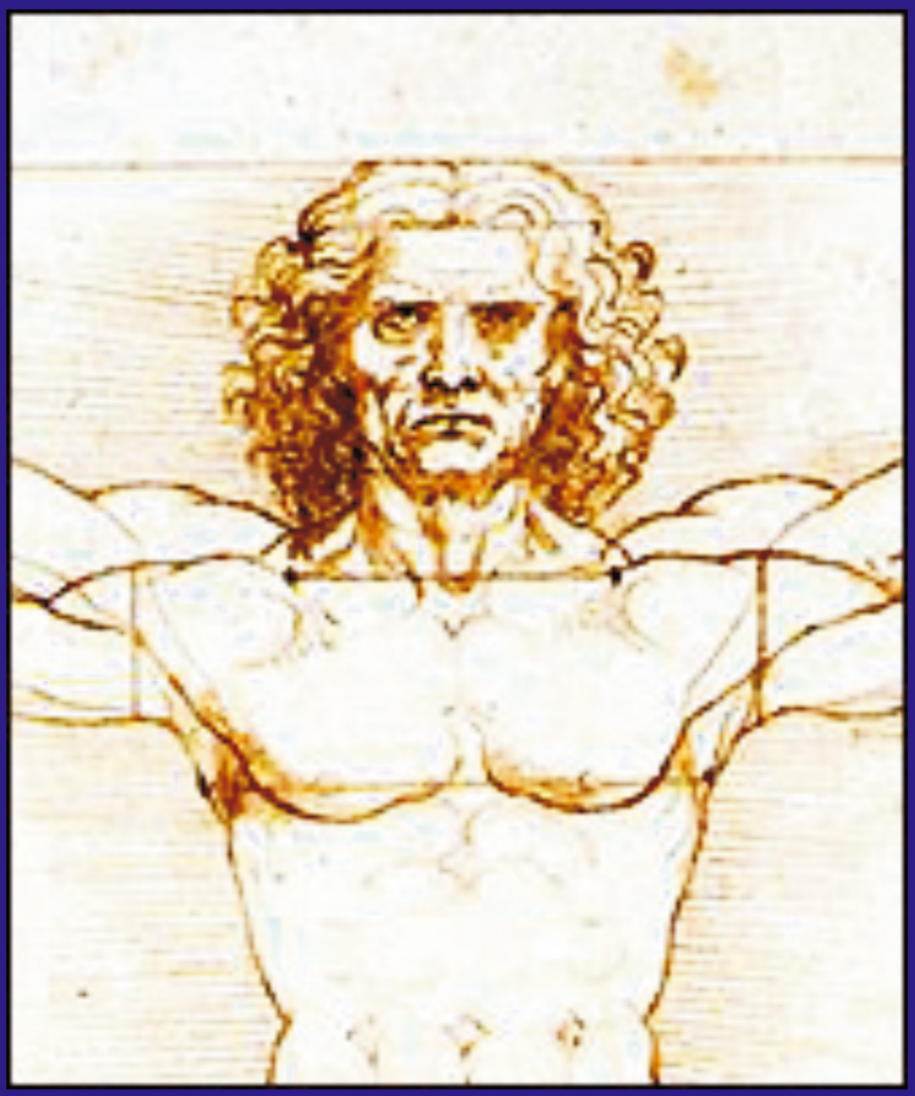
SANAMED

ISSN-1452-662X



Vol 11 (1) 2016.

MEDICINSKI ČASOPIS LEKARA

NOVI PAZAR

SANAMED

ISSN-1452-662X

Izdavač
Udruženje lekara Sanamed, Novi Pazar

ČASOPIS IZLAZI TRI PUTA GODIŠNJE

Adresa uredništva
„SANAMED“, Ul. Palih boraca 52, 36300 Novi Pazar, Srbija
email: sanamednp2006@gmail.com, www.sanamed.rs

Štampa
„ProGraphico“, Novi Pazar

Tiraž
500

Pretplata
Godišnja pretplata: 4500 din. za domaće ustanove; 1500 din. za pojedince; za inostranstvo 75 eura (u dinarskoj protivrednosti po kursu na dan uplate). Pretplatu vršiti na račun 205-185654-03, Komercijalna banka. Za sve dodatne informacije kontaktirati Uredništvo.

SANAMED

ISSN-1452-662X

Publisher
Association of medical doctors “Sanamed”, Novi Pazar

ISSUED THREE TIMES A YEAR

Editorial address
“SANAMED”, St. Palih boraca 52, 36300 Novi Pazar, Serbia
email: sanamednp@gmail.com, www.sanamed.rs

Print
“ProGraphico”, Novi Pazar

Circulation
500

Subscription
Annual subscriptions: 4500 RSD for domestic institutions and 1500 RSD for individuals. For readers abroad, annual subscription is 75 Euro (in Dinar equivalent at the exchange rate on the day of payment). For further instructions and informations, contact Editorial Board.

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SADRŽAJ

- **PRIKAZ SLUČAJA**

A word from the guest editor

Today, 7.3 billion people are living on earth. All 7.3 billion people need air, water, food... Health is the greatest human wealth. Interestingly, the diseases in some way connect people and countries in the world. Diseases are a global challenge of our time that requires cooperation among civilizations to achieve global success. Especially,chronic diseasesas: cardiovascular diseases, cancer, chronic lung and kidney diseases, diabetes, epilepsy, AIDS, mental disorders and stroke. These diseases are an indicator of socio-economic development of states and directly indicate the uneven global distribution of health and wealth. Chronic diseases are leading causes of morbidity and mortality in the world. They represent more than 80% of human lives and medical costs in the world population. World Health Organization (WHO) is working with governments to incorporate chronic diseases into the UN Millennium Development Goals.

Now we are living in an era of globalization. We cannot be healthy if we live in an unhealthy world. World, with active global crises such as: economic, food and energy crises, climate changes, military and migratory crises, make global health efforts even more challenging. Balkan countries should contribute to global health. As doctors, working our human and noble profession, we can appeal: "The power of science and knowledge should be the language and the bridge that brings the nations together. We all must keep investing in science, medicine, education, research and technological development and aim to the well-being of the human kind on Earth and to the future generations that come".

Sanamed journal, has a tremendous privilege to contribute to a global health, by giving us a great opportunity to publish scientific papers and hereby to exchange the medical experience and research.

To be a guest editor of the Sanamed journal is my privilege, honor and a great pleasure. I thank everyone involved in the publication of this issue of the journal. I want especially to thank all members of the editorial board for inviting me to be a guest editor and to wish them a good health, longevity of the journal Sanamed, numerous authors and readers and many cited papers from this journal (in other medical journals).

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A word from the guest editor

Dear Colleagues,

It is a great pleasure and honor for me, to be part of the editorial team for the March 2016 issue of this fast developing scientific journal. SANAMED represents a new bridge connecting the dental teaching and research community from different regional and global institutions. We appreciate the given opportunity to present original research works from Bulgaria.

Let me introduce the team of the department of Oral pathology and Imaging diagnostics of the Faculty of Dental Medicine of the Medical University of Sofia.

The Medical University of Sofia is the oldest institution of higher medical education in Bulgaria. The Faculty of Dental medicine, as part of the MU is a national educational, scientific and medical institution, providing dental education to Bulgarian and Foreign students in Bulgarian and English language, according to Bulgarian medical school traditions and the EU principles of harmonization of dental education.

The Faculty of Dental Medicine consists of eight departments. The 'youngest' one, the 'Department of Oral Pathology and Image Diagnostics', headed by the eminent scientist Prof. Angelina Kisselova, has two units "Image diagnostics" headed by Prof. Hristina Mihailova and "Oral diagnostics" headed by Assoc. prof. Asya Krasteva. An X-rays unit with 3 dental doctors – Ass. Prof. Dr.Yovchev, Dr. Borisov, Dr. Kishkilova and 7 X-rays operators are associated.

The courses included in the programme of the department cover the fields of: "Image diagnostics" "Oral diagnostics", "Dental clinical allergology", and "Oral pathology".

The undergraduate course of "Dental clinical allergology", led by Assoc. Prof. Maria Dencheva, and Ass. Prof. Mariana Tsekova, is recently introduced into the program with the task to teach prevention, diagnosis, treatment and rehabilitation of patients with allergic medical conditions with oral cavity and maxillofacial area expression.

The undergraduate course of "Oral pathology", led by Assoc. Prof. PhD and Ass. Prof. Mariana Tsekova, is focused on the identification and management of systemic diseases affecting the oral and maxillofacial areas. The training course in Oral Pathology (diagnosis) provide students with knowledge and skills to perform a comprehensive overview on the patient' s health and to detect the factors responsible for the onset and specific course of systemic diseases and their impact on maxillo-facial manifestations. The course consists of 30 classes including 15 lectures and 15 clinical exercises.

