulus leads to a decline in specific conditioning [9, 10]. The training program is usually divided into 6 periods: two preparation periods focused on maximum strength, general endurance and muscular endurance; the pre-competition period that focuses on basic specific endurance and rowing technique; two competition periods mainly increasing specific endurance and race preparation, when training reaches "peak" for the championships; and finally, active recovery period [11].

Considering that annual planning and periodization play a great role in muscle adaptation in rowers, the aim of the study was to compare the strength of different muscle groups between training and detraining periods in order to show how periodization affects the adaptation of individual muscle groups.

Material and Methods

This prospective study included 34 rowers, male and female, aged between 15 and 18 years. The study was conducted in the period from August to October 2018. All participants were tested twice, first at the end of the competition season, at the peak of their seasonal performance, and second, before the start of the next preparation season – after the period of detraining. All measurements took place in the Laboratory for Functional Diagnostics of the Department of Physiology, Faculty of Medicine Novi Sad. The study was approved by the Ethical Committee of the Faculty. All participants signed written Informed consent forms.



Graph 1. Absolute (upper panel) and relative (lower panel) strength of different muscle groups measured after the period of training (black bars) and detraining (grey bars). Significant differences between the two periods were found in absolute and relative strength of arm flexors and extensors, and in relative strength of leg extensors. Asterisk (*) indicates the significance at $p < 0.05$

Grafikon 1*. Apsolutne (gornji) i relativne (donji) snage mišićnih grupa merenih nakon perioda treninga (crni stubići) i detreninga (sivi stubići). Značajne razlike između snaga u dva merena perioda nađene su u apsolutnim i relativnim snagama fleksora i ekstrenzora ruku, kao i ekstenzora nogu. Zvezdica (*) označava značajnost na nivou p < 0,05*

Anthropometrics. Body weight and body height were measured using a calibrated, combined weight-height scale, while a measuring tape was used for body circumferences.

Dynamometry. The DYNO (Concept 2, Morrisville, VT, USA) dynamometer was used to measure muscle strength and contraction speed. Three groups of muscles were tested at both points in time: arm flexors, arm extensors, and leg extensors. The testing was standardized in such a way that every subject received the same instructions, went through the warm-up of the same duration and intensity, and

was given an opportunity of a pre-test in order to familiarize with the machine. Additionally, starting and ending angles of the extremities were controlled in order to ensure the maximal consistency of the movement. First three contractions were always given as a physical and psychological preparation and the next five maximal contractions were statistically analyzed using a dynamometer in order to provide the mean values as the output. These data were gathered and subsequently analyzed.

Statistical analysis was performed in SPSS Statistics ver. 20. As anthropometric and dynamometric parameters did not violate the assumptions of normality, the means between two measurements were compared using the t-test for dependent samples. All results were expressed as mean ± standard deviation, and the level of significance was set at $p < 0.05$.

Results

The study included 34 male and female rowers aged 16.5 ± 1 years. Their average height was 182.05 ± 4.5 cm, average weight 74.14 ± 4.68 kg, and they have been training actively for 3.7 ± 1.7 years.

During the detraining period, the strength of arm muscles, both flexors and extensors, decreased significantly when compared to the training period (66.2 ± 10.6 vs. 57.1 ± 12.5 kg in the flexors, $p = 0.034$; 62.4 ± 10.9 vs. 52.5 ± 15.0 kg in extensors, $p = 0.045$). Unlike that, the strength of leg extensors did not change significantly (144.6 ± 17.8 vs. 130.4 ± 23.7 kg, $p = 0.067$) (**Graph 1**).

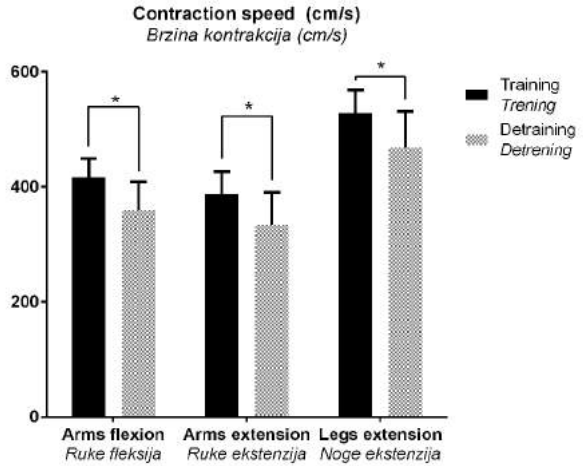
The relative strength was calculated by dividing the absolute muscle strength with the body weight at the testing time. Relative strength of arm muscles decreased significantly following the detraining period (0.89 ± 0.14 vs. 0.77 ± 0.14 in the flexors, $p = 0.015$; 0.84 ± 0.15 vs. 0.7 ± 0.16 in extensors, $p = 0.019$), as shown in the **Graph 1**. Such a significant decrease was also found for the relative strength in the leg extensors (1.95 ± 0.24 vs. 1.76 ± 0.28, $p = 0.041$).

Graph 2 shows that contraction speed decreased significantly after the period of detraining compared to the period of training in all three muscle groups: arm flexors (416.9 ± 32.7 vs. 360.1 ± 47.9 cm/s, $p = 0.002$), arm extensors (387.6 ± 38.9 vs. 334.8 ± 56.0 cm/s, $p = 0.006$) and leg extensors (527.8 ± 40.0 vs. 467.9 ± 63.5 cm/s, $p = 0.005$).

Discussion

In this study, we examined the muscle strength differences in two periods of training and found that absolute and relative strength and velocity of the upper body decreased during detraining. These differences were not found in the lower extremities.

The traditional training periodization, a division of the entire seasonal program into smaller periods was established about sixty years ago, when the knowledge of athletes' preparation was poor and the scientific background insufficient. To this day,



Graph 2. Contraction speed of different muscle groups after the period of training (black bars) and detraining (grey bars). Significant decrease in contraction speed was found in all three muscle groups following detraining. Asterisk (*) indicates the significance at $p < 0.05$

Grafikon 2. *Brzine kontrakcije merenih mišićnih grupa nakon perioda treninga (crni stubići) i detreninga (sivi stubići). Značajno smanjenje brzine kontrakcije je nađeno za sve tri mišićne grupe nakon perioda detreninga. Zvezdica (*) označava značajnost na nivou $p < 0,05$*

sport science has changed tremendously, while the classical periodization has remained at the same level, offering coaches basic guidelines for structuring and planning the training process [12].

Classical periodization protocol has six integral parts, two preparation periods, pre-competition period, two competition periods and active recovery.

Preparation period 1 focuses on maximum strength and general endurance, while preparation period 2 focuses on general endurance and muscular endurance. Strength training is an integral part of preparations, and it is equally important for novices and seniors. Therefore, authors suggest that it may be wise to prioritize weight-training over the preparation period, as senior rowers are likely to cease strength training when the championships start. In terms of rowing performance, strength training should ideally be done twice a week and should primarily target the lower–body. The volume of weight training exercise should be gradually reduced and intensity increased with time, to manage fatigue as the demands of competitive rowing and training increase progressively [13]. Skeletal muscles have the capacity to adapt according to the type and intensity of physical activity they are required to perform. The onset and degree of adaptation depend on the type, intensity and duration of the training stimulus [14]. During these phases, rowers gain strength in both the upper and lower body. This muscle strength is not specialized for any specific sport discipline or movement and can be assessed by commercial dynamometry. Air-braked isoacceleration dynamometers, such as Concept 2 DYNO,

maintain the same resistance during the movement and measure the maximal force of the contraction expressed in kilograms, power in Watts, work in Joules, and contraction speed in cm/s. This type of assessment is suitable for evaluation of strength progress, especially for junior rowers and talent identification programs for rowing as it decreases the potential risk of injury [15].

The pre-competition period focuses on improvement of basic specific endurance and rowing techniques by replacing the gym with on-water trainings, targeting arm flexors and extensors, chest and back muscles. The competition period with the main goal on increased specific endurance, ''super-compensation'' effect and race preparation is a period in which the training reaches peak for the championships. This is the period when athletes display their maximal abilities, i.e. strength, endurance or other sport specific performances. Unlike relative maximal strength, absolute maximum strength is a strong determinant of rowing performance. Lawton et al. reported that peak quadriceps strength together with maximum rate of oxygen consumption (VO_2 max) has been found to be a major predictor for 2000-m performance [13]. In our study, leg extensors' absolute strength at the peak of performance was 144.6 kg, while for arm extensors and flexors it was 66.2 kg and 62.4 kg, respectively. When compared to kayakers tested by Kojić et al., there were no differences in leg extensors' strength, but kayakers showed better results in the strength of both arm flexors (107.9 kg) and extensors (98.9 kg) [16].

After the championships period, cessation of resistance training is typically associated with a diminished physiological function, reductions in maximal voluntary muscle strength, muscle cross-sectional area and neural drive to the muscle [17]. In contrast, some studies have reported partially preserved gains in dynamic muscle strength when resistance training was followed by 6 – 12 weeks and even 30 – 32 weeks of detraining [18]. Detraining period in a rowing annual periodization protocol is based on active recovery. Since we measured muscle strength twice, once after championships and once after detraining, our results showed that although the strength of arm flexors and extensors decreased significantly (by 14% and 16%, respectively), there were no significant changes in the leg extensors in terms of absolute strength, after the period of detraining. A possible explanation is that during detraining, athletes did not completely cease with physical activities. During their active recovery, rowers worked on improving general strength and endurance by running, targeting leg muscles, and eliminated the gym and specific on-water exercises, targeting arm flexors and extensors. Another explanation could be adaptation of the central nervous system, which is induced together with muscular hypertrophy. As a result, the muscle strength can be maintained longer, even after detraining, since nervous factors do not reverse as fast as muscular hypertrophy [19]. Andersen et al. revealed that quadriceps femoris eccentric strength may remain entirely unchanged even after three months of detraining, while concentric strength of the muscles decreases [20]. Our results showed that the concentric strength of the leg extensors did not decrease significantly. It may be explained by the fact that subjects in the mentioned study entirely ceased physical activity during detraining. Great attention should be paid to detraining, since it represents a very sensitive period for an athlete. It should be used to maintain and perfect the technique, because the sequence, modality and the timing of every movement is of paramount importance for the formation of dynamic stereotype. Well learned and memorized dynamic stereotype is a basis for performing the greatest amount of work per unit time, with the least energy expenditure. Based on such a dynamic stereotype, increase in strength and stamina after detraining leads to excellence in results.

Conclusion

Periodization of the annual rowing training program has higher impact on differences in the upper limb muscle adaptation compared to the lower limb muscles in terms of absolute strength. When planning the annual protocol, additional attention should be given to detraining. It should be planned as an active recovery in order to maintain the previously acquired abilities.

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THE PROBLEM OF UNUSABLE TRANSFUSION UNITS

PROBLEM NEUPOTREBLJIVIH TRANSFUZIOLOŠKIH JEDINICA

Dragan RADONJIĆ[1], Mirjana VARJAČIĆ[2] and Milan VUKANOVIĆ[3]

Summary

Introduction. Availability of safe blood and blood products has always been a key strategy for addressing such health–related challenges. The most common reasons for blood wastage are expired blood validity, chylous blood, hemolysis in bags, insufficient amount of blood or extracted blood, damage to the bag during work or processing, blood positive for transmissible diseases, blood suspicious of transmissible diseases. The reasons also include insufficiently educated blood donors in terms of eating before giving blood, sometimes clinician's inadequate therapeutic choice regarding the expiration of individual blood units, and sometimes unplanned taking of less common blood groups. **Material and Methods.** We analyzed those blood units that did not meet the standards, as well as the reasons why this happened in the period from 2009 – 2014 in the Blood Transfusion Center Bar in Montenegro. The aim of this study was to objectively show the reasons for blood wastage in the specified period. **Results.** In the observed period of time, 7.001 units of whole blood were collected. Of those, there were 796 (11.36%) unusable blood units, which is very high according to the world standards. This is important because blood treatment is an extremely expensive and complex method and sometimes it is very difficult to collect rare blood groups. **Conclusion.** Discovering new and analyzing the existing factors that cause unused transfusion units, by planning and introduction of preventive measures and application only of safe blood in the treatment of patients, will significantly reduce the number of unusable blood units and contribute to faster and successful treatment of patients in the future.

Key words: Blood Transfusion; Blood Banks; Blood Safety; Safety Management; Quality Control; Risk Factors

Sažetak

Uvod. Dostupnost sigurne krvi i krvnih proizvoda oduvek je bila ključna strategija za rešavanje izazova u vezi sa zdravljem. Najčešći razlozi za neiskorišćene jedinice krvi su: istekla validnost jedinice, masna – hilozna krv, hemoliza u kesama, nedovoljna količina uzete krvi, oštećenje kese tokom prerade, krv sumnjiva na prisustvo krvlju prenosivih bolesti. Razlozi se nalaze i kod nedovoljno obrazovanih donora krvi u pogledu ishrane pre davanja krvi, neadekvatan izbor krvi za lečenje od strane kliničara kao i neplansko uzimanje jedinica krvi sa retkom krvnom grupom. **Materijal i metode.** Analizirali smo one jedinice krvi koje ne zadovoljavaju navedene standarde kao i razloge zbog kojih se to desilo u periodu 2009−2014. godine u Službi transfuziologije u Baru, Crna Gora. Cilj rada bio je objektivno prikazivanje pravih razloga zbog kojih nisu valjano iskorištene uzete jedinice krvi u navedenom periodu. **Rezultati.** U tom vremenskom periodu prikupljeno je 7 001 jedinica cele krvi. Od toga je u istom periodu bilo neupotrebljivih jedinica krvi 796 ili 11,36% što je prema svetskim normativima veoma mnogo. Ovo je važno, zato što je transfuzija krvi izuzetno skupa i složena metoda, a ponekad je veoma teško dobiti retku krvnu grupu. **Zaključak.** Otkrivanje novih i analiza postojećih faktora koji utiču na pojavu neupotrebljenih transfuzioloških jedinica, uz planiranje i uvođenje preventivnih mera i primenu samo sigurne krvi u lečenju pacijenata značajno će smanjiti broj neiskorišćenih jedinica krvi i doprineti bržem i uspešnijem tretiranju pacijenata u budućnosti.

Ključne reči: transfuzija krvi; banke krvi; bezbednost krvi; sigurnosne mere; kontrola kvaliteta; faktori rizika

Introduction

The availability of safe blood and blood products has always been a key strategy for addressing such health-related challenges. An unused (unusable blood) transfusion unit is a unit of blood that does not meet the European quality standards on the use of safe blood and as such cannot be used for patients who need transfusion [1, 2]. The Blood Transfusion Service at the General Hospital in Bar, under the auspices of the Blood Transfusion Institute of Montenegro, seeks to provide completely safe blood and blood components.

Modern principles of blood treatment require the reimbursement only of that part of blood or blood component that the patient really needs [3, 4]. The use of blood always carries numerous risks, such as

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transmission of infectious diseases, blood transfusion complications (immunological and non-immunological), blood pressure malfunction, bacterial contamination, and many other problems [4]. The blood components used in our institution include whole blood, erythrocytes, platelets, fresh frozen plasma, and plasma rich in platelets.

The most common reasons for blood wastage are expired blood validity, chylous blood, hemolysis in blood bags, insufficient amount of blood or extracted blood, damage to the bag during work or processing, blood positive for transmissible diseases, or blood suspected of transmissible diseases. The aim of this research was to objectively present the reasons why blood units were not properly used in our facility in the period 2009 – 2014, which could have been processed into blood components and as such potentially used in blood treatment of patients who needed transfusion at that time.

Material and Methods

A retrospective epidemiological study was conducted in the period June - December 2016. The data were collected from the blood transfusion registry of the Blood Transfusion Center Bar protocol in Montenegro. The study is the first part of a research (PhD Thesis) which is in the final stage. The data were analyzed using Statistical Package for the Social Sciences (SPSS) version 20 (IBM, USA). We used the methods of descriptive statistics to describe the socio-demographic characteristics, presented as the mean and standard deviation (SD) for numerical and normally distributed data or shown as a frequency and percentage (%) for categorical data.

Results

In the observed period, 8.090 people applied for blood donation, of which 1.089 were rejected **(Table 1)**. In regard to gender, 902 (82.82%) men and 187 (17.18%) women were rejected. About half were aged 36 – 65 years. The least rejected were donors with middle education, 745 (68.41%), and the highest percentage of rejected were workers, 470 (43.16%). The main reason was mostly fear of donating blood. The blood was most frequently given by people with secondary education, while people with high education give blood less frequently.

The reasons why donors were rejected were analyzed. The most common reasons why blood cannot be donated are fatigue, low blood pressure (48.39 ± 4.19%), and elevated blood pressure (26.95 ± 2.88%) **(Table 2)**. In the observed period of time, 7.001 units of whole blood were collected. Of that, there were 796 (11.36%) unusable blood units. Blood was collected and stored in standard blood bags (Terumo - Japan), 350 ml or 450 ml of blood per donor. Anticoagulants, citrate phosphate dextrose (CPD) and citrate phosphate dextrose adenine (CPD-A1) were used in the blood bags for 28 – 42 days. Most blood donations were done at our intended premises (80%), while the rest was collected from voluntary blood donors (20%).

Table 1. Distribution of blood donors by gender, age and occupation
Tabela 1. *Prikaz davalaca krvi prema polu, dobu i zanimanju*

	N	%
Gender/*Pol*		
Male/*Muški*	902	82.82
Female/*Ženski*	187	17.18
Total/*Ukupno*	1089	100%
Age/*Životno doba*		
18 - 25	144	13.22
26 - 35	355	32.60
36 - 65	590	54.18
Total/*Ukupno*	1089	100%
Professional qualifications/*Stručna sprema*		
Low/*Niža*	292	26.82
Middle/*Srednja*	745	68.41
High/*Visoka*	52	4.77
Total/*Ukupno*	1089	100%
Employment Status/*Status zaposlenja*		
Employed/*Zaposlen*	470	43.16
Unemployed/*Nezaposlen*	315	28.93
Retired/*Penzionisan*	17	1.56
Student/*Student*	287	26.35
Total/*Ukupno*	1089	100%

Table 2. Reasons for rejecting blood donors in regard to the disease
Tabela 2. *Razlozi za odbijanje donatora krvi prema vrsti bolesti*

Year	Reasons for rejecting blood donors													
	High blood pressure *Visok krvni pritisak*		Fatigue, low blood pressure *Zamaranje, nizak krvni pritisak*		Fear of giving blood *Strah od vađenja krvi*		Heart disease, diabetes *Srčana oboljenja, dijabetes*		Recent injuries, surgery *Nedavna povreda, operacija*		Other, alcoholism *Ostalo, alkoholizam*		Total *Ukupno*	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%
2009.	87	27.53	156	49.36	14	4.43	23	7.27	31	9.81	5	1.58	316	29.02
2010.	60	27.90	103	47.90	8	3.72	21	9.76	19	8.37	4	1.86	215	19.74
2011.	42	21.98	105	54.97	10	5.23	11	5.75	20	10.47	3	1.57	191	17.45
2012.	53	27.19	86	44.10	7	3.58	18	9.23	25	12.82	6	3.07	195	17.90
2013.	51	29.65	89	45.64	5	2.90	12	6.97	10	5.81	5	2.90	172	15.79
SUM	293	26.90	539	49.49	44	4.04	85	7.80	105	9.64	23	0.21	1089	100.00

Table 3. Number of donated and unused blood units per year
Tabela 3. *Prikaz uzetih i neiskorištenih jedinica krvi po godinama*

Year *Godina*	Number of donated blood units *Broj uzetih jedinica krvi*	Number of unused blood units *Broj neiskorišćenih jedinica krvi*	**%**
2009.	1422	169	11.88
2010.	1436	168	11.69
2011.	1417	159	11.29
2012.	1386	139	10.02
2013.	1340	161	12.01
Total/*Ukupno*	7001	796	11.36

Table 4. Reasons why blood units could not be used
Tabela 4. *Razlozi zbog kojih se jedinice krvi ne mogu koristiti*

Insufficient blood volume *Nedovoljna zapremina krvi*	2009.		2010.		2011.		2012.		2013.		Total/*Ukupno*	
	N	%	N	%	N	%	N	%	N	%	N	%
	21	20.00	25	23.80	19	18.09	18	17.14	22	20.95	105	13.19
Damage to blood bags/*Oštećenje krvnih kesa*	25	23.80	21	20.00	29	27.61	18	17.14	12	11.42	105	13.19
Chylous/*Masna krv*	45	20.45	48	21.81	43	19.54	39	17.72	45	20.45	220	27.64
Hemolysis/*Hemoliza*	16	21.33	14	18.67	12	16.00	15	20.00	18	24.00	75	9.42
Expiration date/*Istekao rok trajanja*	26	21.67	19	15.83	21	17.50	25	20.83	29	24.17	120	15.07
BBD/*KPB*	7	23.33	6	20.00	4	13.33	3	10.00	10	33.33	30	3.76
Suspicion of BBD/*Sumnja na KPB*	29	20.56	35	24.82	31	21.98	21	21.98	25	17.73	141	17.71
Total/*Ukupno*	169	100.00	168	100.00	159	100.00	139	100.00	161	100.00	796	100.00

Legend: BBD – bloodborne diseases/*Legenda: KPB – krvno-prenosive bolesti*

All blood units were processed according to the Standard Operating Procedures (SOPs) for blood processing. Blood collection was done by adequately trained staff of our service using appropriate standardized equipment. Of the total number of collected blood units (7.001), there were 796 (11.36 %) useless blood units in the observed period. Four cases were excluded from the analysis, of which 3 due to erythrocyte clots, and 1 to incorrect bag labeling. During the studied 5-year period, there were 11.37 ± 0.80 of unused blood units on average **(Table 3).**

Most blood units, 220 (27.87%) were not used because of chylous blood in the blood bag. There were 30 (3.76%) blood units positive for transmissible diseases, 120 (15.05%) had an expired shelf life, 105 (13.07%) had damaged bags, and 75 (9.41%) had hemolysis in the bags. In the observed period, 141 (17.71%) blood units were not used due to a suspected transmissible disease **(Table 4).**

In the 5-year period, 30 (3.76%) units were not used due to the presence of a transmissible disease, and the most common reason was treponema pallidum hemagglutination (*TPH*) (syphilis infection) in 16 (53.3%) blood donors **(Table 5).**

Damage to blood bags was found in 105 (13.19%) cases. The most common reason was poor welding

Table 5. Blood units could not be used because of BBDs
Tabela 5. *Jedinice krvi pozitivne na krvno-prenosive bolesti*

Year *Godina*	HBsAg +	HCV +	HIV +	TPH +	Total/*Ukupno*	
					N	%
2009	1	2	0	4	7	23.33
2010	2	1	0	3	6	20.00
2011	1	1	0	2	4	13.33
2012	0	1	0	2	3	10.00
2013	3	1	1	5	10	33.33
Total/*Ukupno*	7	6	1	16	30	99.99

Legend: HBsAg – surface antigen of hepatitis B virus, HCV – hepatitis C virus, HIV – human imunodeficiency virus, TPN – Treponema pallidum hemagglutmation
Legenda: HBsAg – hepatitis B površinski antigen, HCV – virus hepatitisa C, HIV – virus humane imunodeficijencije, TPN – Treponema palidum-hemaglutinacioni test

Table 6. Donor blood wastage in the world
Tabela 6. *Prikaz neiskorišćenih transfuzioloških jedinica u svetu*

Country/*Država*	Percentage/*Postotak (%)*	Country/*Država*	Percentage/*Postotak (%)*
Sweden/*Švedska*	0	Slovenia/*Slovenija*	3.5
Norway/*Norveška*	0	Croatia/*Hrvatska*	3
Netherlands/*Holandija*	1	Serbia/*Srbija*	9
Portugal/*Portugal*	2	Montenegro - Bar/*Crna Gora - Bar*	10.1 – 11.14
Germany/*Nemačka*	2.5	B I H/*Bosna i Hercegovina*	14
France/*Francuska*	2.5	Macedonia/*Makedonija*	13
England/*Engleska*	2.5	Brasil/*Brazil*	19
Spain/*Španija*	3	Argentina/*Argentina*	21
Turkey/*Turska*	3	Russia/*Rusija*	45
Italy/*Italija*	3.5	Ukraine/*Ukrajina*	50
USA/*Sjedinjene Američke države*	3.5	Georgia/*Gruzija*	39
Greece/*Grčka*	5	Lithuania/*Litvanija*	29
Japan/*Japan*	5	Azerbaijan/*Azerbejdžan*	23
China/*Kina*	6	Nigeria/*Nigerija*	40
Australia/*Australija*	8	Kongo/*Kongo*	52
Poland/*Poljska*	8	JAR/*Južnoafrička Republika*	54
Hungary/*Mađarska*	12	Angola/*Angola*	51
Romania/*Rumunija*	1.5	Zambia/*Zambija*	49
Island/*Island*	5.5	Somalia/*Somalija*	55

of the blood bags, in 52 (50.48%) cases, but with a downward trend. After that, frozen plasma damage before dissolution in 20 (19.05%) cases, and frozen plasma damage after dissolution in 18 (17.14%) cases.

Discussion

The most important task of any modern transfusion service is to plan blood collection and consumption as a cornerstone of greater security in the future [3]. Blood treatment is an extremely expensive method, and blood collection has always been an extremely demanding and difficult job, especially in countries like ours, where the standard of living is quite low. In the conditions of struggle for personal material existence, potential and multiple blood donors are often forced to push their planned giving into the second plan.

As with any other service, quality planning is the prerequisite for success [1, 2, 6]. The number of unused blood units usually depends on the quality of content itself, and in Europe and the world it ranges from 2.5 – 3.9%, while the number in highly developed countries is very low, amounting to 0 – 2% (Sweden, Norway, the Netherlands, Portugal) or it is very high (about 55%) in the countries of the former Russian republics and in Africa, mostly directly related to blood borne diseases (acquired immune deficiency syndrome (AIDS), syphilis) [4, 5, 10]. According to the data of the European Union, the percentage of unused blood units in Montenegro amounts to 10.1%, while in our service in Bar, it is 11.37 ± 0.80% on average **(Table**

6). Absolutely the largest number of unused units in our service was related to fresh frozen plasma, due to a short shelf-life (3 months), which was recently solved by purchasing chamber refrigerators with a storage temperature at – 40 degrees C, extending the plasma storage time to three years [1, 5, 8, 11].

Another important cause of unused blood units in our institution is increased amount of fat in the donors' blood [4, 8]. Almost half of the donors (49.49%) were rejected because of fatigue or low blood pressure, while 26.90% were rejected due to high blood pressure.

Inadequate and obsolete equipment, which are unfortunately still being used, as well as the lack of some devices, are mainly the reason for inadequate collection and storage of adequate amounts of blood. Moreover, staff negligence in processing and preparation of blood also contribute to the damage to blood units. The presence and suspicion of transmissible diseases in blood donors is a problem that we face on daily basis. The introduction of centralized blood processing for transmissible diseases (Blood Transfusion Institute) in our country has certainly reduced the processing costs and processing errors, which is a big step forward [3, 5, 11].

Special emphasis is also on the work and education of staff working with blood or acquisition of the transported blood bags [14, 16]. We also noticed a considerable number of blood units with insufficient blood volume. The problem was caused by the lack of devices for measuring the weight of the blood contents in the bags that was also solved by purchasing necessary devices [3, 4].

Hemolysis in erythrocytes in blood bags was usually due to too much content (blood) in the bags, so that the amount of anticoagulant was not sufficient to uniformly integrate with the total amount of erythrocytes in the bag, leading to the formation of clots and hemolytic erythrocytes [6, 7]. The appearance of clots in the bags also occurred due to insufficient and inadequate mixing of contents in the bags when taking blood, but also because of insufficient amount of anticoagulant in the bags.

Wrong labeling of blood bags and replacing blood samples taken (the most common substitute identification numbers and card providers) are errors made by the staff, and they were almost eradicated, but they need to be given special attention, knowing the consequences they can cause [3, 10]. Continuous education of employees and mandatory reporting of errors does not involve penalizing the person who made an error, but improves the quality of work [2–4] in order to overcome the abovementioned problems.

The greatest number of damages to the blood bags refers to poor welding of the sample hose on the blood bags. They are caused by poor quality of the welding machine or inadequate handling of the appliance. We carry out intensive education of the staff to overcome the problems.

We also educate drivers and the personnel who transfer blood between institutions in terms of adequate storage, receipt and handover of blood units that must be transported in accordance with the prescribed standards [1–3].

A damage to the bags of frozen plasma often happens before dissolving, and this is usually accompanied by a slip from the hands of the staff during the extraction of the plasma from the freezer. Then, these bags fall on the floor and break down.

Damage to plasma bags after dissolution, as well as their placement in departments with the placement of other prepared blood derivatives is directly related to the training of the staff. Their most common errors include the destruction of the sterile barrier when connecting the transfusion system and inadequate warming of the blood in the pouches before giving it to the patient. Ensuring good quality control in the future, in the form of quality planning, work and checking everyone's work, should lead to good results that are our common obligation and goal [1–4].

Conclusion

It is clear that the number of unused blood units in our country (10.1%) and in our institution (11.38%) is still high. The leading reasons for this are high presence of fat in the donors' blood, blood suspected of transmissible diseases, expiration of the blood units, insufficient amount of taken blood in the bags, and the damage to the blood bags during processing.

Continuous education should promote a healthy lifestyle with particular reference to safe sex and risky behavior among young people who may be blood donors.

Discovering new and analyzing the existing factors that affect the occurrence of unused transfusion units with better planning, introduction of preventive measures and application only of safe blood in the treatment of patients will significantly reduce the number of unused blood units and contribute to faster and successful treatment of patients in the future.

Respecting European standards regarding the safety of blood, good medical practice and quality control will significantly reduce the number of unsuitable transfusion units, which will lead to faster, better and cheaper health care.