These textbooks and monographs are published to assist undergraduate dental students' performance.

As these disciplines were recently introduced in the new dental curriculum in the Dental school of the Medical university of Sofia, the research and teaching methods are getting improved simultaneously.

The selection of papers was made with the aim to make you familiar with interdisciplinary fields and the implementation of research into education and practice of dentistry.

The first paper reflects the latest research on the influence of common allergens from the professional environment on dental students, dental professionals, and dental technicians when in contact. The second paper presents the observation on the effect of bleaching as a modern approach in esthetic dentistry while taking into consideration the safety parameters of performance.

I hope, all of us will agree that, only through sharing ideas, concepts and scientific findings, we will be able to achieve methodological growth and experience with the science and art of dentistry. SANAMED is a good example of such a cooperation. Therefore, we hope the publications will rise further discussions and common projects.

I would like to express my gratitude towards the notable work of authors and reviewers and to wish the longevity of the Journal SANAMED and the sincerest regards to the wonderful editorial board.

Sincerely,

Prof. Dr Lydia Katrova, DDM, MPH, PhD
Medical University of Sofia
Faculty of Dental Medicine, Sofia, Bulgaria

A word from the editor

Dear colleagues and readers,

it is my honor and pleasure to be able to greet you and thank you for sharing your effort which we all have invested in professional designing of our "SANAMED" journal. With this statement I want to remind you of our small jubilee, ten years of publication of Journal "SANAMED". It is not a small jubilee, but a significant period of time during which we have persistently and courageously worked on improving, despite the obstacles in the way. In addition, to this day Journal has an ascending trend line in terms of quality and content. Notwithstanding the enthusiasm of the editorial team, and regardless of their energy and desire to show their professional content to the world of medicine, problems that were encountered during the work would not be able to had overcome if there were no enthusiastic professional and friendly assistance and support of professional team of experts from world famous Universities and Clinics. With joy, I can say that the number of contributors, very professional elite of high-quality professors from various fields of medical sciences, continues to increase, and that also became a guarantor of value and serious work on this Journal, so neither did we ever abused their names and we have taken our work seriously.

Getting back to the beginning, ie. the first issue of "SANAMED", I have to mention the first two of our friends and reviewers, Prof. Dr. Mirko Rosic from Kragujevac and Prof. Dr. Radivoj Kocic from Nis. From the first day they have accepted our invitation for cooperation and supported us as we have been acquaintances for years. They have believed that our project is a serious work and they were sure in the future success. I thank them for that! At the same time I please all our later, no less significant contributors, of which I think all the best, not to feel disrespected because I have not mentioned their names. Without the enormous contribution of all of them, "SANEMED" would not have this today's quality.

The first issue, in 2006, was opened with these words: "If you opt to serve the one who looks at you with respect, forget the other ones, because they are in the minority. Your eternal pride will be the living image that is all around you, and sometimes in your family, as part of what you have done. This will give you the power to verify and defend the doctrine as the only argument of developed society groups, to persevere and contribute your professional life to something that what will be, while you are alive

and after you remain, an eternal mark which others will remember." Then delivered, this thought is transmitted from issue to issue and has become a "Leitmotif" of the Journal, and the effort of these people has become a kind of endowment for future young authors.

There are also thoughts: "Read to understand. Write to impart. Work to be remembered.". They contain the power of the mind of every man who has dedicated his life to science and humanity, and they are also the motive of our persistent work on the survival of the "SANAMED"' Journal.

This anniversary issue is the crown of the work so far and I believe that all those, who have followed us and cooperated with us, will confirm its quality. Once again I want to thank to our associates, our visiting editors and all those who have written and published in our Journal. Our work has contributed to the spreading of scientific thought throughout the world from a small oasis in Sandzak, Serbia.

Our idea to organize a symposium for this jubilee, with several topics and lectures by world famous names who are our associates, for financial reasons is now questionable. If we provide enough fund, all our associates will be notified and invited.

With respect,

Prim. Dr. Avdo Ceranic
Editor in chief

Riječ urednika

Cijenjeni saradnici i čitaoci,

čast mi je i zadovoljstvo da mogu da vas pozdravim i da vam se zahvalim na zajednički učinjenom trudu koji smo uložili u stručnom oblikovanju našeg „SANAMED“-a. Ovom rečenicom hoću da vas podsjetim na naš mali jubilej, tj. deset godina izlaženja časopisa. To i nije mali jubilej, već značajan period vremena tokom kojeg smo, i pored prepreka na putu, istrajno i hrabro radili na unapređivanju, i do danas časopis ima trend uzlazne linije po kvalitetu i sadržini. Bez obzira na entuzijazam uredničkog tima, i bez obzira na njihovu energiju i želju da se svijetu medicine predstave svojom stručnom sadržinom, probleme sa kojima su se susretali u toku rada ne bi uspjeli da prevaziđu da nam nije bilo svesrdne stručne i prijateljske pomoći i podrške stručnog tima eksperata iz svih krajeva svijeta, sa poznatih svjetskih Univerziteta i Klinika. Sa radošću iznosim da se broj saradnika i dalje povećava i da čini izuzetno stručnu elitu visoko kvalitetnih profesora iz raznih oblasti medicinskih nauka koji su ujedno i postali garant kvaliteta i ozbiljnog rada na ovom časopisu, tako da nismo ni mi smjeli zloupotrijebiti njihova imena i vodimo računa o ozbiljnosti našeg rada.

Kad se vratim na početak, tj. prvi broj „SANAMED“-a, moram da pomenem prva dva naša prijatelja i recenzenta, Prof. dr Mirka Rosića iz Kragujevca i Prof. dr Radivoja Kocića iz Niša. Od prvog dana su prihvatili naš poziv na saradnju i podržali kao da smo se godinama znali. Vjerovali su da to što pokrećemo je ozbiljan rad i bili su sigurni da ćemo uspjeti. Hvala im na tome! Istovremeno molim sve naše kasnije priključene, ništa manje značajne saradnike, o kojima mislim sve nabolje, da ne zamere što njihova imena ne spomenuh. Bez svih njih „SANEMED“ ne bi imao ovaj kvalitet.

Prvi broj časopisa, 2006. godine, otvoren je riječima:

„Ako se opredjelite da služite onome ko na vas gleda sa poštovanjem, zaboravite one druge, jer su u manjini. Vaš vječiti ponos će biti živa slika koja je svuda oko vas, a ponekada i u vašoj porodici, kao dio onoga što ste vi uradili. To će vam dati snagu da potvrdite i branite nauku kao jedini argument razvijenog društva, da istrajete i posvjetite svoj radni vijek onome što će, dok ste živi i poslije vas, ostati vječiti zapis da vas drugi pamte i budete sa živi-

ma.“ Tada izrečena, ova misao se prenosi iz broja u broj časopisa i postala je „light motiv“, a trud ovih ljudi je postao svojevrsna zadužbina za mlade buduće stvaraoce.

Tu su i misli: „Čitaj da shvatiš. Piši da preneseš. Uradi da te pamte.“ U njima je sadržana snaga svakog umnog čovjeka koji svoj život posvijeti nauci i čovjeku, kao i motiv našeg istrajnog rada na opstanku časopisa.

Ovaj jubilarni broj je kruna dosadašnjeg rada i vjerujem da svi oni koji su nas pratili i sarađivali sa nama potvrdit će njegov kvalitet. Još jednom hvala našim saradnicima, našim gostujućim urednicima i svima onima koji su pisali i objavljivali u našem časopisu. Naš zajednički rad je doprineo širenju naučne misli širom svijeta iz jedne male oaze u Sandžaku, Srbiji.

Naša ideja da za ovaj jubilej sazovemo i organizujemo simpozijum sa nekoliko tema i predavanja poznatih svetskih imena koji su naši saradnici, iz finansijskih razloga je za sada pod znakom pitanja. Ukoliko obezbijedimo sredstva svi naši saradnici će biti obaviješteni i pozvani.

S poštovanjem,

Prim. dr Avdo Ćeranić
glavni i odgovorni urednik

IKO Company

zajedno gradimo budućnost

Iko Company d.o.o. je porodična firma koja posluje od 2005 godine. Naša osnovna delatnost je trgovina građevinskim materijalom i proizvodnjom. Spremno prihvatamo i pratimo sve promene koje kretanja na tržištu postavljaju pred nas. U prvom redu velikom fleksibilnošću u prilagođavanju asortimana i kvalitetu asortimana, kao i spremnošću na saradnju sa projektantima i graditeljima.

Možemo se pohvaliti da smo do sada učestvovali u izgradnji mnogih višespratnica kao i preko 1000 stambeno - poslovnih objekata. Što je najvažnije mi nemamo nezadovoljnih poslovnih partnera, a najveća nagrada nam je kada po završenom poslu poslovni partner kaže da mu je bila čast što je sa nama sarađivao. Prodajni i proizvođački pogoni zauzimaju površinu od preko 400 m2 i locirani su u neposrednoj blizini zelene pijace, neposredno pored magistralnog puta Novi Pazar - Beograd. Blizina ove saobraćajnice uveliko pojednostavljuje kako dopremanje repromaterijala tako i otpremanje gotovih proizvoda. Iko Company proizvodi fert gredice i vrši obradu betonskog gvožđa. U našoj ponudi su sve vrste materijala za grube radove od temelja do krova.

Od 2015. godine Iko Company d.o.o. učestvuje u izgradnji i projektovanju najmodernije višespratnice smeštene u najluksuznijem delu grada Novog Pazara, u ulici Kosančićeva, nadomak Gradskog stadiona. Lokacija se nalazi u blizini osnovne škole, bolnice, nadomak srednje medicinske škole, u neposrednoj blizini dečijeg vrtića.

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Čitaj da shvatiš

Piši da preneseš

Uradi da te pamte

* * *

Read to understand

Write to impart

Work to be remembered

Avdo Ćeranić

SANAMED
2016; 11(1): 15–20
ISSN-1452-662X

DOI: 10.5937/sanamed1601015N
UDK: 616.853-001-089.5
ID: 222050060
Original article

DOES THE ADDITION OF DEXAMETHASON TO LOCAL ANESTHETIC PROLONG THE ANALGESIA OF INTERSCALEN PLEXUS BRACHIALIS BLOCK IN PATIENTS WITH SHOULDER SURGERY?

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Primljen/Received 30. 01. 2016. god.

Prihvaćen/Accepted 01. 03. 2016. god.

Abstract: **Introduction:** Peripherial nerve blocks is a suitable alternative to general anesthesia especially for one-day case surgery. Interscalene approach of plexus brachialis block as much as supraclavicular and infraclavicular provide reliable, safe, effective, low cost and most complete anesthesia with satisfactory postoperative analgesia for upper limb surgery. Postoperative analgesia of plexus brachialis blocks can be prolonged by using different drugs as adjuvants with local anesthetics. Dexamethasone has been shown to prolong the duration of postoperative analgesia when given as an adjunct for peripheral nerve blocks. The investigation was randomized, prospective, double blinded and controlled study.

Objective: The study was designed to compare the effects of dexamethasone administered as an adjunct to bupivacaine in interscalene brachial plexus block on the onset, duration and postoperative analgesia in patients under the shoulder surgery.

Methods: A prospective, double-blind study was undertaken in patients scheduled for shoulder surgeries under the interscalene brachial plexus block. We enrolled 60 patients, ASA I-II both sexes, aged 19-65 years, weighing 54-89 kg, divided to two groups G1 and G2. The brachial plexus block was performed by interscalene approach and mixture of 2% lidocaine (12 ml) and 0.5% bupivacaine (22 ml) either alone or combined with dexamethasone (4 mg). The block was performed by using double technique neurostimulator/ultrasound technique.

Results: In our investigation we found a significant increase in onset and duration of motor and sensory block in Group G2 (with dexamethasone) as compared to Group G1 patients ($p < 0.01$).

Conclusion: Addition of dexamethasone to local anesthetic drugs in interscalene plexus brachialis block, significantly prolongs the duration of analgesia and motor block in patients undergoing shoulder arthroscopy. Moreover, it is a remarkably safe and cost effective method of providing postoperative analgesia.

Key words: regional anesthesia, interscalene plexus block, adjuvants, dexamethasone.

INTRODUCTION

Peripherial nerve blocks is a suitable alternative to general anesthesia especially for one-day case surgery. Interscalene approach of plexus brachialis block as much as supraclavicular and infraclavicular provide reliable, safe, effective, low cost and most complete anesthesia with satisfactory postoperative analgesia for upper limb surgery. Pneumothorax, hemothorax, Horner's syndrome and phrenic nerve block are the potential complications (1). Generally, a major limitation of peripheral nerve blocks can be a limited duration of analgesia (2). In order to circumvent that limitation, peripheral nerve catheters that offer continuously delivery of local anesthetics have been proposed as an efficient method of postoperative analgesia (3). Nevertheless, peripheral nerve catheters are costly and can be cumbersome to manage in the outpatient surgical setting (3, 4). Also, postoperative analgesia of peripheral nerve blocks can be prolonged by using different drugs as adjuvant with local anesthetics, such as morphine, ephedrine, pethidine, clonidine, dexmedetomidine, butorphanol, buprenorphine, midazolam (5, 6, 7). However, these may lead to certain side-effects such as sedation, psychomimetic effects, respiratory depression, pruritis, etc (6, 7). The ideal adjuvant that acts to prolong anesthesia and improve clinical outcomes while maintaining a favorable side effect profile, remains undiscovered.

Recently, several studies have examined the use of perineural dexamethasone in order to prolong analgestic duration of peripheral nerve blocks with variable results. However, the aggregated effect of perineural dexamethasone on analgesia outcomes has yet to be quantified. In addition, the safety of perineural dexamethasone also needs to be further examined (8). Dexamethasone is a systemic glucocorticoid commonly used to reduce postoperative nausea/vomiting, pain and to improve quality of recovery after surgery. Preliminary studies suggest that its addition can impressively prolong the duration of analgesia of peripheral nerve block with minimal adverse effects (7). The exact mechanism of dexamethasone's action is still unknown. It has been suggested that dexamethasone may prolong block duration by increasing the activity of inhibitory potassium channels on nociceptive C-fibers or by causing vasoconstriction via glucocorticoid receptor mediated nuclear transcription modulation (8,9). Dexamethasone's suppression of inflammatory mediators, including prostaglandins (PGE2), may also play a role. Indirect evidence has supported the assumption that dexamethasone acts locally, however recent studies have suggested a systemic effect may be responsible for its clinical effect and intravenous administration may give similar results (9).

The investigation was randomized, prospective, double blinded and controlled study. The purpose of this study was to compare the effects of dexamethasone administered as an adjunct to bupivacaine in interscalene plexus brachialis block, on the onset and duration of analgesia and motor blockade at the patients with shoulder surgery.

MATERIAL AND METHODS

After ethical committe approval and informed consent, we enrolled 60 patients, ASA I-II of either sexes, aged 19-65 years, weighing 54-89 kg, undergoing shoulder surgery. The brachial plexus block was performed by interscalene approach and mixture of lidocaine and bupivacaine either alone or combined with dexamethasone. The block was performed by using double technique neurostimulator/ultrasound technique.

Exclusion criteria in this investigation were:

- Refusal to regional anesthesia
- ASA Grade 3 and 4
- Any bleeding disorder in patient with anticoagulants
- Severe respiratory disease
- Neuro deficit involving brachial plexus
- Local infection at the injection site
- History of allergy to local anaesthetic
- Patients with a history of peptic ulcer disease, diabetes mellitus, hepatic or renal failure (contraindication to steroids, or systemic use of corticosteroids within 6 months before surgery)
- Pregnant women

Investigations: X-ray chest, basic laboratory investigations, EKG (electrocardiogram). All the patients were premedicated with tablets from the group of benzodiazepams, night before surgery and one hour prior to surgery.

Baseline parameters were recorded by attaching all the basic monitoring devices like oxygen saturation (SpO2), electrocardiogram (EKG), noninvasive blood pressure (NIBP). Patients were randomly divided in two groups, G1 and G2 with 30 of them in each group. Group G1: Patients received mixture of 2% lidocain (12 ml) and 0.5% bupivacaine (22 ml) plus 1 ml 0.9% normal saline, making a total volume of 35 ml, through the interscalene approach of plexus brachialis.

Group G2: Patients received mixture of 2% lidocain (12 ml) and 0.5% bupivacaine (22 ml) plus 4 mg (1 ml) dexamethasone, making a total volume of 35 ml, through the interscalene approach of plexus brachialis.

The following parameters were studied:

- *Onset of sensory block* was tested by using pin prick method along the distribution of the shoulder and humerus i.e. the time from injection to onset of analgesia in five time intervals (min) 0, 10, 15, 20, 25 and 30 min. Sensory block was graded according to the following scale: 0 = no block (normal sensation), 1 = partial block (decreased sensation), and 2 = complete block (no sensation). The first time interval "0" we do not analyzed, because in all 60 patients we had not noticeable changing in sensory and motor block, so the real first examinated time interval was 10 min.

- *Duration of analgesia:*

During the procedure, anesthesia was considered satisfactory if the patient did not complain of any pain or discomfort and if no sedation was necessary.

Post operative follow up was carried out in the recovery and post operative ward. The duration of analgesia was noted according to 0-10 visual analogue score (VAS) for pain at every half an hour for first 10 hours and then hourly till 24 hours.

When the patients began to experience the worst pain VAS $\geq$ 5, it was considered that analgesic action of the drugs was terminated and rescue analgesic given.