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A FOODBORNE NOROVIRUS OUTBREAK AMONG THE FILM CREW IN THE AUTONOMOUS PROVINCE OF VOJVODINA, SERBIA

EPIDEMIJA TROVANJA HRANOM IZAZVANA NOROVIRUSOM MEĐU ČLANOVIMA FILMSKE EKIPE U AUTONOMNOJ POKRAJINI VOJVODINI, SRBIJA

Mirjana ŠTRBAC[1] and Mioljub RISTIĆ[1, 2]

Summary

Introduction. Norovirus is one of the most common causes of acute gastroenteritis in the world. The aim of this study was to describe characteristics of an outbreak of norovirus infection and present all the steps of an outbreak investigation. **Material and Methods.** A retrospective cohort study was conducted among all individuals who ate food from the same restaurant. All the exposed persons filled out an adapted questionnaire that is routinely used in patients with food poisoning. **Results.** This paper presents a norovirus outbreak among film crew members and measures taken to control the epidemic. Gastroenteritis was diagnosed in 20 exposed persons. In most patients, symptoms lasted 1 - 3 days, and every third patient sought medical attention. The predominant clinical manifestations were vomiting and diarrhea. The food that probably caused the infection were sandwiches with ham, cheese and lettuce and microbiological analysis confirmed that the outbreak was caused by norovirus. **Conclusion.** Although the source of this outbreak remains unclear, the results of environmental investigation of the restaurant showed several irregularities in the kitchen that may have caused norovirus transmission.

Key words: Norovirus; Disease Outbreaks; Foodborne Diseases; Gastroenteritis; Surveys and Questionnaires; Epidemiology; Signs and Symptoms; Risk Factors

Sažetak

Uvod. Norovirus je jedan od najčešćih uzročnika akutnog gastroenteritisa u svetu. Cilj ovog istraživanja bio je da se opišu karakteristike jedne epidemije izazvane norovirusom i prikažu sve etape u sprovođenju istraživanja epidemije. **Materijal i metode**. Sprovedena je retrospektivna kohortna studija među svim osobama koje su konzumirale hranu iz istog restorana. U istraživanju je za sve eksponirane osobe korišćen epidemiološki upitnik prilagođen za anketiranje pacijenata kod trovanja hranom. **Rezultati**. Ovaj rad prikazuje epidemiju norovirusom među članovima filmske ekipe i preduzete mere kontrole ove epidemije. Kod ukupno 20 izloženih osoba registrovan je gastroenteritis. Kod većine pacijenata, simptomi su trajali 1−3 dana, a svaki treći pacijent zatražio je medicinsku pomoć. U kliničkoj slici dominirali su povraćanje i proliv. Inkriminisana namirnica bio je sendvič sa šunkom, sirom i zelenom salatom. Mikrobiološkim ispitivanjima je potvrđeno da je uzročnik epidemije norovirus. **Zaključak**. Iako je izvor ove epidemije ostao nepoznat, rezultatima ispitivanja radne sredine prepoznato je nekoliko nepravilnosti u kuhinji restorana, čime je verovatno omogućeno širenje norovirusa.

Ključne reči: Norovirus; epidemija bolesti; bolesti uzrokovane hranom; gastroenteritis; istraživanja i upitnici; epidemiologija; znaci i simptomi; faktori rizika

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Introduction

Norovirus (NoV), a member of the Caliciviridae family, is a single-stranded ribonucleic acid (RNA) virus with low infectious dose. It is one of the most common causes of acute gastroenteritis in the world and affects all age groups, with the most common genogroup II, genotype 4 [1, 2]. Symptomatic NoV infection is characterized by acute onset of nausea, vomiting, abdominal cramps, and diarrhea [3].

In foodborne outbreaks caused by NoV, the food can be contaminated by an infected person who is in the acute phase of the disease, but also by food handlers who are asymptomatic carriers [2].

Viruses, including NoV, are difficult to isolate from food, in contrast to bacteria, which can replicate in food. Therefore, identification of viral pathogens in the stool of patients and comprehensive

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Abbreviations
NoV – norovirus
GII.4 – genogroup II, genotype 4
IPHV – Institute of Public Health of Vojvodina
RR – relative risk
RT-PCR – real-time polymerase chain reaction

epidemiological investigation are very important for the detection of outbreaks caused by NoV [3].

Due to the lack of laboratory diagnostic facilities and limited surveillance of NoV infections in Serbia, there is no data about the incidence in the population, but common reports of gastroenteritis with probable viral etiology [4] indirectly indicate that NoV infection is present in our country with a similar incidence as in the European Union [5].

On the 15th December 2015, a physician from an Emergency Department informed the Center for Disease Control and Prevention of the Institute of Public Health of Vojvodina (IPHV) about five members of a film crew with symptoms of diarrhea and/or vomiting. Those members were admitted on the same morning. Within the next four hours, an additional crew member appeared with similar symptoms. All patients had eaten food from the same restaurant. Immediately after receiving this information, an IPHV Outbreak Team initiated an outbreak investigation, and in cooperation with the sanitary and veterinary inspection, visited the Emergency Department, the restaurant, and the patients' accommodation.

The aim of this investigation was to find the source and all possible modes of transmission during this outbreak, and to identify and exclude potential risk factors.

Material and Methods

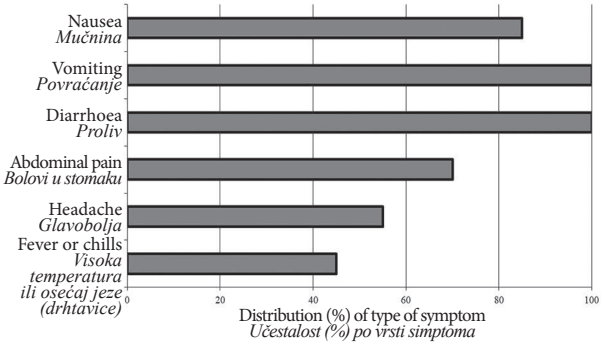
A retrospective cohort study was conducted among all subjects who ate food that was delivered from a restaurant to the patients' accommodation. We defined an outbreak case as a person who ate some meals from the same restaurant for two days (on the 13th and 14th December 2015) and developed diarrhea and/or vomiting within the following three days. Information on the process of preparation, serving and food delivery to the patients' accommodation during these two days in collaboration with the sanitary inspection were obtained. The investigators adapted a standard questionnaire, routinely used for patients with foodborne diseases. The questionnaire was based on the information from the restaurant with a list of food items which were served during the two days before the outbreak occurrence. Additionally, there were questions on demographic data such as the time and date of onset, clinical features, and the duration of specific signs/symptoms of NoV infection, as well as the time of food consumption.

After data collection, a descriptive and univariate analysis was carried out. Also, the relative risk (RR) values with 95% confidence interval (CI) were calculated. Statistical significance was set at $p <$

Table 1. Demographic and clinical characteristics of outbreak cases due to norovirus infection
Tabela 1*. Demografske i kliničke karakteristike slučajava u epidemiji izazavnoj norovirusom*

Characteristics/*Karakteristike*	Number of cases/*Broj slučajeva* *
Sex/*Pol*	
Male/*Muškarci*	11
Female/*Žene*	9
Age (years)/*Uzrast (godine)*	
20 - 29	14
30 - 39	4
40 - 49	2
Place of residence/*Mesto prebivališta*	
Bečej	2
Others **/*Ostalo*	18
Duration of symptoms//*Trajanje simptoma*	
Less than one day/*Kraće od jednog dana*	2
1 - 3 days/*Jedan do tri dana*	12
≥ 3 days/*Tri i više dana*	6
Seeking healthcare/*Poseta zdravstvenoj ustanovi*	6
Hospitalization/*Hospitalizacija*	0
Deaths/*Smrtni ishod*	0

Legend: * One member of the film crew reported to have had diarrhea one night before the others, but he did not meet the case definition and was not included in the outbreak cases; ** Cases from other places of Serbia (Belgrade, Aleksandrovac, Palić)
*Legenda: * Jedan član filmske ekipe prijavio je da je imao dijareju jednu noć pre ostalih, ali on nije ispunio definiciju slučaja i nije bio uključen kao slučaj ove epidemije; ** Slučajevi iz drugih mesta Srbije (Beograd, Aleksandrovac, Palić)*



Graph 1. Frequency of clinical signs/symptoms of outbreak cases due to norovirus infection
***Grafikon 1**. Učestalost kliničkih znakova/simptoma među obolelima u epidemiji izazvanoj norovirusom*

0.05. Data analysis was performed using the SPSS version 21 software.

Results

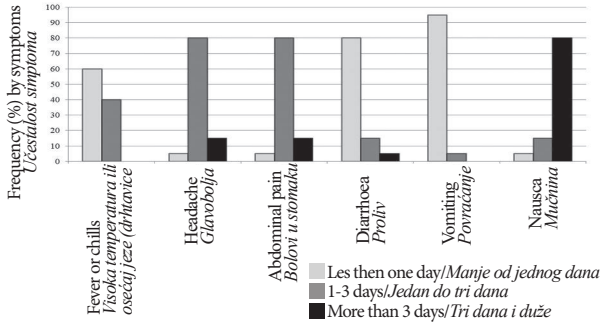
Epidemiological investigation

None of the interviewed food handlers or kitchen employees reported having been sick in the weeks before to the outbreak, but the chief cook was not at work on the day when the outbreak was investigated.

Descriptive epidemiology

A total of 30 film crew members filled out the questionnaire and 20 of them were diagnosed with infection. Out of total cases, 11 were males and 14 were aged between 20 and 29 (age range of 21 – 44 years). Of all the film crew members, only two patients with symptoms were from the place of outbreak, while the rest were from other places in Serbia. In most patients (12/20) the symptoms lasted 1 – 3 days, and every third patient sought medical attention (**Table 1**).

In regard to symptoms, all patients reported vomiting and/or diarrhea (**Graph 1**).



Graph 2. Duration of signs/symptoms of outbreak cases due to norovirus infection
***Grafikon 2**. Trajanje kliničkih znakova/simptoma među obolelima u epidemiji izazvanoj norovirusom*

In 80% of all patients, nausea was the symptom with the longest duration (more than three days), but in 95% of all patients, vomiting lasted less than a day. None of them had fever, chills or vomiting longer than three days (**Graph 2**).

The date and time of symptom onset for 20 cases are shown in **Graph 3**. In accordance with the information about two different dates of exposure to suspicious food items, most cases had symptoms 40 hours after consuming the food on the 13th December, and 16 hours after food consumption on the 14th December, with the most registered cases on the 15th December, between 02.00 to 04.00 a.m.

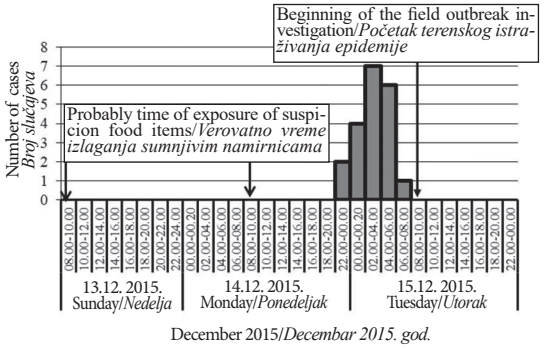
Analytic epidemiology

There were three meals a day (breakfast, lunch and dinner). All three meals were prepared in the kitchen of the restaurant and delivered to the members of the film crew who were accommodated in their apartments, a few kilometers away from the restaurant. The meals were delivered by a vehicle which was not equipped for safe food transportation.

Considering the two-day period before the outbreak, we identified a total of six food items that were probably related to symptom development. The same food items (sandwiches) were served on both days during breakfast, leading to the highest attack rate among the exposed subjects (RR: 2.8 vs. RR: 3.9, $p < 0.05$). Although the RR for green beans was more than one, there was not a statistically significant difference among the exposed persons and those who were not (**Table 2**).

Environmental investigation

After the sanitary inspection, there were several irregularities in the restaurant's kitchen. More precisely, there were incorrect washing routines, storage of fresh foods and prepared meals, as well as inadequate management and control of cooling the heat-treated foods. In addition, there was evidence of insufficient cleaning and disinfection of work surfaces in the kitchen. Furthermore, there



Graph 3. Epidemic curve of outbreak cases due to norovirus infection by date and time of onset in regard to food consumption
***Grafikon 3**. Epidemijska kriva - slučajevi epidemije izazvani norovirusom po datumu i vremenu početka tegoba u odnosu na vreme konzumiranja namirnica*

Table 2. Relative risk of food item consumption among outbreak cases due to norovirus infection
***Tabela 2**. Relativni rizik konzumiranih namirnica za nastanak epidemije izazvane norovirusom*

Food at each meal by date and time of consumption *Hrana pri svakom obroku prema datumu i vremenu konzumacije*	Exposed/*Izloženi*			Not exposed/*Neizloženi*			Relative risk/*Relativni rizik obolevanja u odnosu prema konzumiranoj namirnici (95% CI)*	p
	Number of outbreak cases *Broj obolelih u epidemiji*	Total number of participants/ *Ukupan broj ispitanika*	Attack rate *Učešće obolelih u ukupnom broju izloženih (%)*	Number of cases *Broj obolelih u epidemiji*	Total number of participants *Ukupan broj ispitanika*	Attack rate *Učešće obolelih u ukupnom broju neizloženih* (%)		
13. 12. 2015.								
Breakfast */*Doručak*								
Sandwiches with ham, cheese and lettuce salad/*Sendviči sa šunkom, sirom i zelenom salatom*	17	20	85.0	3	10	30.0	2.8 (1.1-7.4)	0.0343
Lunch **/*Ručak*								
Moussaka (mashed potatoes, eggs and minced meat)/*Musaka (krompir, jaja i mleveno meso)*	13	22	59.1	7	8	87.5	0.7 (0.4-1.0)	0.0771
Dinner ***/*Večera*								
Mashed potatoes, roast pork and canned pepper salad/*Pire krompir, svinjsko pečeno meso i salata od konzervirane paprike*	15	23	65.2	5	7	71.4	0.9 (0.5-1.6)	0.7482
14. 12. 2015.								
Breakfast */*Doručak*								
Sandwiches with ham, cheese and cabbage salad/*Sendviči sa šunkom, sirom i kupus salatom*	18	21	85.7	2	9	22.2	3.9 (1.1-13.3)	0.0321
Lunch **/*Ručak*								
Green beans, bread and canned pepper salad/*Zeleni pasulj, hleb i salata od konzervirane paprike*	16	22	72.7	4	8	50.0	1.5 (0.7-3.0)	0.3201
Dinner ***/*Večera*								
Mixed meat (steak, chicken, bacon, sausage), bread and green salad/*Mešano meso (biftek, piletina, slanina, kobasica), hleb i zelena salata*	15	22	68.2	5	8	62.5	1.1 (0.6-2.0)	0.7791

Legend: *Consumed between 8.00 - 10.00 a.m.; **Consumed between 1.00 - 3.00 p.m.; ***Consumed between 6.00 - 8.00 p.m.
*Legenda: * Konzumira se između 8,00 i 10,00 sati; ** Konzumira se između 13,00 i 15,00 sati; *** Konzumira se između 18,00 i 20,00 sati*

were cockroaches on the floor and the walls of the kitchen during the investigation. The kitchen staff did not routinely wear gloves when handling ingredients and food items. In light of the observed irregularities, the sanitary authorities immediately ordered a sanitary examination of food handlers and of all the kitchen staff. On the 15th December, after the sanitary inspection, the restaurant's kitchen was closed, until the correction of all sanitary defects.

In accordance with the Guidelines for microbiological criteria in Serbia [6], samples obtained from the kitchen work surfaces and the cutlery, showed a large number of Coliform bacteria, which is a common bacterial indicator of sanitary quality of food and water.

Microbiological investigation

The stool samples of two patients and 11 members of the kitchen staff were tested for bacterial pathogens (Salmonella spp., Shigella spp., Campylobacter spp.) and viruses (norovirus, rotavirus and astrovirus) at the microbiology and virology laboratories of the IPHV. The stool samples were extracted using the Ribo Virus commercial kit

(Sacace, Biotechnologies, Italy) according to the manufacturer's instructions. Using the real-time polymerase chain reaction (RT-PCR), nucleic acid for NoV, rotavirus and astrovirus was performed. In addition, all 11 nasal and nasopharyngeal swabs of the kitchen staff were tested for Staphylococcus aureus and Streptococcus pyogenes.

Furthermore, according to the recommendations of the sanitary and veterinary inspections, samples of the kitchen work surfaces, the cutlery and fresh barbecue sausages were tested for bacterial pathogens in the microbiological laboratory of the IPHV. It was not feasible to perform a microbiological analysis of the food items served during the two suspicious days because it was depleted prior to the outbreak investigation.

Norovirus was confirmed in the stool samples of two patients (genogroup II), without further genotyping. However, the stool samples of 11 kitchen staff were negative for NoV. Stool samples for bacterial pathogens of two patients and 11 the kitchen employees were negative. Moreover, the nasal and nasopharyngeal swabs of 11 kitchen staff were negative for Staphylococcus aureus and Streptococcus pyogenes.

In accordance with the recommendations of the Law on Food Safety of the Republic of Serbia [7], the microbiology tests of fresh barbecue sausages showed genus Listeria, species Listeria innocua and a large number of the Enterobacteriaceae. With available laboratory capacities, no further tests were carried out.

Discussion

A sudden onset and short duration of this outbreak where all cases were registered within a 10-hour period, suggested that food was the probable source of the outbreak. Considering the facts that all of the exposed persons, as well as the suspicious restaurant (linked to this outbreak), used the water from the same source and since the investigation of the outbreak did not register an increasing number of cases with gastroenteritis in the general population, the water was excluded as a potential source of this outbreak.

As is known, the clinical features of NoV infection are vomiting, followed by abdominal cramps, fever and watery diarrhea. The illness usually lasts for two to three days, but the duration can be longer [3, 8]. In this outbreak, considering two different time points of probable exposure to the incriminated food (on the 13th and 14th of December) and the time and date when the first and last outbreak cases were registered, the minimum incubation period was 10 hours while the maximum was 42 hours. Among all patients, the illness started with nausea, the symptom with the longest duration. Vomiting and diarrhea were registered in all cases, and vomiting lasted less than a day in 95% of all patients.

Regarding the outcome of this outbreak, we found that it did not have serious public health consequences, without any evidence of secondary transmission of the NoV infection to the general population. However, despite the fact that the outbreak was registered in a small exposed group, the number of infected persons was high (attack rate: 66.7%; 20/30). This phenomenon can be explained by the fact that the exposure to the same incriminated food items happened twice before the outbreak had been registered. Although there were no hospitalizations or deaths recorded, it seems that a high infectious dose of NoV through two exposures probably contributed to the large percentage (30%) of sick persons who requested medical care.

It is a known fact that NoV has a low infectious dose (approximately from 10 – 18 to 1000 viral particles), which allows an easy spread of NoV through droplets, by fomites, and person-to-person contact. Among close contacts, the secondary attack rate of NoV is 30% or more [8–10]. In accordance with this, an explosive occurrence of this outbreak may have been contributed by the fact that one member of the film crew reported to have had diarrhea a night before the others. Although he did not meet the case definition, he could have spread the infection by contact.

Although person–to-person transmission is very common in NoV outbreaks [1], secondary cases were not detected in our investigation. An explanation for this probably lies in the fact that except for two patients, all the other members of the film crew left the place of outbreak immediately after the beginning of outbreak, and thus potential secondary cases might not have been reported in this area.

The results of the microbiological analysis of two stool samples confirmed that the outbreak was caused by NoV. However, genus Listeria, species Listeria innocua, was also detected in the samples of fresh sausages. The clinical presentation of foodborne NoV infection and gastrointestinal disease caused by Listeria monocytogenes are similar. As is known, patients with Listeria become ill within 24 to 48 hours after exposure to the contaminated food (rice salad, chocolate milk, corn salad) [11]. After analyzing the RR to all food items, we excluded Listeria in "mixed meat with fresh barbecue sausages" as the cause of this outbreak.

In the outbreak investigated here, the specific source of infection remains unclear. Results of other authors suggest that the freshly prepared sandwiches can be the source of NoV infection, especially those that contain egg mayonnaise. The same study determined that soup, although being a warm product, could have been the source of NoV infection [9]. We revealed evidence that sandwiches (served for two breakfasts) were the possible sources of the outbreak. Our results also suggest that green beans may be considered as a suspicious food item (RR: 1.5), but the difference between the exposed and not exposed persons was not statistically significant.

Regarding the observed course of this outbreak, it is not possible to explain why no other customers of the restaurant had some symptoms of infection. This could probably be explained by the fact that people who did not belong to the film crew (other

customers of the restaurant) had eaten the same food as the outbreak cases, except for the sandwiches.

The food handlers have already been identified as a potential source of NoV transmission in several studies [9, 12–14]. The identification of asymptomatic food handlers is very important during NoV outbreaks [2, 15]. Results of others authors showed that the food handlers could be a source of the outbreak even in a situation when they denied any gastrointestinal illness during the outbreak period. For example, in previously published research, additional investigations showed that the child (infant) of a healthy food handler had been sick with watery diarrhea two days before the food handler prepared the incriminated meals. Hence, this member of the kitchen staff did not need to be sick, but may have been contaminated after changing the baby's diapers if he did not wash his hands properly [16].

The concentration of NoV excreted in stool samples of infected individuals among the infected people decreases rapidly and, becomes practically undetectable within 2 – 3 days [12]. We were not absolutely sure if asymptomatic kitchen employees had a role in the spread of the virus in this outbreak, because their stool samples were tested more than 72 hours after the first suspicious meal had been served. Interestingly, the kitchen chief of the restaurant was not at work on the day when the outbreak was investigated and he did not provide a stool sample for laboratory testing. In the absence of symptoms among all tested kitchen staff, negative laboratory results of their stool samples, and the absence of appropriate laboratory capacity for testing of paired serum samples from the kitchen employees, we were not able to directly confirm our hypothesis about the source of this outbreak.

On the other hand, several other facts indicated that this outbreak was potentially classified as a foodborne outbreak of NoV infection. The cause of this outbreak was confirmed using RT-PCR method and the clinical features were typical for NoV infection. Despite the fact that the source of infection was not directly confirmed, results of univariate analysis of the exposure showed that eating sandwiches was associated with an increased risk of infection. The sandwiches were previously recognized as the cause of NoV outbreak [17], and lettuce was the common source of infection [18, 19]. Furthermore, high levels of Coliform bacteria, which were found on the restaurant's kitchen work area surfaces, are indicating that the kitchen was unsanitary. Additionally, considering that NoV remains viable on surfaces for as long as two weeks [20] and due to the fact that the food delivery was carried out in lunch boxes by a vehicle not equipped for the safe food transportation, we believe that these facts probably contributed to the contamination of food items before the consumption.

Conclusion

Our report represents the first detailed epidemiological study of a foodborne outbreak due to the norovirus infection in Serbia, and we recognized several gaps during the investigation. For the recognition of the outbreak type, the probable source, the reservoir of infection, as well as the route of transmission, it is necessary to carry out an immediate and comprehensive investigation. Outbreak conclusions and consequently control measures about certain outbreaks may be inadequate without appropriate laboratory support for the confirmation of certain pathogens.

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CASE REPORTS
PRIKAZI SLUČAJEVA

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Case report
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RENAL ACTINOMYCOSIS – A CASE REPORT

BUBREŽNA AKTINOMIKOZA – PRIKAZ SLUČAJA

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Summary

Introduction. Actinomycosis of the urogenital tract mainly manifests with formation of renal and perirenal abscesses. When it comes to treating renal lodge abscesses caused by Actinomyces bacteria, the method of choice is mainly surgical evacuation of purulent collections, followed by administration of parenteral penicillin or cephalosporin antibiotics during a six week period. The definitive diagnosis is made based on the antibiogram findings, isolation of Actinomyces israelii from abscess collection, as well as by characteristic histological findings. The exact incidence and prevalence of urogenital actinomycosis is still unknown. **Case Report**. A 54-year-old female patient was admitted to the Emergency Department of the Clinical Center of Vojvodina for triage. She complained of pain in the left lumbar and gluteal region, weakness, malaise, and fever. She was treated with corticosteroids under the diagnosis of vasculitis five months prior to admission. Based on clinical, laboratory blood and urine tests, ultrasound examination of the abdomen and contrast CT of the abdomen and pelvis, the diagnosis of left kidney abscess was made. It also spread to the retroperitoneum (iliopsoas muscle, gluteus maxuimus and ipsilateral inguinal region). Urgent operative exploration of retroperitoneum and kidney was performed. A lumbotomy was performed in the left half of the retroperitoneum with evacuation of abscesses, as well as partial nephrectomy of the lower half of the left kidney. Subsequently, the obtained antibiogram of operatively sampled aspirate, renal actinomycosis was histopathologically verified. The surgically removed tissue that was sent for histopathology showed presence of connective tissue infiltrated with a pronounced inflammatory infiltrate composed of lymphocytes, plasma cells, histiocytes and granulocytes with numerous microabscesses and actinomycosis colonies.

Key words: Actinomycosis; Kidney Diseases; Abscess; Retroperitoneal Space; Urinary Tract Infections; Diagnosis; Signs and Symptoms; Urologic Surgical Procedures

Sažetak

Uvod. Na nivou urogenitalnog trakta aktinomikoza se uglavnom manifestuje stvaranjem renalnih i perirenalnih apscesa. Metoda lečenja apscesa bubrega i bubrežne lože, koji su uzrokovani baketrijama iz genusa *Actinomyces,* jeste hiruška evakuacija gnojne kolekcije uz parenteralnu terapiju penicilinima ili cefalosporinskim antibioticima u trajanju od šest nedelja. Definitivna dijagnoza se postavlja na osnovu nalaza biograma i izolacije *Act. israelii* iz apscesne kolekcije kao i na osnovu karakterističnog patohistološkog nalaza. Tačna incidencija i prevalencija urogenitalne aktinomikoze nije poznata. **Prikaz slučaja**. Pacijentkinja starosti 54 godine javila se u Trijažnu ambulantu Urgentnog centra Kliničkog centra Vojvodine zbog bolova u predelu leve lumbalne i glutealne regije, slabosti, malaksalosti i febrilnosti. Poslednjih pet meseci lečena je kortikosteroidima kod imunologa, pod dijagnozom vaskulitisa. Na osnovu kliničke slike, laboratorijskih nalaza krvi i urina, ultrazvučnog pregleda abdomena i kontrasne kompjuterizovane tomografije abdomena i male karlice postavljena je dijagnoza apscesa levog bubrega koji iradira u retroperitoneum, u *m. iliopsoas*, *m. gluteus maxuimus* i ingvinalnu regiju ipsilateralno. Izvršena je hitna operativna eksploracija retroperitoneuma i bubrega. Lumbotomijom je pristupljeno levoj polovini retroperitoneuma uz evakuaciju apscesa i ektomiju donjeg pola levog bubrega. Naknadno je dobijen nalaz biograma sa antibiogramom operativno uzorkovanog aspirata i patohistološke verifikacije da se radi o aktinomikozi bubrega. U patohistološkom nalazu tkiva koje je operativno odstranjeno bilo je prisutno vezivno masno tkivo sa izraženim zapaljenskim infiltratom koji je sastavljen od limfocita, plazmocita, histiocita i granulocita sa brojnim mikroapscesima i kolonijama aktinomikoze.

Ključne reči: aktinomikoza; bolesti bubrega; absces; retroperitonealni prostor; infekcije urinarnog trakta; dijagnoza; znaci i simptomi; urološke hirurške procedure

Introduction

Certain infectious diseases, although relatively rare in clinical practice, may lead to serious consequences, including death. One of such diseases is renal actinomycosis. Renal abscesses usually occur due to secondary hematogenous dissemination from a focus elsewhere in the body (purulent changes of

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Abbreviations
ED – Emergency Department
CT – computed tomography

the skin, lungs, bones, and other organs), although they can develop through direct extension from the surrounding structures. The most common pathogens that cause renal abscess are Staphylococcus aureus and Escherichia coli. The most common predisposing pathological conditions for the development of renal medullary abscesses are diabetes mellitus and urinary tract calculi. Given all the benefits of the development of modern medicine, one must not forget the importance of various kinds of immunosuppression [1 - 3]. The treatment consists of surgical evacuation of purulent collection, followed by use of antibiotic therapy (especially in case of large, limited renal abscess). Purulent content must be collected and sent for microbiological testing [1 - 3]. Actinomyces israelii is the best known representative of the genus Actinomyces, which includes anaerobic and microaerophilic Gram-positive filamentous bacteria, that coexist as saprophytes in the gastrointestinal tract and vagina. In general, bacteria of the genus Actinomyces are transitional microorganisms between bacteria and fungi. Other members of the genus are: Actinomyces odontolyticus, Actinomyces naeslundii (viscous) and Actinomyces Erikson. In an affected organism, bacteria form colonies. Colonies manifest as a yellow solid grain, a few millimeters in diameter (normally up to 2 mm), when observed by a light microscope. Microscopic materials are made up of filaments which are referred to as hyphae (hyphae are in general more characteristic for fungi than bacterial microorganisms). Actinomyces species are rather resistant; in dry environment, at the room temperature and when not exposed to direct sunlight, they can survive up to two months. They are sensitive to most antibiotics, penicillin included. Antigen structure of bacteria of the genus Actinomyces is not fully explored [4]. So far, there have not been any registered cases of actinomycosis transmission among humans, as well as from animals to humans. There is a widespread view that actinomycosis infection is of endogenous origin, caused by the disruption of balance in both local and systemic immune response. Bacteria are usually found in the tonsillar crypts, carious teeth, as well as other parts of the mouth. The theory is that the microorganism alone cannot cause an infection, but it becomes a pathogen in symbiosis with other microorganisms. Science does not know much of acquired immunity after an Actinomyces israelii. A specific prophylaxis does not exist [4]. The exact incidence of actinomycosis is not known either. In the United States, in the late 20th century, the annual incidence of all cases of actinomycosis was 1 case per 300.000 persons. Actinomycosis of the urogenital tract mainly manifests in the form of renal and perirenal abscess. When it comes to the treatment of the renal lodge abscesses caused by Actinomyces bacteria, the method of choice is mainly surgical evacuation of purulent collections, followed by parenteral penicillin or cephalosporin antibiotics during a six week period. The definite diagnosis cannot be made before antimicrobial susceptibility test is done and Actinomyces israelii is isolated from the abscess collection. Characteristic histological findings include characteristic hyphae [1–11]. Incidence of cervicofacial and thoracic actinomycosis is much higher compared to the abdominal and pelvic actinomycosis.