- *Onset of motor block* is the time from injection to the inability of the patient to move his/her fingers or raise their hand. Motor block was measured at 10, 15, 20, 25 and 30 min by assessing the following motor functions: flexion at the elbow (musculocutaneous nerve), extension of the elbow and the wrist (radial nerve), op-

position of the thumb and index finger (median nerve), and opposition of the thumb and small finger (ulnar nerve). Motor block was graded according to the following scale: 0 = no block (full muscle activity), 1 = partial block (decreased muscle activity), and 2 = complete block (no muscle activity).

- *Duration of motor block* postoperatively was assessed every hour by asking the patients to move their fingers, hand, flexion and extension at the elbow. This time was recorded and taken as cessation of motor block effect.

Possible side effects of brachial plexus block

Incidence of drowsiness, pruritus, nausea/vomiting, Horner's syndrome, phrenic nerve palsy, pneumothorax, respiratory depression and sign of symptoms for local anaesthetic toxicity were looked for and noted, if any.

During the anesthesia plexus brachialis block is *excellent* if there is no discomfort or pain, *good* (mild pain or discomfort, no need for additional analgesics), *fair* (pain that required additional analgesics) or *poor* (moderate or severe pain that needed fentanyl or general anesthesia). In the circumstance of inadequate action of the block, the block would be supplemented with general anaesthesia. If in case surgery was unduly prolonged and the effect of the block wore off, rescue analgesia with IV hypnotic and analgetic would be given.

Statistical analysis

The data obtained in this study was arranged in tables and presented in frequencies and percentage. The analysis used Student's unpaired t-test, SPSS ver. 20 was used.

RESULTS

The patients data of analgesia were presented as level 1 = partial block (decreased sensation) and level 2 = complete block (no sensation). They were displayed through five time intervals as frequencies and percentage in two examined groups (Table 1).

Table 1. *Comparison of onset of analgesia*

Level of analgesia	Time interval (min)	G1	G2	Level of significance
1	10	3 (10%)	25 (83%)	p ≤ 0,01
	15	24 (80%)	5 (17%)	p ≤ 0,01
	20	9 (30%)	1 (3%)	/
	25	2 (7%)	1 (3%)	/
	30	2 (7%)	2 (7%)	/
2	10	/	/	/
	15	4 (13%)	23 (77%)	p ≤ 0,01
	20	21 (70%)	28 (93%)	p ≤ 0,01
	25	28 (93%)	28 (93%)	n.s.
	30	28 (93%)	28% (93%)	n.s.

Table 2. *Comparison of onset of motor block*

Level of motor block	Time interval (min)	G1	G2	Level of significance
1	10	4 (13%)	26 (87%)	p ≤ 0.01
	15	23 (77%)	7 (23%)	p ≤ 0.01
	20	3 (10%)	1 (3%)	/
	25	2 (7%)	1 (3%)	/
	30	2 (7%)	2 (7%)	/
2	10	/	1 (3%)	/
	15	15 (17%)	21 (70%)	p ≤ 0.01
	20	26 (87%)	28 (93%)	p ≤ 0.05
	25	28 (93%)	28 (93%)	n.s.
	30	28 (93%)	28 (93%)	n.s.

Table 3. *Comparison of duration of analgesia and motor block*

Variable	Groups	Mean ± SD (hr)	Level of significance
Duration of analgesia	G1	9.3 ± 1.25	p ≤ 0.01
	G2	16.1 ± 2.55	
Duration of motor block	G1	6.6 ± 1.50	p ≤ 0.01
	G2	10.5 ± 2.30	

The analysis showed significant difference (p ≤ 0,01) in level 1 between data in two time intervals (10 min., 15 min.). In level 2 data from group of patients with dexamethasone (G2) have significant increase of complete analgesia (77% and 93%). In last two intervals (25 min., 30 min.) the data were not significant, because the interscalene plexus block was established.

The motor block was established in the first time interval with significant high percent of patients with dexamethasone (table 2). In Group 1, most of patients (77%) had incomplete motor block in the first 15 minutes. The appearance of complete motor block began between 20-25 min. The difference is significant in mentioned time interval.

Duration of motor block and duration of analgesia were prolonged in dexamethasone group compared to control group. Statistical difference between examined groups in both variables was significant (p ≤ 0,01). Interscalene plexus block anesthesia was unsuccessful in four patients (two of each group). Additional side effects as potential complications like Horner's syndrome was found in 6 patients from group G1 and 4 from group G2.

DISCUSSION

Interscalene plexus brachialis block is a simple, safe, low cost, effective technique of regional anesthesia having advantages over general, especially for one day case shoulder surgery. Interscalene plexus brachialis block over general anesthesia provide postoperative longer period of analgesia without problems associated with general anesthesia (4, 10). Prolonging surgical anesthesia and analgesia is of significant interest in regional anesthesia, especially in plexus brachialis block. There are two solutions in order to increase the duration of analgesia in these blocks, a) using peripheral nerve catheters which offer continuously delivery of local anesthetics and b) adding the adjuvants in local anesthetic (3, 4). Nevertheless, peripheral nerve catheters are costly and can be cumbersome to manage in the outpatient surgical setting (4).

The adjuvants added in plexus brachialis block such as morphine, ephedrine, pethidine, clonidine, dexmedetomidine, butorphanol, buprenorphine, midazolam provide prolongation of sensory and motor block. Recently, the addition of a glucocorticoid specifically, dexamethasone, has been studied with high quality outcome. Many literature reviews concluded that analgetic effect of dexamethasone works by:

- reducing the transmission in unmyelinated C-fibers through inhibiting the activity of potassium channels, that will decrease the amount of pain sensed by patient
- causes a degree of local tissue vasoconstriction and provides a slower uptake of local anesthetic
- dexamethasone exhibits a potent anti-inflammatory effect and inhibits the release of inflammatory mediators like interleukins and cytokines, it promotes the release of antiinflammatory mediators leading to decreased postoperative pain (11, 12).

In our study we evaluated 60 patients with shoulder artroscopy, that underwent the interscalene plexus brachialis block. Dexsamethasone 4 mg was used as a adjuvant added in local anesthetics. The most recent study included the higher dose of dexamethasone such as 8 mg, 10 mg, so the main point in our study was to investigate if the dose of 4 mg dexamethasone affects the onset of sensation and motor block as well, if this corticosteroid prolongs duration of analgesia and motor blockade, compare to group of patient without dexamethason in interscalene block (13, 14). The results in our study shows that the onset of sensation (level 1) in G2 (with dexamethasone) in 87% of patients were performed in the first time interval (10 min), and the interscalene block was completely established between 15-20 min, compare to G1 group where the block in most of patients was resolved between 20-25 min. (p ≤ 0.01). The motor block was established in the first time interval with significant higher percentage of patients in group G2 (with dexamethasone). In Group 1, the most patients (77%) had incomplete motor block in the first 15 minutes. The appearance of complete motor block began between 20-25 min. The difference between two groups is significant in mentioned time interval (p ≤ 0.01).

In one study by Shrestha BR, onset of action was 10-30 minutes in local anesthetic group (mean 18.15 ±

4.25) and 10-20 minutes (mean 14.5 ± 2.10) in the local anesthetic plus steroid, group. They found statistically significant difference between two groups (15). However another study by Ali Movafegh, found that the onset time of sensory and motor blockade was similar in both groups (with and without dexamethasone) (16).

In our study the duration of analgesia in dexamethasone group G2 was 16,1 ± 2,55h longer than in G1 9.39 ± 1,25 (P ≤ 0.01). The mean duration of motor block in G2 was 10,5 ± 2,30 h and in G1 6,6 ± 1,50h (P ≤ 0.01). Cummings reported that dexamethasone prolonged analgesia from interscalene blocks using ropivacaine and bupivacaine, with the effect being stronger with ropivacaine (17). Pathak reported that the duration of analgesia and motor block were significantly prolonged in patients (with dexamethasone) with supraclavicular plexus block undergoing upper limb surgery, compared to the control group (without dexamethasone) (13). Parrington showed that dexamethasone added to mepivacaine prolongs the duration of analgesia (332 min vs. 228 min in control group) after supraclavicular brachial plexus block. The onset time of sensory and motor blocks were similar in both groups (14).

In a randomized, control trials by Desmet et al. and Shahedha et al. a study was performed on intravenous dexamethasone and its equality to perineural dexamethasone in prolonging the analgesic duration of a single-shot interscalene block with ropivacaine (5, 18).

The efficiency of dexamethasone in prolonging the duration of analgesia and motor block in patients operated under the plexus brachialis blocks, were noticed also in other peripherial blocks like peribulbar block in posterior segment eye surgery, axillary block, sciatic block etc (19, 20).