Figure 1. Abdominal CT scan of the patient (contrast intravenous phase) – showing an abscess that involves the lower pole of left kidney and the surrounding musculature
Slika 1. *Kompjuterizovana tomografija abdomena pacijenta (kontrasna faza) – pokazuje apscesnu kolekciju koja zahvata donji pol levog bubrega i okolnu muskulaturu*

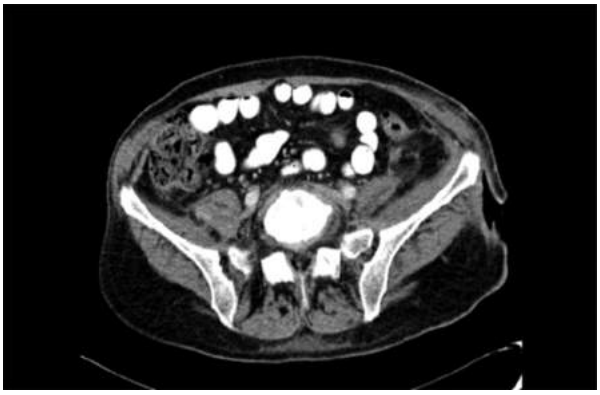

Figure 2. Pelvic CT scan of the patient - contrast intravenous phase
Slika 2. *Kompjuterizovana tomografija male karlice pacijentkinje – kontrasna faza*

Case Report

A 54-year-old female patient was admitted to the Emergency Department (ED) of the Clinical Center of Vojvodina for triage. She complained of pain in the left lumbar and gluteal region, weakness, fatigue and fever (body temperature to 39 °C). Symptoms debuted two weeks prior to admission to the ED, and

have gradually got worse. Five months prior to admission, the patient had been treated at the Department of Dermatology and the Department of Nephrology and Immunology of the Clinical Center of Vojvodina, where she was diagnosed with vasculitis and received Prednisone (10 mg a day). These admissions were due to nodular inflammatory changes with purulent-hemorrhagic secretion on the skin of the lower extremities. Such pustules first appeared in January 2013. The analysis made at that time showed slightly positive antineutrophil cytoplasmic antibodies (ANCA), while proteinase-3 (PR-3) and myeloperoxidase (MPO) antibodies were proven to be negative. Immunofixation serum was M component. The Medical Advisory Board of the Department of Nephrology indicated corticosteroid treatment, which consequently induced disappearance of pustules. The pustular biopsy indicated a structure resembling rheumatoid nodule. The patient had active dental foci that were repaired during the hospital stay. Thoracic computed tomography (CT) showed signs of infiltration in the right upper lung lobe. A consulting pulmonologist indicated bronchoscopy after discharge, which was not performed. The patient suffers from bipolar affective disorder and receives Velahibin tbl. (75 mg daily), as recommended by a psychiatrist. The patient denied other chronic diseases as well as surgical interventions.

Physical examination at the ED revealed a painful fluctuating tumefaction in the left lumbar lodge, tender on palpation. Laboratory tests of blood and urine were done. Urine sediment contained a large number of leukocytes, epithelial cells and bacteria, as well as two renal epithelial cells; qualitative test was positive for nitrites and proteins. Blood test results showed leukocytosis - Leu 20.87 x 10*9/l (Neu 17.54x10*9/l). C-reactive protein was 216.4 mg/l. Urea, creatinine, acidum uricum, as well as electrolytes, were within reference values. The abdominal ultrasound showed a heterogeneous lesion, with central zones of echogenicity and peripheral vascularization, localized in the central part of left kidney, 73 x 49 mm in size. The left kidney lesion primarily corresponded with an abscess, although other etiology could not be excluded. The right kidney was of normal size, with normal parenchyma, and no signs of calculosis and hydronephrosis. There was no sign of free fluid in the abdominal cavity. In the superficial structures of the right superiliac region, a hypoechoic mass (partly unclear and partly clearly limited), with anechoic central areas (that may correspond to areas of colliquation), was visualized. Based on these findings, the attending urologist made a decision to urgently perform a contrast CT of the abdomen and pelvis **(Figures 1 and 2)**. The CT showed that the left kidney was increased, its larger diameter of 13 cm. An inhomogeneous, hypodense lesion, with clear postcontrast increase of density was seen in the interpolar region and lower pole of the kidney. Its diameters were 8 x 5 cm, most consistent with an inflammatory etiology. This lesion was structurally similar to ones visualized in the regions of the left m. iliopsoas and m. gluteus maximus, as well as in the groin part, on the same side; all lesions were connected via channels. The right kidney and ureter were both without any pathology, and the excretory function of both kidneys was preserved. The liver was enlarged, its sagittal diameter of 17 cm in the medial clavicular line, of correct contours and a diffusely reduced density. Its structure was disrupted with fatty infiltrations, as well as a 2 cm dual zone hypodensity, corresponding to cysts. There was also an 11 mm gallbladder calculus, as well as a great number of small stones. The CT of the abdomen and pelvis was otherwise unremarkable.

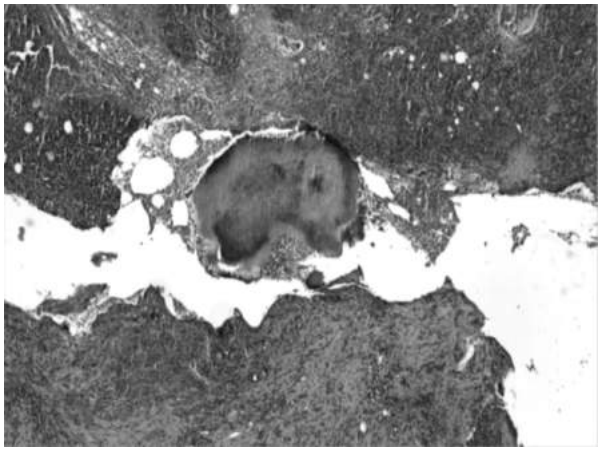

Figure 3. Histopathological preparation of the surgically removed tissue under a light microscope
Slika 3. *Patohistološki preparat operativno odstranjenog tkiva pod svetlosnim mikroskopom*

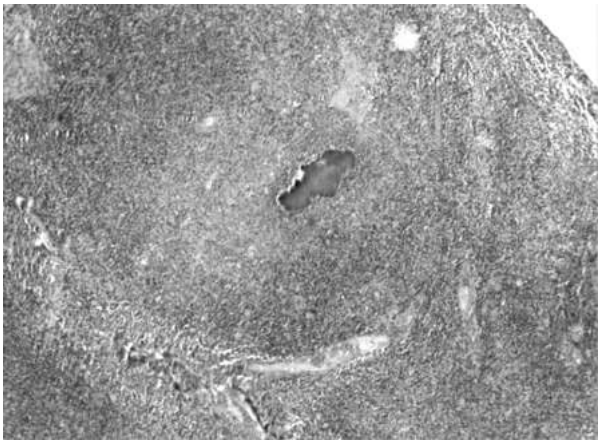

Figure 4. Histopathological preparation of the surgically removed tissue under a light microscope
Slika 4. *Patohistološki preparat operativno odstranjenog tkiva pod svetlosnim mikroskopom*

Urgent surgical exploration of the retroperitoneal space and kidneys with evacuation of pus was performed immediately, using lumbar incision with a left retroperitoneal approach. Around 2.000 ml of limpid

light yellow and thick liquid was evacuated, containing small, irregularly shaped, dark yellow particles, as well as a smaller amount of brownish pus. The evacuated pus was sent for microbiology testing. Then, a partial nephrectomy was performed - the lower pole of the left kidney that was affected by purulent process had been removed, and sent for histopathological examination. The peritoneum and the retroperitoneum were drained. The surgical wound was closed in layers. The surgeon made an incision and evacuated the gluteal collection that had the same characteristics as the previously described one. The patient was postoperatively admitted to the Department of Urology, Clinical Center of Vojvodina, where she stayed for three weeks. The initial parenteral antibiotic therapy included ceftriaxone 2 g/12h for 10 days and metronidazole 500 mg/8h for 7 days. After receiving the antibiogram results, as well as histopathological verification of renal actinomycosis, the therapy was changed to parenteral amoxicillin/clavulanic acid at dose of 1200 mg/12 h for 10 days. The antibiotic treatment continued after discharge for additional 20 days, but the patient received trimethoprim/sulfamethoxazole tablets, 960 mg/12 h.

Histopathological analysis of surgically removed tissue showed connective tissue and fat with an inflammatory infiltrate composed of lymphocytes, plasma cells, histiocytes and granulocytes, with numerous colonies and microabscesses containing actinomycosis **(Figures 3 and 4)**. During several months of follow-up, the patient had been in good physical condition, and all laboratory results were within reference values.

Control CTs of the thorax, abdomen and pelvis, performed at follow-ups, showed persisting lesions in the right lung, liver, gallbladder and spleen. Further treatment, after discharge was done by a specialist in infectious diseases.

Discussion

Actinomyces israelii is a microorganism that rarely causes an infection in humans [1–9]. Actinomycosis mainly affects the neck and mediastinum and less often the abdomen and lower pelvis. In almost all cases reported in the literature, actinomycosis is described as a chronic, slowly progressive infection [2, 4]. The progression of the disease and our patient's medical history (considering clinical manifestations and duration of the disease) corresponds to the clinical picture of actinomycosis. There are few cases of urinary tract infections with actinomyces in the literature, mainly as complications of enterovesical and vesicovaginal fistulas, almost always in females [2, 7–9]. In most cases, it occurs among patients who are either immunocompromised or have had major surgeries of the urinary tract [2, 4–9]. The presented patient received a five-month-long continuous immunosuppressive therapy that led to a progress when it comes to pustules on the lower extremities, but on the other hand, it triggered further dissemination of actinomyces infection, due to decreased immune response. Previously described changes of the lung parenchyma corresponded to bacteria from the genus Actinomyces, but histopathological verification was necessary for definitive diagnosis. There are not many reported clinical cases of renal and perirenal abscesses. All of the described cases of pelvic actinomycosis included ascites, pleural effusions and pelvic lymphadenopathy. In almost all cases, the diagnosis was based on microbiological and histopathological changes in surgically removed tissue [2, 4–9]. An abscess is an infectious process that can easily induce sepsis, and if not adequately and aggressively treated, it may easily lead to permanent renal failure, or even death [1–3]. Renal abscesses are a particular problem from the standpoint of urgent urology, especially when one needs to decide whether to perform an urgent surgical exploration and evacuation, or conduct a conservative treatment with antibiotics prior to intervention [2–4, 7–9, 11–21]. In most described literature cases, actinomycosis infection (disregarding anatomic localization of process itself), is characterized by fever, weakness and fatigue. Laboratory blood test results revealed a leukocytosis (caused by an increase in neutrophil granulocyte absolute value), as well as an increased value of C-reactive protein [2–4, 7–9, 11–21]. In almost all cases, the inflammatory collection was revealed by CT of the corresponding part of the body, and the final diagnosis was based on histological findings. Most patients are over 55 years old. When it comes to our case report, the diagnosis was established based on worldwide accepted clinical procedures. According to the age, the presented patient fits the age population in which actinomycosis is usually diagnosed.

The main problem, after studying actinomycosis nearly 80 years, is that initial factor that leads to the infection is still not fully known. Commonly recognized initial factors are immunosuppression and violation of integrity of mucous membranes of the gastrointestinal, respiratory and urogenital tract (caused either by trauma, or surgical intervention). However, until now, none of them has been fully confirmed, nor are they entirely discarded. Our patient was receiving immunosuppressive therapy and had a dental focus that certainly might have been the initial point of entry of actinomyces into the systemic circulation. Another question is, how many patients are there in our everyday clinical practice, presenting with common infectious syndromes, among whom an underlying actinomycosis diagnose is unrecognized. Absence of a specific laboratory test for detection of specific antibodies against actinomycosis antigens disables setting the diagnosis without histopathological evaluation. This delays the beginning of adequate therapy and raises the cost of treatment.

Conclusion

Although renal and retroperitoneal abscesses caused by bacteria from the Actinomyces genus are

relatively rare compared to other etiologies, it is logical to assume a probable increase in this form of urinary tract changes, especially having in mind a constantly growing number of persons with immunodeficiency, as well as the rapid aging of the global population. Also, there is an increasing number of patients whit comorbidities who are subjected to invasive surgical procedures, such as, for example, radical cystectomy in urology. Considering all the above mentioned, actinomycosis has an important place when it comes to differential diagnosis of solid masses as well as purulent collections of the urogenital tract.

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POSTTRAUMATIC DISRUPTION OF THE RIGHT MAIN BRONCHUS – A CASE REPORT

POSTTRAUMATSKA DISRUPCIJA DESNOG GLAVNOG BRONHA – PRIKAZ SLUČAJA

Bojan KOLEDIN[1], Miloš KOLEDIN[1,2], Ivan KUHAJDA[1,2] and Slađana KOLEDIN[2,3]

Summary

Introduction. Tracheobronchial disruption is a rare disorder, usually accompanied by a severe blunt chest trauma that quite rarely appears as an isolated event. **Case Report.** This is a case report of a right main bronchus disruption, due to an injury to the right hemithorax, caused by a falling tree trunk. The disruption was accompanied by mediastinal emphysema, fractures of the 4th and 5th ribs on the right side and compound sternal fracture. The patient was operated in general anesthesia, through right thoracotomy approach, followed by successful right main bronchus reconstruction by interrupted suture technique, without anatomic resection of the lung parenchyma. **Conclusion.** Although this injury is rare, with suspicion of bronchial rupture, bronchoscopy confirms the diagnosis and leads to better prognosis.

Key words: Bronchi; Thoracic Injuries; Wounds and Injuries; Bronchoscopy; Pneumothorax; Thoracic Surgical Procedures; Chest Tubes; Treatment Outcome

Sažetak

Uvod. Traheobronhijalna disrupcija predstavlja redak poremećaj i obično je povezana sa ozbiljnim, tupim traumama grudnog koša, dok se izuzetno retko javlja izolovano. **Prikaz slučaja.** Ovo je prikaz slučaja disrupcije desnog glavnog bronha koji je nastao prilikom pada stabla u predelu desnog hemitoraksa. Disrupcija desnog glavnog bronha je bila praćena medijastinalnim emfizemom, prelomom IV i V rebra sa desne strane i dvostrukim prelomom sternuma. Pacijent je operisan u opštoj anesteziji kada mu je urađena desna torakotomija i sutura desnog glavnog bronha pojedinačnim šavovima bez anatomske resekcije plućnog parenhima. **Zaključak.** Iako spada u retke povrede, sumnja na traheobronhijalnu disrupciju uz neodložnu primenu bronhoskopije, dovešće nas do željene dijagnoze, a samim tim i bolje prognoze.

Ključne reči: bronhi; povrede grudnog koša; rane i povrede; bronhoskopija; pneumotoraks; grudna hirurgija; torakalni dren; ishod lečenja

Introduction

The incidence of tracheobronchial disruptions due to blunt trauma of the chest is very low, accounting for 1 – 2.8% of all injuries. Most patients with this type of blunt injury, up to 80%, do not survive transportation to the hospital [1–3]. The accurate diagnosis fails to be established in almost 68% of the cases. A high clinical suspicion index and adequate interpretation of radiological findings are crucial for the diagnoses of these injuries, enabling an urgent surgical intervention with a primary suture of the airways. The proper treatment reduces the risk of death, as well as partial or total bronchial stenosis [2–4].

Case Report

A 44-year-old male patient was transferred from a regional hospital with right chest injuries induced by a falling tree trunk a day prior to admission. On admission, the patient was tachypneic, spontaneously breathing, his oxygen saturation was 82% with a breathing mask applied, anxious, hemodynamically stable, with

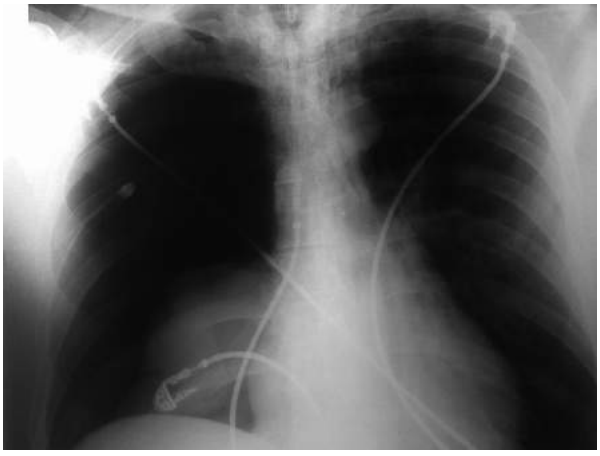

Figure 1. Chest X-ray on admission
Slika 1. *Rendgenski snimak grudnog koša prilikom prijema*

a chest tube placed in the right hemithorax and persistent air leak through the applied drain. The chest drain

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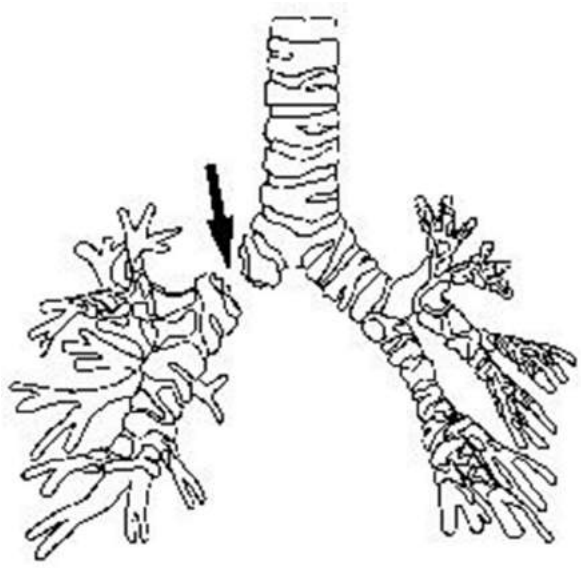

Figure 2. Schematic presentation of the bronchial tree with a right main bronchus disruption
Slika 2. *Shematski prikaz bronhijalnog stabla sa oštećenjem desnog glavnog bronha*

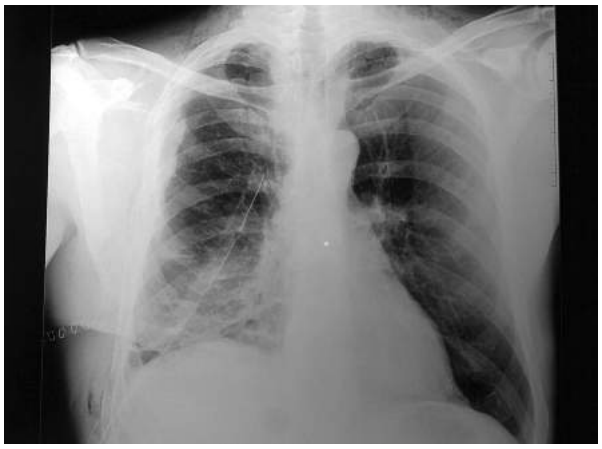

Figure 3. Post surgery chest X-ray
Slika 3. *Rendgenski snimak grudnog koša posle operacije*

tube was placed in the intensive care unit of the regional hospital. Radiologically, the drain was properly positioned, but the right pneumothorax persisted **(Figure 1)**. Detailed medical history revealed that the patient had a long history of alcohol abuse. The chest X-ray on admission showed a 4th rib fracture and a pneumothorax on the right. The chest computed tomography showed a total pneumothorax on the right side, a mediastinal shift, as well as a 5th rib fracture and a compound fracture of the sternum. Since a right main bronchus rupture was suspected, a bronchoscopy was performed, revealing a disruption of the right main bronchus. Following a short-course preoperative management, the patient underwent right exploratory thoracotomy in general anesthesia. Complete rupture of right main bronchus was found 1.5 – 2 cm distally to the carina **(Figure 2)**. Considering that the time from the injury was 24 hours, primary repair with debridement was performed by interrupted sutures and two chest tubes were placed. The postoperative course was without complications; there was no air leakage, fallen lung sign or pneumothorax **(Figure 3)**. On the 3rd and 4th postoperative days the chest tubes were removed. Control chest X-ray revealed no signs of either pneumothorax or emphysema. On the 5th postoperative day, the patient was discharged for home treatment.

Discussion

The first case of tracheobronchial tree traumatic rupture was reported by Webb in 1848, following the autopsy of a male patient who had been run over by a car [5]. First successfully primary surgical treatment of the tracheobronchial rupture was performed by Scannell in 1951 [6]. It is believed that the mechanism of injury includes a combination of anteroposterior chest compression, causing stress on the carina, while the lungs still remain in contact with the lateral chest wall, and a rapid elevation of the intraluminal pressure due to the glottis closure reflex [3, 6]. Over 80% of these injuries develop 2 cm from the tracheal carina and most of them have been registered in young patients with a relatively elastic chest wall [3, 6, 7].

There are two clinical presentations documented, depending on the peribronchial tissue status (intact/non intact). A large rupture will induce a total pneumothorax, inducing dyspnea impossible to resolve, a condition which may further go bad if a chest tube is introduced. In this case, the diagnosis is clear, usually requiring an emergency intervention [1, 3].

If peribronchial tissues are intact, the manifested symptoms may be very mild, such as minimal pneumothorax and minimal air leak in the mediastinum. This condition is difficult to recognize on a standard chest X-ray [8]. These situations require a high clinical suspicion index, especially in young patients when the mechanism of injury suggests a rupture of the airways. If an injury of the airways is suspected, bronchoscopy should be performed. However, these procedures should be carried out in the operating room in total anesthesia, due to the risk of disruption of the peribronchial tissue, so that an endobronchial tube can be introduced distally beside the disruption, or a two-lumen tube may be introduced in case a disruption is not visualized [7, 10].

Conclusion

Once the diagnosis of bronchial disruption is established, surgical treatment offers the best long-term prognosis; open surgery with debridement and end to end anastomosis if it is possible. There are cases when lung resection is needed. Recently, there are attempts to perform this procedure via uniportal video assisted thoracic surgery approach.

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HISTORY OF MEDICINE
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DEVELOPMENT OF THE CITY HOSPITAL IN NOVI SAD – PART II

RAZVOJ GRADSKE BOLNICE U NOVOM SADU – DRUGI DEO

Dušanka DOBANOVAČKI[1], Nada VUČKOVIĆ[1, 2], Radmila GUDOVIĆ[1], Vladimir SAKAČ[1, 3], Milanka TATIĆ[1, 4] and Vesna TEPAVČEVIĆ[5]

Summary
At the end of the Second World War, the General State Hospital had seven departments, the same facilities, and the same bed capacity as in the pre-war period. In the newly formed state of Yugoslavia, intensive growth and modernization of the hospital began, despite the great financial difficulties. The hospital became the Main Provincial Hospital and new departments and services were established. Mainly during the 1960s and 1970s, ten new surgery departments were established, which later became independent clinics. The surgery departments occupied pavilions 1, 2, 3 and 4. Complex and contemporary abdominal and thoracic surgeries were performed. The Department of Internal Diseases became the Clinic of Internal Diseases and in 1964 it was moved to a newly equipped four-story building. The Clinic of Gynecology and Obstetrics was founded and it was moved into a modern, purpose-built facility with a 230 bed capacity for adult patients and 105 for newborns. Rapid progress has also been made in the development of the Clinic of Infectious Diseases, Clinic of Eye Diseases, Clinic of Ear, Nose and Throat Diseases, Neurology and Psychiatry Clinics, Clinic of Dermatovenereology Diseases, Medical Rehabilitation Clinic – as well as a modern laboratory, X-ray, blood transfusion, and polyclinic services. After the establishment of the Faculty of Medicine and the Clinical Center of Vojvodina, this large tertiary medical institution is the source of pride for Novi Sad. Founded 110 years ago, the hospital is still dedicated to providing better healthcare for patients.
Key words: History of Medicine; History, 20th Century; Hospitals; Tertiary Care Centers; Yugoslavia

Sažetak
Posle završetka Drugog svetskog rata bolnica je imala ista odeljenja, broj postelja i opremu kao i pre rata. U novoosnovanoj državi Jugoslaviji, uprkos značajnim finansijskim teškoćama, u bolnici je započeo intenzivan razvoj i modernizacija. Bolnica je postala Glavna pokrajinska bolnica, osnivala su se nova odeljenja i servisi. Uglavnom tokom šezdesetih i sedamdesetih godina dvadesetog veka, deset novih hirurških odeljenja je osnovano koja su kasnije postala samostalne klinike. Hirurško odeljenje je zauzelo prostor u paviljonima 1, 2, 3 i 4. Izvode se kompleksne i savremene abdominalne i grudne operacije. Odeljenje za unutrašnje bolesti postaje Klinika za interne bolesti i 1964. godine preseljava se u novu opremljenu četvorospratnu zgradu. Klinika za ginekologiju i akušerstvo je osnovana i preseljava se u moderan, namenski građen objekat sa kapacitetom 230 postelja za odrasle i 105 za novorođenčad. Brz napredak uticao je i na razvoj Klinike za infektivne bolesti, Klinike za oftalmologiju, Klinike za bolesti uva, grla i nosa, Klinike za neurologiju i psihijatriju, Klinike za dermatovenorologiju, Klinike za medicinsku rehabilitaciju – sve praćeno modernom laboratorijskom i rendgenološkom službom, transfuzionim i poliklinickim servisima. Posle osnivanja Medicinskog fakulteta i Kliničkog centra Vojvodine, ova velika tercijerna medicinska institucija je ponos Novog Sada. Podignuta pre 110 godina bolnica je i dalje posvećena poboljšanju zdravlja obolelih.
Ključne reči: istorija medicine; istorija, 20. vek; bolnice; centri tercijarne nege; Jugoslavija

The names of the City Hospital and its managers through the history

City Hospital (1909)
190(7)9 – 1919 Dr. Alexander Schossberger
General State Hospital (1921)
1919 – 1932 Dr. Đura Trifković
1932 – 1941 Dr. Risto Miletić Šain
1941 – 1944 Hungarian Military Administration
1945 – 1946 Dr. Radivoj Kalenić
Main Provincial Hospital (1946)
1946 – 1952 Dr. Nestor Teodorović
1952 – 1958 Dr. Đorđe Maletić
1959 – 1961 Dr. Svetislav Cvejić

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Clinical Hospital (1963)
1961 – 1969 Dr. Imre Miller
1969 – 1974 Prof. Dr. Aleksandar Svirčević
1974 – 1977 Prim. Dr. Lazar Ilić
All Clinics are independent, under the authority of the Faculty of Medicine Novi Sad 1977 – 1997
Clinical Center Novi Sad (1997)
1997 – 2000 Prof. Dr. Đorđe Janjić
Clinical Center of Vojvodina (2002)
2001 – 2003 Prof. Dr. Pavle Milošević
2003 – 2006 Prof. Dr. Dragomir Damjanov
2006 – 2015 Prof. Dr Dragan Drašković
2015 – 2016 Doc. Dr. Ivan Levakov
2016 – 2019 Prof. Dr. Petar Slankamenac
2019 – Prof. Dr. Edita Stokić

Period after Second World War

At the end of the Second World War, the General State Hospital had seven departments, the same facilities, and the same number of bed capacity as in the pre-war period [1]. In the newly formed state, the Federal People's Republic of Yugoslavia, despite the great financial difficulties, intensive development and modernization of medicine, hospital services and public health system began, covering all categories of the population. The hospital became the Main Provincial Hospital in 1996; new departments and services were established, expanding the activities and educating young medical staff - doctors and nurses.

In 1945, buildings for the *Admitting Department* and the dispensary station were built with the entrance from the Hajduk Veljkova street. The *Department of Surgery* was expanded in the First and Second Pavilions, where the First and Second Surgical Departments were established. Complex and latest abdominal and chest surgeries were performed. In the period from 1952 - 1958, the surgical services were expanded, young doctors were hired, and anesthesia was conducted by specialist in anesthesiology [1]. In 1955, the surgical block was transformed, and the Emergency Surgery Unit [2] was set up in the basement of the Pavilion 1.

The Section of Orthopedics, established in 1928, became the *Orthopedic-Traumatology Department* in 1956, and it is still located in the basement of the Pavilion 2. Not before 1963/4, the department was moved to Pavilion 6: the orthopedic patients were on the ground floor, and traumatologic on the first floor [2] (upgraded in 1945) [3, 4].

In 1948, the Urology Section was established, which became a *Department of Urology* in 1952. It was located in the basement of the *Surgery Department*, the patients were nursed by nuns and in 1953 it had a 50 bed capacity [5, 6].

In 1956, within the *Second Surgery Department, a Pediatric Surgery* ward was established. In 1957, the child surgical pathology became a separate entity, and in 1959 it became a *Pediatric Surgery and Orthopedics Department* [7]. Expansion of the surgical program and the need to increase the bed capacity led to the union of the pediatric services, and the Institute for Mother and Child Health Care was established in 1977 in a specially built building at 10 Hajduk Veljkova Street [7].

In 1960, both Surgery Departments were united into the Surgery Clinic and an intensive development of new surgical branches started [8]. Initially, the Clinic was located in three and then in four separate buildings (Pavilions 1, 2, 3, 6) plus an Orthoperdic Department in Sremska Kamenica, with a total of 411 bed capacity and 41 employees [9]. In the course of the 60s and 70s of the twentieth century, the departments became independent clinics **(Figure 1)**:

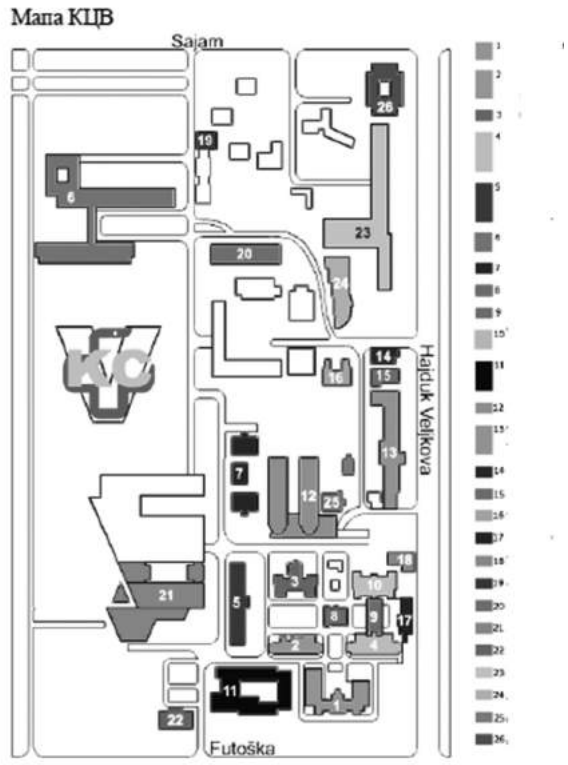
– Clinic of Abdominal, Endocrine and Transplantation Surgery,
– Clinic of Orthopedic Surgery and Traumatology,
– Clinic of Neurosurgery,
– Clinic of Urology with a Dialysis Unit, which became the Dialysis Center in 1970 [5, 6],
– Clinic of Vascular and Transplantation Surgery,
– Clinic of Plastic and Reconstructive Surgery,
– Clinic of Maxillofacial and Oral Surgery,
– Clinic of Anesthesia and Intensive Care [10].

In 1985, the Surgery Clinic became the Institute of Surgery and today it is a part of the Clinical Center of Vojvodina, founded in 2002.