CONCLUSION

Addition of dexamethasone to local anesthetic drugs in interscalene plexus brachialis block, significantly prolongs the duration of analgesia and motor block in patients undergoing shoulder artroscopy and is a remarkably safe and cost effective method of providing post operative analgesia. A patient with reduced pain and a reduced need for additional analgesics post operatively is always a satisfied customer.

Conflict of interest

The authors declare are no conflict of interest.

Abbreviations

PGE2 — Prostaglandins
ASA — American Association of Anesthesiologists
EKG — Electrocardiogram
SpO_2 — Oxygen Saturation
NIBP — Non invasive blood pressure
VAS — Visual Analogue Scale
SPSS — Statistical Package for the Social Sciences

Sažetak

DA LI DODATAK DEKSAMETAZONA LOKALNOM ANESTETIKU PRODUŽAVA TRAJANJE ANALGEZIJE KOD INTERSKALENSKOG BLOKA PLEKSUSA BRAHIJALISA KOD PACIJENATA SA OPERACIJOM RAMENA?

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Uvod: Blokovi perifernih nerava su odgovarajuća zamena za generalnu anesteziju, posebno u jednodnevnim, kratkim hirurškim intervencijama. Interskaleni blok pleksusa brahijalisa, podjednako kao i supraklavikularni i infraklavikularni obezbeđuje pouzdanu, sigurnu, efektivnu, ekonomičnu i najkompletniju anesteziju sa zadovoljavajućom postoperativnom analgezijom za operacije gornjeg ekstremiteta. Postoperativna analgezija bloka pleksusa brahijalisa može biti produžena uz korišćenje drugih lekova kao dodataka lokalnim anesteticima. Deksametazon, primenjen kao dodatni lek, za blokiranje perifernih nerava, pokazao se kao odličan lek, koji produžava vreme postoperativne analgezije. Studija je randomizovana, prospektivna i dvostruko slepa i kontrolisana studija.

Cilj: Studija je dizajnirana da uporedi efekte deksametazona, koji je primenjen kao dodatak bupivakainu u interskalenskom bloku pleksusa brahijalisa na početku, tokom trajanja i postoperativne analgezije kod pacijenata, podvrgnutih operaciji ramena.

Metoda: Prospektivnoj, dvostruko slepoj studiji su podvrgnuti pacijenti, kojima je zakazana operacija

ramena pod interskalenim blokom pleksusa brahijalisa. Uključili smo 60 pacijenta, ASA I-II oba pola, uzrasta 19-65 godina, težine 54-89 kg, podeljenih u dve grupe G1 i G2. Blok brahijalnog pleksusa je izveden interskalenim pristupom i miksturom 2% lidokaina (12 ml) i 0,5% bupivakaina (22 ml) bilo samih ili u kombinaciji sa deksametazonom (4 mg). Blok je postignut korišćenjem duple tehnike, neurostimulator/ultrazvuk tehnike.

Rezultati: U našem istraživanju smo našli značajan porast na početku i tokom trajanja, motornog i senzornog bloka u Grupi 2 (sa deksametazonom) u poređenju sa Grupom 1 ($p < 0,01$).

Zaključak: Dodavanje deksametazona lokalnim anesteticima u interskalenom bloku pleksusa brahialisa, značajno produžava vreme trajanja analgezije i bloka motornih funkcija kod pacijenata podvrgnutih artroskopiji ramena. Šta više, pokazao se kao izuzetno siguran i ekonomičan metod u obezbeđivanju postoperativne analgezije.

Ključne reči: regionalna anestezija, interskalenskii blok pleksusa, adjuvansi, deksametazon.

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SANAMED
2016; 11(1): 21–27
ISSN-1452-662X

DOI: 10.5937/sanamed1601021L
UDK: 616.248-057.875
ID: 222056204
Original article

PILOT STUDY OF CONTACT SENSITIZATION OF FORMALDEHYDE-RELEASERS, FORMALDEHYDE AND GLUTARALDEHYDE IN DENTAL STUDENTS

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Primljen/Received 18. 01. 2016. god. Prihvaćen/Accepted 01. 03. 2016. god.

Abstract: **Introduction:** Occupational allergic contact sensitization is common in dental personnel. Some of the most common occupational allergens in dental practice are some formaldehyde-releasers, formaldehyde and glutaraldehyde.

Aim: The aim of the present study was to evaluate the rate of contact sensitization to formaldehyde, quaternium-15, imidazolidinyl urea, diazolidinyl urea, and to glutaraldehyde in students of dental medicine and dental patients.

Material and methods: A total of 50 participants were included in the study: 40 students of dental medicine exposed to formaldehyde-releasers, formaldehyde and glutaraldehyde during the course of their education; 10 dental patients without occupational exposure to the latter substances served as a control group. All of them were patch-tested with the studied allergens.

Results: The sensitization rate to formaldehyde was significantly higher in the group of dental patients if compared to the one of dental students ($\chi^2 = 5.37$; $p = 0.021$). Positive skin patch test reactions to quaternium-15 and to imidazolidinyl urea were observed only in the group of dental students. A significantly higher rate of sensitization to diazolidinyl urea, if compared to the one to imidazolidinyl urea ($\chi^2 = 5.4$; $p = 0.02$) and to quaternium-15 ($\chi^2 = 6.76$; $p = 0.009$), as well as to glutaraldehyde, if compared to the one to quaternium-15 ($\chi^2 = 3.96$; $p = 0.04$) for the whole studied population was established. For the whole studied population, significantly increased rate of concomitant sensitization to formaldehyde and glutaraldehyde ($\chi^2 = 6.18$ $p = 0.013$), as well as to diazolidinyl urea and to glutaraldehyde was established ($\chi^2 = 9.12$ $p = 0.003$).

Conclusions: We consider the importance of exposure to diazolidinyl urea, quaternium-15, imidazolidinyl urea and glutaraldehyde during the course of practical education in dentistry for the onset of sensitization. The exposure to formaldehyde is ubiquitous and is difficult to distinguish the roles of environmental and occupational exposures. The promotion of proper personal protection as well as adequate information on occupational chemical hazards should start as early as during the first years of education in dentistry.

Key words: contact sensitization, students of dental medicine, formaldehyde, formaldehyde-releasing preservatives, glutaraldehyde.

INTRODUCTION

Occupational allergic contact sensitization is common in dental personnel, since in their daily activities they are exposed to the numerous chemical agents. Some of the most common healthcare allergens present biocides, commonly applied for sterilization of medical devices that are sensitive to normal heat or steam sterilization processes (glutaraldehyde) and disinfection of surfaces (quaternary ammonia compounds). Increased rates of sensitization to the majority of the above-mentioned allergens among dental specialists are reported (1). Preservatives are biocidal chemicals added to cosmetics, topical medicaments, consumer goods, foods, and industrial products to protect them against microbial spoilage and to protect the consumer

against infection (2). They prevent growth of bacteria, molds, yeast, and algae in body, skin, and hair care products, personal care products, domestic preparations, and industrial products (3, 4). Preservatives were identified as the most common cosmetic contact allergens in several recent studies (5, 6), but they are applied in various materials used in everyday dental practice as well. They can be classified into three broad categories: antimicrobials, antioxidants, and ultraviolet light absorbers. The antimicrobial agents can be further divided into formaldehyde preservatives, formaldehyde-releasers, and non-formaldehyde-releasing preservatives.

Formaldehyde is an inexpensive biocidal preservative used in a wide range of products, such as tissue specimen and cadaveric preservation solutions, nail polish, wrinkle-free fabrics, etc. In dentistry it is used as an ingredient of root canal filling materials, or could leach from dental composites. In the reported North American Contact Dermatitis Group (NACDG) frequency data, formaldehyde ranked seventh, with 5.8% positive reactions noted in the 4,308 patients referred for testing (7). This high rank as well as formaldehyde's ubiquity and important role as a top allergen have been noted for the last 75 years (8). Its historical importance stems from its effectiveness in preventing contamination of personal hygiene products (9). Notably, it is also 1 of only 5 chemicals that have been listed by the Consumer Product Safety Commission as "strong sensitizers" since 1961 (10). Formaldehyde is the American Contact Dermatitis Society Contact Allergen of the Year for 2015. The exposure is widespread, and contact allergy might be difficult to suspect in the individual dermatitis patient (11).

Formaldehyde-releasing preservatives (FRP) were developed to avoid formaldehyde-induced contact allergies assuming that the formaldehyde release level would not be sufficient from the releaser to cause a skin reaction (12). However, many of them have also been demonstrated to be contact allergens, some related to the release of formaldehyde, while others by their own chemical properties (13). Formaldehyde-releasing preservatives include quaternium-15, diazolidinyl urea, imidazolidinyl urea, 2-bromo-2-nitropropane-1.3-diol, and 1,3-Dimethylol-5,5-dimethylhydantoin DMDM hydantoin (14). They are among the leading contact allergens and are found in many medications, household cleansers, and personal health products (9). It is important for people to be aware of sources of formaldehyde exposure and understand that many products containing formaldehyde or FRPs may not indicate this on their labels. A study by Rastogi reported that 33% of 67 moisturizers evaluated did not have proper labeling in regards to their formaldehyde/FRP content (15).