The *Department of Internal Diseases* remained in Pavilion 3 and increased the number of beds after the separation of the Maternity Ward. In 1962, the *Department of Internal Diseases* became the Clinic of Internal Diseases and in 1964 it was moved to a new well-equipped building in the hospital, with four floors and a 200 bed capacity. On the ground floor, there was an ambulance for emergency cases with a laboratory and an X-ray unit. New departments [9] were established, that will later become clinics of the Clinical Center of Vojvodina:

– Clinic of Cardiology with cabinets and an intensive care unit for patients with myocardial infarction. After the Institute of Cardiovascular Diseases in Sremska Kamenica was established, the Clinic was relocated and became independent (1977),
– Clinic of Pulmonology, that was later moved to the Institute of Tuberculosis and Lung Diseases in Sremska Kamenica [9],
– Clinic of Nephrology and Clinical Immunology,
– Clinic of Endocrinology, Diabetes and Metabolic Diseases,
– Clinic of Gastroenterology and Hepatology,
– Clinic of Hematology.

The *Department of Gynecology and Obstetrics* became an independent department in 1947 in the Pavilion 6. Although the rebuilding started before the war, two new floors were added to the building after the end of the Second World War [3, 11]. The department had an operating room and a delivery room [12, 13]. Since 1952, part of the bed capacity of the *Department of Gynecology and Obstetrics* was in the Pavilion 4, which was reconstructed by the addition of new wings. In this part, patients with „septic conditions" and women with planned abortions were placed [11]. Since 1947,



Scheme 1. Today's sketch and arrangements of hospital pavilions in Clinical Center of Vojvodina:
1, 2, 3 and 4. Clinics of surgery specalities
5. Clinics for internal diseases
6. Clinics for neurology and psychiatry
7. Clinic for infectios diseases
8. Clinic for skin and venereal diseases
9. Clinic for ear, nose ant throath diseases
10. Clinic for eye diseases
Chapel of Saint apostle and gospel Luka
11. Clinic for medical rehabilitation
12. Policlinics
13. Laboratory and Radiology
14. Center for forensic medicine, toxicology and molecular genetic
15. Pathology and hystology centre
16. Hospital pharmacy and supply
17. Dialysis departmet
18. Admission department
19. Metadonic centre
20. Techical and supply department
21. Emergency centre
22 Board house
23. Faculty of medicine
24. Faculty of pharmacy
25. Department Pasteour
26. Transfusiology department

Shema 1. Današnji nacrt i raspored bolničkih objekata u Kliničkom centru Vojvodina:
1, 2, 3 i 4. Klinike za hirurška oboljenja
5. Klinike za internistička oboljenja
6. Klinike za neurologiju i psihijatriju
7. Klinika za infektivne bolesti
8. Klinika za kožno-venerične bolesti
9. Klinika za bolesti uha, grla i nosa
10. Klinika za očne bolesti
Bolnička crkva Sv. Apostola i evangeliste Luke
11. Klinika za medicinsku rehabilitaciju
12. Poliklinika
13. Centar za laboratorijsku medicinu, Radiologija
14. Centar za sudsku medicinu, toksikologiju i molekularnu genetiku
15. Centar za patologiju i histologiju
16. Centar za medicinsko snabdevanje, bolnička apoteka
17. Odeljenje za dijalizu
18. Prijem bolesnika
19. Metadonski centar
20. Služba za tehničko-uslužne poslove
21. Urgentni centar
22. Uprava KCV
23. Medicinski fakultet
24. Farmaceutski fakultet
25. Pasterov zavod
26. Zavod za transfuziju krvi

pregnant women were legally required to give birth at maternity hospitals, so a large number of pregnant women were being admitted. That is why, an out of hospital Maternity Ward at 30 Gajeva Street with a 20 bed capacity was established and worked until 1951. In the period of 4 years, about 2.000 uncomplicated deliveries were performed [14]. In 1963, the Clinic of Gynecology and Obstetrics was founded and moved to a modern and purpose-built facility in Branimira Ćosića Street [11] with a 230 bed capacity for adult patients and 105 for newborns. The scope of services has increased, organizational changes have been made several times including foundation of clinics, departments, and sections, of which the most important were:

– Department of Perinatology,
– Department of Gynecology,
– Institute of Pregnancy Pathology,
– Institute of Human Reproduction, and
– Department of Fetal Medicine and Prenatal Diagnosis.

In 1945, the *Department of Infectious Disease* became independent, with a 20 bed capacity, mainly for the treatment of children affected by scarlet fever, diphteria and small pox [15]. In 1960, the Department became the Clinic of Infectious Diseases [16] and it was treating all infectious diseases. After moving to the premises of the Hygiene Institute in 1969, the Clinic of Infectious Diseases increased the bed capacity to 110 where all infectious diseases [16] were treated [16] and since the establishment of the Faculty of Medicine it has become the teaching and research hospital. The construction meant for connecting the Admitting Block and the Intensive Care Unit started in 1995 [16, 17].

Tuberculous patients were treated on the ground floor of the Pavilion 6 until 1947, and later in the buildings of the Regional Hospital for the Treatment of Tuberculosis at the Provincial Hospital at 37 Branimira Cosica Street - Pavilion Betania [13] till 1960, when the Institute of Tuberculosis and Lung Diseases

was established in Sremska Kamenica. The Betanija Pavilion was built in 1900, supported by the Episcopal-Methodist Church in America and it was a hospital-sanatorium for the mentally ill patients [18, 19]. In 1960, tuberculosis patients were moved to the Institute of Tuberculosis and Lung Diseases in Sremska Kamenica. After the establishment of the Faculty of Medicine in Novi Sad, the Clinic of Infectious Diseases has become a teaching hospital with a capacity of 110 beds.

The Department of Ophthalmology was located on the first floor of Pavilion 5, and it was mainly dealing with research in the field of trachoma and surgery of anomalies caused by the disease [20]. Later, ophthalmooncology, modern ophthalmology and eye microsurgery were developed.

The Department of Ear, Nose and Throat Diseases was located in the basement and ground floor of Pavilion 5, and since 1957 had a 52 bed capacity. Since 1963, it has expanded its bed capacity and child pathology occupaing the ground floor of the building [9]. In the same year, it became the Clinic of Ear, Nose and Throat Diseases for the treatment of otological problems, throat microsurgery, phoniatrics, and Rhinology and Allergology Departments were intensively developed. In 1977, an addition to the building was built with a modern operating theatre [21].

Dermatovenereology diseases were mainly treated through the outpatient department or the State Hygiene Institute [22, 23], but the patient rooms were inadequately located just across the reception office. In 1952, the Department moved to a very small facility in Kisačka street with a 65 bed capacity and a small handy laboratory. The Clinic of Dermatovenerology was founded in 1963, in 1965 it was moved to the hospital in the upgraded building of Pavilion 4 [13]. The Clinic developed separate branches for mycology, allergology and child dermatology.

The Hospital for the Mentally ill patients was founded in 1949, and in 1951 it became an independent *Neuropsychiatric Department* located in the building of the current hospital pharmacy until 1966 [1] when a modern purpose-built building was built, the last in a series of hospital pavilions and where the current Clinic for Neuropsychiatry is located [9].

The Radiology Department, established in 1928, in 1952, it was transferred to an adapted building of the hospital. In 1965, the department became an Institute and it was located on the ground floor of the newly constructed building of the Polyclinic; adequate medical staff was employed and new equipment was purchased. In 1973, the Institute became the Institute of Radiology with two Departments: for diagnostics and radiotherapy [24].

The Central Clinical Laboratory, founded in 1946, was transformed into the Institute of Diagnostics Laboratory of the Clinical Hospital in 1973, and in 1985 it was transferred to the Polyclinic [1, 25]. Today it is the Center for Laboratory Medicine and it is located in the new Polyclinic.

The Blood Transfusion Station of the III Yugoslav Army was founded in 1944 [26], but after the end of the Second World War, it became the Blood Transfusion Station of the General Provincial Hospital in 1949 [1]. In 1958, a new wing was built on the surgery Pavilion 1 and the Blood Transfusion Station was moved there. In 1963, the station became the Blood Transfusion Institute of the Provincial Hospital. An increased number of surgeries and modernization of the operational program set new tasks for the institute regarding supply of blood and blood derivatives [27]. A new building was built for blood transfusion services and its work started at the beginning of 1988. Since 1994, the Blood Transfusion Institute received a new equipment, trained and specialized staff and with the introduction of modern technology in the preparation and distribution of blood and its derivatives, today, the Blood Transfusion Institute of Vojvodina is as independent medical facility which has maintained the basic program orientation regarding the collection, testing, and preparation of blood products for its users.

The Department of Dentistry was established in 1949 and in 1991 it was transformed into the Institute of Dentistry. Today it is located in the building so-called „Forest Hospital" [1].

In 1951, several utility facilities were added to the hospital: technical-mechanical services, warehouses, kitchen, heat rooms and laundry rooms [1, 12].

The Rehabilitation Center with 68 patient beds [13] was founded as part of the Main Provincial Hospital in 1959, at the initiative of the Association of Disabled War Veterans, which became the Department of Physical Medicine and Rehabilitation in 1960 [1]. In 1973, a new building was added to the hospital, and the Clinic of Medical Rehabilitation, with 120 beds and over 10 specialized cabinets were established in 1990 [9, 28].

Since 1941, the *Pathology Service* has been operating in inadequate premises until 1958/9, when a facility for the needs of pathological anatomy was adapted. It became a Department in 1962, an Institute of Pathology in 1970 [29]. Today, it is the Center of Pathology and Histology. In 1960, the Center of Forensic Medicine with Criminology and Toxicology was established [9], whereas today it is the Center of Forensic Medicine, Toxicology and Molecular Genetics.

The Specialist Polyclinic was a part of the City Health Center until 1959, and then became a part of the Main Provincial Hospital. In 1965, a purpose-built building was designed in the Hajduk Veljkova Street to provide outpatient interdisciplinary specialist and subspecialist healthcare including: consultative examinations, complex diagnostic tests, minor surgical interventions, and some therapeutic modalities. In the following decades, the needs for modern diagnostic methods have increased, as well as the the number of patients, so a new Polyclinic of the Clinic Center was built and started working in 2001, whereas the old has become the Diagnostic Department of the Institute of Radiology and partly the laboratory of the Clinical Center [30].

Hospital chapels were common until the Second World War, after which they were banned, but are being built in Serbia since the late 20th century [12]. In the basement of the Eye Clinic and the Ear, Nose and Throat Clinic, on the north side, is the entrance to the Hospital Chapel dedicated to the *Holy Apostle and Evangelist Luke*. The former prison hospital was renovated and became the hospital chapel in 2008 [31].

The omnipresence of practical and scientific medicine in each segment of health culture, expansion of the existing and establishment of new hospital and outpatient-preventive health services, created conditions for the establishment of the *Faculty of Medicine* in Novi Sad on May 18, 1960 [32]. The hospital service has become a scientific institution and a modern teaching base for medical education of young people, responsible for scientific research and expansion of modern aspects of treatment, prioritizing financing and equipment [8]. Then, the Main Provincial Hospital became the teaching base of the Faculty of Medicine and in 1963 became a Clinical Hospital. Eighteen new departments were established with a 1.070 bed capacity, and 120 doctors specialists were employed [13].

The Clinical Center of Vojvodina has entered the 21st century as a tertiary health institution established in 2002. It consisted of 27 professional health units, with a capacity of 1.425 beds, 1.892 health workers, of which 612 were doctors specialists (http://www.kcv.rs) **(Scheme 1)**. The major goal of the Clinical Center of Vojvodina is early detection, treatment and rehabilitation of patients, professional development and specialization of all health workers, and cooperation with other institutions dealing with the health of the population. The Emergency Center was built in 2010, and it is a modern high-standard institution intended for all emergency conditions.

During the past 110 years, the City Hospital in Novi Sad has passed hard times, but has always had a scientific spirit with continuous improvement of quality work and professional services. Being part of the Faculty of Medicine, many generations of doctors and health professionals have proven themselves with their knowledge and dedication in the daily struggle for better health and life of patients. The mission of the first doctors of the City Hospital was transferred to the next generations, a mission of practicing professional and scientific medicine, in agreement with the Hippocratic code of ethics in medicine. The respect for tradition and present was, and will always be, part of the timeless spirit present in every corner of these buildings.

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UPUTSTVO ZA AUTORE

Časopis ***Medicinski pregled*** objavljuje radove koji prethodno nisu objavljeni niti poslati u drugi časopis. U Časopisu mogu biti objavljeni radovi iz različitih oblasti biomedicine, koji su namenjeni lekarima različitih specijalnosti.

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1. Uvodnici – do 5 strana. Sadrže mišljenja ili diskusiju o posebno značajnoj temi za Časopis, kao i o podacima koji su štampani u ovom ili nekom drugom časopisu. Obično ih piše jedan autor po pozivu.

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3. Pregledni članci – do 10 strana. Predstavljaju sistematsko, sveobuhvatno i kritičko izlaganje problema na osnovu analiziranih i diskutovanih podataka iz literature, a koji oslikavaju postojeću situaciju u određenom području istraživanja. Literatura koja se koristi u radu mora da sadrži najmanje 5 radova autora članka iz uže naučne oblasti koja je opisana u radu.

4. Prethodna ili kratka saopštenja – do 4 strane. Sadrže izuzetno važne naučne rezultate koje bi trebalo objaviti u što kraćem vremenu. Ne moraju da sadrže detaljan opis metodologije rada i rezultata, ali moraju da imaju sva poglavlja kao originalni članci u sažetoj formi.

5. Stručni članci – do 10 strana. Odnose se na proveru ili prikaz prethodnog istraživanja i predstavljaju koristan izvor za širenje znanja i prilagođavanja originalnog istraživanja potrebama postojeće nauke i prakse.

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8. Ostali članci – U časopisu Medicinski pregled objavljuju se feljtoni, prikazi knjiga, izvodi iz strane literature, izveštaji sa kongresa i stručnih sastanaka, saopštenja o radu pojedinih zdravstvenih organizacija, podružnica i sekcija, saopštenja Uredništva, pisma Uredništvu, novosti u medicini, pitanja i odgovori, stručne i staleške vesti i članci napisani u znak sećanja (*In memoriam).*

Priprema rukopisa

Kompletan rukopis, uključujući tekst rada, sve priloge i propratno pismo, treba poslati na elektronsku adresu koja je prethodno navedena.

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– mora da sadrži izjavu svih autora da se radi o originalnom radu koji prethodno nije objavljen niti prihvaćen za štampu u drugim časopisima;

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Tekst rada treba da bude napisan u programu *Microsoft Word* za *Windows*, na A4 formatu stranice (sve četiri margine 2,5 cm), proreda 1,5 (isto važi i za tabele), fontom *Times New Roman*, veličinom slova 12 *pt*. Neophodno je koristiti međunarodni sistem mernih jedinica (*SI*), uz izuzetak temperature (° *C*) i krvnog pritiska (*mmHg*).

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Naslovna strana treba da sadrži: kratak i sažet naslov rada, bez skraćenica, skraćeni naslov rada (do 40 karaktera), imena i prezimena autora (ne više od 6) i afilijacije svih autora. Na dnu strane treba da piše ime, prezime i titula autora zaduženog za korespondenciju, njena/njegova adresa, elektronska adresa, broj telefona i faksa.