For over 40 years, glutaraldehyde was the primary choice for disinfecting heat-sensitive medical devices, such as dental equipment and endoscopic instruments, and its toxicity has been well described, and its use has been associated with dermatitis and occupational asthma. Increased rates of sensitization to the majority of the above-mentioned allergens among dental specialists are reported (1). Quite a few data in the available literature was found concerning the rate of contact sensitization to these substances among dental students.

AIM

The aim of the present study was to evaluate the rate of contact sensitization to formaldehyde, some formaldehyde-releasing preservatives and to glutaraldehyde in students of dental medicine and dental patients.

MATERIAL AND METHODS

Subjects

A total of 50 participants were included in the study: 40 students of dental medicine from the Faculty of Dental Medicine, Medical University – Sofia (19 male and 21 female, mean age 25.30 ± 9.1), exposed to formaldehyde, some formaldehyde-releasing preservatives and to glutaraldehyde during the course of their practical education (Group E); 10 randomly selected dental patients (4 male and 6 female, mean age 47.70 ± 17.6), without occupational exposure to the investigated substances served as a control group (Group C). The mean age of the individuals from Group C was significantly higher if compared with Group E ($t = -5.6$, $p < 0.005$). General characteristics of the studied subjects are presented in Table 1. The study was approved by the Medical Ethics Board at Medical University – Sofia. All the participants were informed about the purpose of the study and gave their written informed consent.

Methods

Skin patch testing with formaldehyde (2.0%/aq), quaternium-15 (1.0%/pet), imidazolidinyl urea (2.0%/pet), diazolidinyl urea (2.0%/pet), and glutaraldehyde (0.2%/pet, Chemotechnique Diagnostics) was performed according to the Jadassohn & Bloch classical methods for diagnosis of contact allergy, by placing the allergens in IQ-Ultra hypoallergenic patches of Chemotechnique Diagnostics (IQ Chambers®, Vellinge, Sweden). Lack of anti-allergic medication constituted a mandatory condition before placing the patches and during the testing. Patches with allergens were applied on the back of the tested individuals, reading of the test was perfor-

med on day 2, several hours after removing the patches, with control revision on day 3. Interpretation of reaction sites was based on the method recommended by the International Contact Dermatitis Research Group (ICDRG). Interpretation key based on recommendations by the ICDRG was applied.

Statistical analysis. The statistics were calculated with SPSS 19.0. The following statistics available for cross-tabulation were used: multiple correspondent analysis, Chi -square test, Fisher Exact Test for statistical significance. Values of $p < 0.05$ were accepted as statistically significant.

RESULTS

Data concerning the frequency of positive patch test reactions to the studied preservatives in the investigated groups are summarized in Table 2.

As shown in Table 2, the highest was the frequency of positive skin patch test among dental students to glutaraldehyde, and the lowest – to quaternium-15; among the whole studied by us population of 50 individuals, the established frequency of sensitization was highest to diazolidinyl urea, lowest – again to quaternium-15. The sensitization rate to formaldehyde was significantly higher in the group of dental patients if compared with the one of dental students ($\chi^2 = 5.37$; $p = 0.021$). No statistically significant differences between Group E and Group C regarding the rates of sensitization to the other studied allergens were revealed ($p > 0.05$). Furthermore, for the whole studied population, a significantly higher rate of sensitization to diazolidinyl urea, if compared to the one to imidazolidinyl urea ($\chi^2 = 5.4$; $p = 0.02$) and to quaternium-15 ($\chi^2 = 6.76$; $p = 0.009$), as well as to glutaraldehyde, if compared to the one to quaternium-15 ($\chi^2 = 3.96$; $p = 0.04$) was established. The statistical analysis of the results didn't reveal other significant differences in sensitization rates.

The distribution of concomitant/cross sensitization to the included in the study preservatives in the group of dental students and the in whole population is presented in Table 3 and Table 4. Significantly higher rate of concomitant sensitization to diazolidinyl urea and to glutaraldehyde was established ($\chi^2 = 9.12$ $p = 0.003$). Furthermore, significantly increased rate of concomitant sensitization to formaldehyde and glutaraldehyde was revealed ($\chi^2 = 6.18$ $p = 0.013$). The rate of concomitant sensitization to formaldehyde and to glutaraldehyde for the group of dental students was (15.0%). No statistically significant differences regarding the sensitization rates and the type of exposure, age and gender characteristics of the studied population were revealed.

DISCUSSION

Aldehydes, e.g. formaldehyde, FLP preservatives and glutaraldehyde represent an important class of disinfectants, broadly used throughout the world for various purposes. They are well known for their irritant and/or allergenic properties, and are of daily concern in

Table 1. *General characteristics of the studied groups*

Group	Respondents			
	age (years) (M ± SD)	male [n (%)]	female [n (%)]	total [n (%)]
Students of dental medicine	25.30 ± 9.1	19 (47.5)	21 (52.5)	40 (80.0)
Patients without occupational exposure	47.70 ± 17.6	4 (40.0)	6 (60.0)	10 (20.0)

Table 2. *Distribution of positive skin patch test reactions to the studied allergens among the studied groups*

STUDIED ALLERGEN	Positive reactions in dental students N (%)	Positive reactions in control group of dental patients N (%)	Positive reactions Total N (%)
Formaldehyde	9 (22.5)	6 (60.0) $\chi^2 = 5.37$; $p = 0.021$	15 (30.0)
Quaternium-15	6 (15.0)	–	6 (12.0)
Imidazolidinyl urea	7 (17.5)	–	7 (14.0)
Diazolidinyl urea	12 (30.0)	5 (50.0)	*** 17 (34.0)* **
Glutaraldehyde	13 (32.5)	1 (10)	14 (28.0)

* $\chi^2 = 5.4$, $p = 0.02$; ** $\chi^2 = 3.96$, $p = 0.04$; *** $\chi^2 = 6.76$, $p = 0.009$

Table 3. *Distribution of the concomitant/cross sensitization between the studied preservatives in the group of dental students (n = 40)*

N°	ALLERGEN	1	2	3	4	5
1	Imidazolidinyl urea	7	1	2	3	2
2	Quaternium-15	1	6	2	3	3
3	Diazolidinyl urea	2	2	12	8	5
4	Glutaraldehyde	3	3	8	13	6
5	Formaldehyde	2	3	5	6	9

* The numbers on the first row of the table indicate the corresponding allergen from column 2

Table 4. *Distribution of the concomitant/cross sensitization between the studied preservatives in the whole population (n = 50)*

N°	ALLERGEN	1	2	3	4	5
1	Imidazolidinyl urea	7	1	2	3	2
2	Quaternium-15	1	6	2	3	3
3	Diazolidinyl urea	2	2	17	8***	10
4	Glutaraldehyde	3	3	8	14	6**
5	Formaldehyde	2	3	10	6	15

* The numbers on the first row of the table indicate the corresponding allergen from column 2
** Significantly increased rate of concomitant sensitization to formaldehyde and glutaraldehyde ($\chi^2 = 6.18$ $p = 0.013$)
*** Significantly increased rate of concomitant sensitization to diazolidinyl urea and to glutaraldehyde ($\chi^2 = 9.12$ $p = 0.003$)

occupational and/or environmental dermatology. Formaldehyde is the undisputed "leader" of aldehydes. Its use is so ubiquitous that it has always been present in the baseline series of patch tests (16). Occupational formaldehyde allergy is common in workers using protective creams, detergents, and liquid soaps. According to the FDA Voluntary Cosmetic Registration Program database, about 20% of personal health products and cosmetics contain a FRP, with imidazolidinyl urea as the most common (17). According to Latorre (2011) the most frequent allergens are formaldehyde (1.72%), imidazolidinyl urea (1.05%), quaternium-15 (0.88%), and diazolidinyl urea (0.79%) (18). Kadivar et al. (2015) reported significantly more work-related allergic contact dermatitis, especially to formaldehyde, quaternium-15, and glutaraldehyde among health care workers (19). Almost 80% of patients were exposed to quaternium-15 through a moisturizer; hair care products and makeup were also common sources (13). According to our results, the sensitization rate to ***quaternium-15*** was 12% for the whole population, but positive skin patch test reactions were observed only in the group of dental students. We could consider the importance of the exposure to disinfectants during the course of their practical education for the onset of the sensitization.