2. Sažetak

Sažetak ne može da sadrži više od 250 reči niti skraćenice. Treba da bude strukturisan, kratak i sažet, sa jasnim pregledom problema istraživanja, ciljevima, metodama, značajnim rezultatima i zaključcima.

Sažetak originalnih i stručnih članaka treba da sadrži uvod (sa ciljevima istraživanja), materijale i metode, rezultate i zaključak.

Sažetak prikaza slučaja treba da sadrži uvod, prikaz slučaja i zaključak.

Sažetak preglednih članaka treba da sadrži Uvod, podnaslove koji odgovaraju istima u tekstu i Zaključak.

Navesti do 10 ključnih reči ispod sažetka. One su pomoć prilikom indeksiranja, ali autorove ključne reči mogu biti izmenjene u skladu sa odgovarajućim deskriptorima, odnosno terminima iz *Medical Subject Headings*, *MeSH*.

Sažetak treba da bude napisan na srpskom i engleskom jeziku. Sažetak na srpskom jeziku trebalo bi da predstavlja prevod sažetka na engleskom, što podrazumeva da sadrži jednake delove.

3. Tekst članka

Originalni rad treba da sadrži sledeća poglavlja: Uvod (sa jasno definisanim ciljevima istraživanja), Materijal i metode, Rezultati, Diskusija, Zaključak, spisak skraćenica (ukoliko su

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Prikaz slučaja treba da sadrži sledeća poglavlja: Uvod (sa jasno definisanim ciljevima), Prikaz slučaja, Diskusija i Zaključak.

Uvod

U poglavlju Uvod potrebno je jasno definisati predmet istraživanja (prirodu i značaj istraživanja), navesti značajne navode literature i jasno definisati ciljeve istraživanja i hipoteze.

Materijal i metode

Materijal i metode rada treba da sadrže podatke o vrsti studije (prospektivna/retrospektivna, uslove za uključivanje i ograničenja studije, trajanje istraživanja, demografske podatke, period praćenja). Detaljno treba opisati statističke metode da bi čitaoci rada mogli da provere iznesene rezultate.

Rezultati

Rezultati predstavljaju detaljan prikaz podataka koji su dobijeni istraživanjem. Sve tabele, grafikoni, sheme i slike moraju biti citirani u tekstu rada i označeni brojevima po redosledu njihovog navođenja.

Diskusija

Diskusija treba da bude koncizna, jasna i da predstavlja tumačenje i poređenje rezultata studije sa relevantnim studijama koje su objavljene u domaćoj i međunarodnoj literaturi. U poglavlju Diskusija potrebno je naglasiti da li su postavljene hipoteze potvrđene ili nisu, kao i istaknuti značaj i nedostatke istraživanja.

Zaključak

Zaključci moraju proisteći isključivo iz rezultata istraživanja rada; treba izbegavati uopštene i nepotrebne zaključke. Zaključci koji su navedeni u tekstu rada moraju biti u saglasnosti sa zaključcima iz Sažetka.

4. Literatura

Potrebno je da se literatura numeriše arapskim brojevima redosledom kojim je u tekstu navedena u parentezama; izbegavati nepotrebno velik broj navoda literature. Časopise bi trebalo navoditi u skraćenom obliku koji se koristi u *Index Medicus* (*http://www.nlm.nih.gov/tsd/serials/lji.html*). Pri citiranju literature koristiti Vankuverski sistem. Potrebno je da se navedu svi autori rada, osim ukoliko je broj autora veći od šest. U tom slučaju napisati imena prvih šest autora praćeno sa *et al*.

Primeri pravilnog navođenja literature nalaze se u nastavku.

Radovi u časopisima

∗ Standardni rad

Ginsberg JS, Bates SM. Management of venous thromboembolism during pregnancy. J Thromb Haemost 2003;1:1435-42.

∗ Organizacija kao autor

Diabetes Prevention Program Research Group. Hypertension, insulin, and proinsulin in participants with impaired glucose tolerance. Hypertension 2002;40(5):679-86.

∗ Bez autora

21st century heart solution may have a sting in the tail. BMJ. 2002;325(7357):184.

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Magni F, Rossoni G, Berti F. BN-52021 protects guinea pig from heart anaphylaxix. Pharmacol Res Commun 1988;20 Suppl 5:75-8.

∗ Sveska sa suplementom

Gardos G, Cole JO, Haskell D, Marby D, Pame SS, Moore P. The natural history of tardive dyskinesia. J Clin Psychopharmacol 1988;8(4 Suppl):31S-37S.

∗ Sažetak u časopisu

Fuhrman SA, Joiner KA. Binding of the third component of complement C3 by Toxoplasma gondi [abstract]. Clin Res 1987;35:475A.

Knjige i druge monografije

∗ Jedan ili više autora

Murray PR, Rosenthal KS, Kobayashi GS, Pfaller MA. Medical microbiology. 4th ed. St. Louis: Mosby; 2002.

∗ Urednik (urednici) kao autor (autori)

Danset J, Colombani J, eds. Histocompatibility testing 1972. Copenhagen: Munksgaard, 1973:12-8.

∗ Poglavlje u knjizi

Weinstein L, Shwartz MN. Pathologic properties of invading microorganisms. In: Soderman WA Jr, Soderman WA, eds. Pathologic physiology: mechanisms of disease. Philadelphia: Saunders; 1974. p. 457-72.

∗ Zbornik radova sa kongresa

Christensen S, Oppacher F. An analysis of Koza's computational effort statistic for genetic programming. In: Foster JA, Lutton E, Miller J, Ryan C, Tettamanzi AG, editors. Genetic programming. EuroGP 2002: Proceedings of the 5th European Conference on Genetic Programming; 2002 Apr 3-5; Kinsdale, Ireland. Berlin: Springer; 2002. p. 182-91.

∗ Disertacija

Borkowski MM. Infant sleep and feeding: a telephone survey of Hispanic Americans [dissertation]. Mount Pleasant (MI): Central Michigan University; 2002.

Elektronski materijal

∗ Članak iz časopisa u elektronskom formatu

Abood S. Quality improvement initiative in nursing homes: the ANA acts in an advisory role. Am J Nurs [Internet]. 2002 Jun [cited 2002 Aug 12];102(6):[about 1 p.]. Available from: http://www.nursingworld.org/AJN/2002/june/Wawatch.htmArticle

∗ Monografija u elektronskom formatu

CDI, clinical dermatology illustrated [monograph on CD-ROM]. Reevs JRT, Maibach H. CMEA Multimedia Group, producers. 2nd ed. Version 2.0. San Diego:CMEA;1995.

∗ Kompjuterska datoteka

Hemodynamics III: the ups and downs of hemodynamics [computer program]. Version 2.2. Orlando (FL): Computerized Educational Systems; 1993.

5. Prilozi (tabele, grafikoni, sheme i slike)

BROJ PRILOGA NE SME BITI VEĆI OD ŠEST!

Tabele, grafikoni, sheme i slike se postavljaju kao posebni dokumenti.

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– Ako su tabele, grafikoni, sheme ili slike već objavljene, navesti originalni izvor i priložiti pisano odobrenje autora za njihovo korišćenje.

– Svi prilozi će biti štampani kao crno-bele slike. Ukoliko autori žele da se prilozi štampaju u boji, obavezno treba da plate dodatne troškove.

6. Dodatne obaveze

AUTORI I SVI KOAUTORI RADA OBAVEZNO TREBA DA PLATE GODIŠNJU PRETPLATU ZA ČASOPIS *MEDICINSKI PREGLED*. U PROTIVNOM, RAD NEĆE BITI ŠTAMPAN U ČASOPISU.

INFORMATION FOR AUTHORS

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– It must contain the proof given by the author that the paper represents an original work that it has neither been previously published in other journals nor is under consideration to be published in other journals.

– It must confirm that all the authors meet criteria set for the authorship of the paper, that they agree completely with the text and that there is no conflict of interest.

– It must state the type of the paper submitted (an original study, a review article, a preliminary report, a professional article, a case report, history of medicine).

The manuscript:

General instructions.

Use Microsoft Word for Windows to type the text. The text must be typed in font *Times New Roman*, page format A4, space 1.5 (for tables as well), margins set to 2.5 cm and font size 12pt. All measurements should be reported in the metric system of the International System of Units – SI. Temperature should be expressed in Celsius degrees (°C) and pressure in mmHg.

The manuscript should contain the following elements:

1. The title page.

The title page should contain a concise and clear title of the paper, without abbreviations, then a short title (up to 40 characters), full names and surnames of the authors (not more than 6) indexed by numbers corresponding to those given in the heading along with the full name and place of the institutions they work for. Contact information including the academic degree(s), full address, e-mail and number of phone or fax of the corresponding author (the author responsible for correspondence) are to be given at the bottom of this page.

2. Summary.

The summary should contain up to 250 words, without abbreviations, with the precise review of problems, objectives, methods, important results and conclusions. It should be structured into the paragraphs as follows:

– Original and professional papers should have the introduction (with the objective of the paper), materials and methods, results and conclusion

– Case reports should have the introduction, case report and conclusion

– Review papers should have the introduction, subtitles corresponding to those in the paper and conclusion.

The authors should provide up to 10 keywords below the summary. These keywords will assist indexers in cross-indexing the article and will be published with the summary, but the authors' keywords could be changed in accordance with the list of Medical Subject Headings, MeSH of the American National Medical Library.

The summary should be written in both languages, English as well as Serbian. The summary in Serbian language should be the translation of the summary in English; therefore, it has to contain the same paragraphs.

3. The text of the paper.

The text of original studies must contain the following: introduction (with the clearly defined objective of the study), materials and methods, results, discussion, conclusion, list of abbreviations (if used in the text) and not necessarily, the acknowledgment mentioning those who have helped in the investigation and preparation of the paper.

The text of a case report should contain the following: introduction (with clearly defined objective of the study), case report, discussion and conclusion.

Introduction contains clearly defined problem dealt with in the study (its nature and importance), with the relevant references and clearly defined objective of the investigation and hypothesis.

Materials and methods should contain data on design of the study (prospective/retrospective, eligibility and exclusion criteria, duration, demographic data, follow-up period). Statistical methods applied should be clear and described in details.

Results give a detailed review of data obtained during the study. All tables, graphs, schemes and figures must be cited in the text and numbered consecutively in the order of their first citation in the text.

Discussion should be concise and clear, interpreting the basic findings of the study in comparison with the results of relevant studies published in international and national literature. It should be stated whether the hypothesis has been confirmed or denied. Merits and demerits of the study should be mentioned.

Conclusion must deny or confirm the attitude towards the 0based solely on the author's own results, corroborating them. Avoid generalized and unnecessary conclusions. Conclusions in the text must be in accordance with those given in the summary.

4. References are to be given in the text under Arabic numerals in parentheses consecutively in the order of their first citation. Avoid a large number of citations in the text. The title of journals should be abbreviated according to the style used in Index Medicus (http://www.nlm.nih.gov/tsd/serials/lji.html). Apply Vancouver Group's Criteria, which define the order of data and punctuation marks separating them. Examples of correct forms of references are given below. List all authors, but if the number exceeds six, give the names of six authors followed by 'et al'.

Articles in journals

∗ *A standard article*

Ginsberg JS, Bates SM. Management of venous thromboembolism during pregnancy. J Thromb Haemost 2003;1:1435-42.

∗ *An organization as the author*

Diabetes Prevention Program Research Group. Hypertension, insulin, and proinsulin in participants with impaired glucose tolerance. Hypertension 2002;40(5):679-86.

∗ *No author given*

21st century heart solution may have a sting in the tail. BMJ. 2002;325(7357):184.

∗ *A volume with supplement*

Magni F, Rossoni G, Berti F. BN-52021 protects guinea pig from heart anaphylaxix. Pharmacol Res Commun 1988;20 Suppl 5:75-8.

∗ *An issue with supplement*

Gardos G, Cole JO, Haskell D, Marby D, Pame SS, Moore P. The natural history of tardive dyskinesia. J Clin Psychopharmacol 1988;8(4 Suppl):31S-37S.

∗ *A summary in a journal*

Fuhrman SA, Joiner KA. Binding of the third component of complement C3 by Toxoplasma gondi [abstract]. Clin Res 1987;35:475A.

Books and other monographs

∗ *One or more authors*

Murray PR, Rosenthal KS, Kobayashi GS, Pfaller MA. Medical microbiology. 4th ed. St. Louis: Mosby; 2002.

∗ *Editor(s) as author(s)*

Danset J, Colombani J, eds. Histocompatibility testing 1972. Copenhagen: Munksgaard, 1973:12-8.

∗ *A chapter in a book*

Weinstein L, Shwartz MN. Pathologic properties of invading microorganisms. In: Soderman WA Jr, Soderman WA, eds. Pathologic physiology: mechanisms of disease. Philadelphia: Saunders; 1974. p. 457-72.

∗ *A conference paper*

Christensen S, Oppacher F. An analysis of Koza's computational effort statistic for genetic programming. In: Foster JA, Lutton E, Miller J, Ryan C, Tettamanzi AG, editors. Genetic programming. EuroGP 2002: Proceedings of the 5th European Conference on Genetic Programming; 2002 Apr 3-5; Kinsdale, Ireland. Berlin: Springer; 2002. p. 182-91.

∗ *A dissertation and theses*

Borkowski MM. Infant sleep and feeding: a telephone survey of Hispanic Americans [dissertation]. Mount Pleasant (MI): Central Michigan University; 2002.

Electronic material

∗ *A journal article in electronic format*

Abood S. Quality improvement initiative in nursing homes: the ANA acts in an advisory role. Am J Nurs [Internet]. 2002 Jun [cited 2002 Aug 12];102(6):[about 1 p.]. Available from: http://www.nursingworld.org/AJN/2002/june/Wawatch.htmArticle

∗ *Monographs in electronic format*

CDI, clinical dermatology illustrated [monograph on CD-ROM]. Reevs JRT, Maibach H. CMEA Multimedia Group, producers. 2nd ed. Version 2.0. San Diego:CMEA;1995.

∗ *A computer file*

Hemodynamics III: the ups and downs of hemodynamics [computer program]. Version 2.2. Orlando (FL): Computerized Educational Systems; 1993.

5. Attachments (tables, graphs, schemes and photographs).

THE MAXIMUM NUMBER OF ATTACHMENTS ALLOWED IS SIX!

– Tables, graphs, schemes and photographs are to be submitted as separate documents, on separate pages.

– Tables and graphs are to be prepared in the format compatible with Microsoft Word for Windows programme. Photographs are to be prepared in JPG, GIF, TIFF, EPS or similar format.

– Each attachment must be numbered by Arabic numerals consecutively in the order of their appearance in the text

– The title, text in tables, graphs, schemes and legends must be given in both Serbian and English languages.

– Explain all non-standard abbreviations in footnotes using the following symbols *, †, ‡, §, | |, ¶, **, † †, ‡ ‡ .

– State the type of color used and microscope magnification in the legends of photomicrographs. Photomicrographs should have internal scale markers.

– If a table, graph, scheme or figure has been previously published, acknowledge the original source and submit written permission from the copyright holder to reproduce it.

– All attachments will be printed in black and white. If the authors wish to have the attachments in color, they will have to pay additional cost.

6. Additional requirements

SHOULD THE AUTHOR AND ALL CO-AUTHORS FAIL TO PAY THE SUBSCRIPTION FOR MEDICAL REVIEW, THEIR PAPER WILL NOT BE PUBLISHED.