Imidazolidinyl urea is the second most common preservative used in cosmetic products (lotions, creams, hair conditioners, shampoos, deodorants) and topical drugs and affected 2.9% of patch test patients in 2005––2006 (20). It releases 1/8 of the amount of formaldehyde that quaternium-15 releases and is considered to be safer for patients with formaldehyde sensitivity (13). Cheng et al. (2014) evaluated patch test data at the National Skin Centre, Singapore, from 2006 to 2011. Sensitization frequencies among 3177 patients tested to preservatives in the standard series were all greater than 1% for, among other allergens, quaternium 15 (1.43%), and less than 1% for imidazolidinyl urea. A rate of 0% was seen for formaldehyde (3). The results from our study indicate the importance of imidazolidinyl urea as a sensitizer in exposure during the educational process in dentistry – positive skin patch test reactions were established again only in the group of dental students.

Diazolidinyl urea affected 3.7% of patch test patients in 2005–2006 (20). Main sources are cosmetics (hair care products, body lotions, barrier creams and liquid soaps), topical medications, cleaning agents and detergents (21). Diazolidinyl urea is considered to be a stronger sensitizer than imidazolidinyl urea (13,22). The latter statement was confirmed by the results from

our pilot study. Sensitized to diazolidinyl urea were 30% from the group of dental students and 50% from the individuals from the group of dental patients. For comparison, no positive skin patch test reactions to imidazolidinyl urea among dental patients were established. Furthermore, the rate of sensitization to diazolidinyl urea in the whole studied by us population was the highest (34%) if compared to the other studied preservatives, and was established to be significantly higher if compared to the ones for imidazolidinyl urea and for quaternium-15 for the whole studied population.

Concomitant contact allergy to formaldehyde and formaldehyde-releaser remains common. Furthermore, contact allergy to a formaldehyde-releaser was nearly always concomitant with another formaldehyde-releaser (23). A high degree of cross-reaction of diazolidinyl urea to formaldehyde and a lower cross-reaction associated with imidazolidinyl urea were reported (21). A common cross-reaction involves formaldehyde and quaternium-15; diazolidinyl urea cross-reacts with imidazolidinyl urea (2). Larotte et al. (2011) describe a subgroup of 25 patients who were sensitized to both imidazolidinyl urea and diazolidinyl urea, and only 24% of these were also sensitized to formaldehyde (18). According to Warshaw (2015), compared with the previous decade, positivity rates for all formaldehyde-releasing preservatives significantly decreased (formaldehyde - 6.6%; quaternium 15 - 6.4%; diazolidinyl urea - 2.1%; imidazolidinyl urea 1.6%) (24). Results from the present pilot study confirm our previous observation for high sensitization rates to formaldehyde in both dental students and dental patients (25). Our data confirm the observations of Maier et al. (2009) about a high degree of cross-reaction of diazolidinyl urea to formaldehyde, but the statistical analysis revealed a significantly higher rate of concomitant sensitization to diazolidinyl urea and to glutaraldehyde. No similar data were found in the available literature.

Glutaraldehyde is used as a disinfectant, as a tanning agent in leather, liquid fabric softener, as embalming fluid, in electron microscopy, as pharmacological agent used for hyperhidrosis and antifungal purposes. Owing to the known toxicities and sensitizing properties of glutaraldehyde, less offensive and presumably safer alternatives, such as ortho-phthalaldehyde, have been introduced (1). Health care workers were more likely to have work-related allergic contact dermatitis, especially, among other to glutaraldehyde (26). Warshaw et al. (2015) documented the North American Contact Dermatitis Group (NACDG) patch-testing results from 2011, to 2012. According to them, as compared with previous reporting periods positive reaction rates statistically increased for glutaral (1.5%) and paraben mix (1.4%) (24). The results obtained in our pilot study categorically confirm the later findings – the sensitization rates for glutaraldehyde were the highest observed in the group of dental students (32.2%), and more than threefold higher if compared with the one in the group of dental patients (10%). Furthermore, significantly higher rate of concomitant sensitization to formaldehyde and glutaraldehyde was revealed, being 66.7% for the group of dental students. Our findings categorically confirm the role of exposure to glutaraldehyde in dental practice for the onset of sensitization.

CONCLUSION

We consider the importance of exposure to diazolidinyl urea, quaternium-15, imidazolidinyl urea and glutaraldehyde during the course of practical education in dentistry for the onset of sensitization. The sensitization rates for glutaraldehyde were the highest observed in the group of dental students. The exposure to formaldehyde is ubiquitous and is difficult to distinguish the roles of environmental and occupational exposures. High rate of concomitant sensitization to diazolidinyl urea and to glutaraldehyde was revealed. Previously reported observations about high rate of concomitant sensitization to formaldehyde and glutaraldehyde were confirmed. The promotion of proper personal protection as well as adequate information on occupational chemical hazards should start as early as during the first years of education in dentistry.

Acknowledgement. The study was granted by the Medical University, Sofia – Project No. 4-C/2014 "Pilot investigation of urinary bisphenol A in students of dental medicine, students from Dental Technician School and in dental professionals, exposed during the practical education."

Conflict of interests

The authors declare there is no conflict of interests.

Abbreviations

NACDG — North American Contact Dermatitis Group

FRP — Formaldehyde-releasing preservatives

ICDRG — International Contact Dermatitis Research Group

Sažetak

PILOT STUDIJA KONTAKTNE SENZITIVNOSTI NA FORMALDEHID-POJAČIVAČE, FORMALDEHID I GLUTARALDEHID KOD STUDENATA STOMATOLOGIJE

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Uvod: Profesionalna kontaktna alergijska senzibilizacija je česta kod stomatološkog osoblja. Najčešći alergeni u stomatološkoj praksi su formaldehid-pojačivači, formaldehid i glutaraldehid.

Cilj: Cilj ovog rada bio je da se odredi stepen kontaktne senzibilizacije na formaldehid, kvaternium-15, imidazolidinil ureu, diazolidinil ureu i na glutaraldehid kod studenata stomatologije i stomatoloških pacijenata.

Materijal i metode: Ukupno 50 učesnika je uključeno u studiju: 40 studenata stomatologije je bilo izloženo formaldehid-pojačivačima, formaldehidu i glutaraldehidu tokom svoje nastave; 10 stomatoloških pacijenata bez profesionalnog izlaganja supstancama je služilo kao kontrolna grupa. Svi navedeni učesnici studije su bili izloženi patch testu na navedene alergene.

Rezultati: Nivo senzibilizacije na formaldehid je bio značajno viši u grupi stomatoloških pacijenata, u poređenju sa grupom studenata ($\chi^2 = 5.37$; $p = 0.021$). Pozitivni kožni patch testovi na kvaternijum-15 i na imidazolidinil ureu su uočeni samo u grupi studenata stomatologije. Uočen je značajno viši nivo senzibilizacije na diazolidinyl ureu, u poređenju sa rezultatima dobijenim na imidazolidinyl ureu ($\chi^2 = 5.4$; $p = 0.02$) i na kvaternijum-15 ($\chi^2 = 6.76$; $p = 0.009$), kao i na glutaraldehid, ako se poredi sa rezultatima dobijenim na kvaternijum-15 ($\chi^2 = 3.96$; $p = 0.04$) za celu ispitivanu populaciju. Za celu ispitivanu populaciju, zapažen je značajno viši nivo prateće senzibilizacije na formaldehid i glutaraldehid ($\chi^2 = 6.18$ $p = 0.013$), kao i na diazolidinil ureu i na glutaraldehid ($\chi^2 = 9.12$ $p = 0.003$).

Zaključak: Razmatrali smo značaj izloženosti i razvoj senzibilizacije na diazolidinyl ureu, kvaternijum-15, imidazolidinyl ureu i glutaraldehid tokom praktične nastave stomatologije. Izloženost formaldehidu je ubikvitarna i veoma je teško razlikovati posledice koje formaldehid ima u životnoj sredini i u profesionalnoj izloženosti. Unapređenje zaštite osoblja kao i adekvatna informisanost o opasnostima, koje prete od izloženosti ovim supstancama, treba da se započne što pre, po mogućstvu u prvoj godini studija stomatologije.

Ključne reči: kontaktna senzibilizacija, studenti stomatologije, formaldehid, zaštita od formaldehid-pojačivača, glutaraldehid.

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SANAMED
2016; 11(1): 29–34
ISSN-1452-662X

DOI: 10.5937/sanamed1601029P
UDK: 616.8-009.3-056.24
ID: 222049036
Original article

TYPES OF TREMOR IN PATIENTS WITH CEREBROVASCULAR DISEASES AND CARDIOVASCULAR EVENTS

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Primljen/Received 18. 01. 2016. god. Prihvaćen/Accepted 28. 02. 2016. god.

Abstract: **Introduction:** Tremor can occur as a part of the clinical picture of cerebrovascular diseases. Many patients with cerebral stroke have cardiovascular diseases as a comorbidity or complication of stroke; sometimes cardiovascular events can lead to embolic stroke.

Aim: To present types of tremor in patients with cerebrovascular diseases and cardiovascular events and diabetes mellitus type 2, clinical characteristics of tremor and investigations used.

Material and methods: In our study we included 36 patients, 24 men and 12 women, that were examined and followed for 3 years, from 2012-2015. All patients were subjected to the following investigations: neurological examination, laboratory analysis, computerized tomography of brain, magnetic resonance imaging and electroencephalography. In cardiovascular patients we also performed Doppler sonography of carotid arteries, electrocardiography, cardiac ultrasound. The patients were examined and treated by cardiologists.

Results: Of all patients 22% had cerebral infarction, 41% atherosclerosis, 36% multiple lacunar infarctions and 28% diabetes mellitus type 2. Three patients with cerebral infarction had chorea, hemiballismus, dystonia and dystonic tremor, three had postural tremor and two cerebellar intention tremor. Atherosclerotic patients had atherosclerotic action tremor, while diabetic patients predominantly had with action-type tremor. Electroencephalography showed irritative basic brain activity with slow waves, while carotid arteries stenosis was diagnosed by Doppler sonography. Computerized tomography of the brain and magnetic resonance imaging revealed cerebrovascular diseases in certain areas. Patients with cardiomyopathy, rhythm disorders, high blood pressure, hyperlipidemia was investigated and medically treated by a cardiologist.

Conclusion: In cerebrovascular diseases different types of tremor can occur as a result of damage of the extrapyramidal system.

Key words: tremor, basal ganglia, atherosclerotic tremor, cardiovascular events.

INTRODUCTION

Atherosclerosis of small blood vessels, multiple lacunar infarctions and ischemic lesions of the white matter due to atherosclerosis are the most common factors for the occurrence of abnormal movement disorders and parkinsonian symptoms. Atherothrombosis due to cardiac embolism, especially when caused by cardiac arrhythmia is also the cause of tremor and other movement disorders. Tremor can occur as a symptom of cerebrovascular insult, such as brain infarction predominantly or hemorrhagic stroke. In the post stroke patients not only tremor but also other dyskinetic movements can be presented (1). One of the most common type is cerebellar tremor that occurs in cerebellar infarction. Rubral tremor is a slow coarse tremor exacerbated by posture or voluntary movements. Three cases of rubral tremor were observed following stroke. Tremor was similar in all three cases. Lesions in some parts of the thalamus, midbrain and cerebellum can cause this tremor which responds well to levodopa therapy (2). Tremor can also occur in the infarction of the brain stem. Many patients with cerebral strokes also have cardiovascular diseases as a comorbidity or a complication of the cerebrovascular brain stroke. In these patients, in the acute period, many metabolic disorders and electrolyte disbalance can occur which causes the occurrence of tremor. Tremor is also present in

patients with diabetes mellitus associated with diabetic neuropathy that is the complication of diabetes. Vascular Parkinsonism is a special clinical entity which can occur in cerebrovascular diseases and post stroke patients; sometimes it is called atherosclerotic Parkinsonism when atherosclerosis is present mainly in the small and medium brain blood vessels and is manifested with parkinsonian symptoms predominantly on the lower extremities and postural tremor. Atherosclerotic Parkinsonism is typically presented in patients with long term hypertension and cardiomyopathy and diabetic patients when the tremor is more often present symptom (3, 4).

AIM

The aim of the article is to present some types of tremor that occur in patients with cerebrovascular diseases, such as larger cerebral infarctions, small multiple lacunar infarctions and atherosclerosis with cardiovascular events and in diabetes mellitus type 2, and clinical characteristics of tremors that occurred in our patients and used investigations.

MATERIAL AND METHODS

In our study 36 patients, 24 men and 12 women, were examined and followed at the Department for Movement Disorders, University Neurology Clinic in Skopje, during the period of 3 years, from 2012-2015. Among the studied patients, 8 (22%) of them had cerebral infarction, two cerebellar infarction (0.5%), 15 (41%) were with atherosclerotic changes of small and medium brain blood vessels and 13 (36%) had multiple lacunar infarctions of the brain. We also separated 3 patients from those with cerebral infarction, one with infarction in the putamen, one woman with infarction in the subthalamic nucleus and one in the globus palidus.

In this study all 36 patients had tremor as a part of the clinical picture of the cerebrovascular disease. In all patients a complete examination of neurological status was made, as well as laboratory analysis of blood glucose, neuromorphologycal investigations, CT-scan and MRI of the brain, while neurophysiological investigations involved electroencephalography (EEG) and Doppler sonography of the carotid arteries. Total serum lipids, cholesterol and triglycerides in the blood were also measured. Patients with cardiological diseases were examined and treated by cardiologists. Seven patients with atherosclerosis, three with cerebral infarctions and six with multiple lacunar infarctions had cardiomyopathy. EEG was performed on the 18-channel EEG apparatus using 4 standard montages in which the electrodes were placed on the scalp according to the 10-20 international SI system. Doppler sonography of the common, internal and external carotid artery and vertebral arteries was performed in all patients with color duplex transcranial doppler in 2 patients. Doppler of the carotid arteries was performed on a color duplex sonography apparatus. Electrocardiography (ECG) was done in all patients as well as cardiac ultrasound. Most of the responders were investigated and medically treated by the cardiologist.

RESULTS

CT scan revealed ischemic lesions of the white matter due to atherosclerosis in 15 patients with a slightly consecutive ventricular dilatation in two patients. CT also revealed multiple lacunar infarctions in the basal ganglia in the areas of the putamen, globus palidus and subthalamic nucleus and as well as multiple lacunar infarctions in the internal capsule, the brain stem mainly in the pons, thalamus and white matter. CT scan revealed cerebral infarction in another five patients. MRI findings were similar to those of CT and showed only more pronounced areas of ischemia in the white matter.

The women with subthalamic infarction, due to the lenticulostriate artery occlusion, had hemibalistic movements on the side contralateral to infarction. The movements were developed with a sudden onset and diminished in the follow-up period. MRI showed infarction in the subthalamic nucleus on the side contralateral of hemibalistic movements. The men with infarction in the putamen presented with chemichoreatic movements. His MRI revealed infarction on the side which was contralateral to the side of chemichoreatic movements. The third patient had dystonia and later on developed dystonic tremor. MRI of this patient also revealed infarction in the globus palidus on the contralateral side from dystonia. His dystonic tremor presented as oromandibular dystonic tremor that was irregular and disappeared when the patient touched the chin. In the 6-month follow-up period of a 6-month dystonia of the contralateral limb and dystonic tremor diminished but were still present.

EEG changes were registered in 16 patients with vascular Parkinsonism and three with cerebral infarction. Most common changes were irritative basic brain activity with slow waves in the posterior areas billateraly and unilateral theta activity. On doppler sonography six patients showed stenosis of the common carotid artery bifurcation with hemodynamic changes in four, atheromatosis of the external carotid artery in two and three were with stenosis of the common carotid artery without hemodynamic changes. In two patients transcranial color duplex sonography was performed which

Table 1. *Presentation of the types of patients with cerebrovascular diseases with tremor*

Types of cerebrovascular diseases	Number of patients total 36 (24 men and 12 women)	Percent (%)
Atherosclerosis	15	41
Diabetes mellitus type 2	10	28
Multiple lacunar infarctions	13	36
Cerebral infarctions	8	22

revealed hyperechogenicity of the mesencephalon right side without morphological and hemodynamic changes of the intracranial blood vessels. Laboratory tests showed increased total serum lipids, and the elevation of cholesterol fraction and triglycerides in all atherosclerotic patients and in 11 with lacunar infarctions.

Seven patients with atherosclerosis had a chronic ischemic cardiomyopathy established by the cardiologist. Dilated cardiomyopathy was revealed in three patients with cerebral infarctions and as well as in six with multiple lacunar infarctions.

Three of the patients (28%) with multiple lacunar infarctions and seven (46%) with atherosclerosis had a diabetes mellitus type 2 with diabetic neuropathy due to unregulated chronic hyperglycemia. They had chronic high glucose levels in blood and consequently signs of diabetic neuropathy. A laboratory test revealed high blood glucose level in all of them.

Three patients with cerebral infarction had irregular postural tremor; in two the tremor was in the legs which became more pronounced by walking and was associated with low-frequency muscle fatigue. Two patients with cerebellar infarction had cerebellar intention tremor of the same side with infarction. It was tremor at rest, more pronounced in posture and even more severe on intention. They had cerebellar infarction on CT and MRI scans. The patients with atherosclerosis (41%) and multiple lacunar infarctions (36%) presented signs of atherosclerotic vascular Parkinsonism, predominantly affecting the lower extremities. In these patients tremor at rest was not present except in one patient, but it was not pill-rolling tremor with a higher frequency.

All other patients with atherosclerotic Parkinsonism had atherosclerotic tremor which was a high-frequency action tremor, irregular, while patients with atherosclerotic changes in the cerebellar blood vessels had an additional intention tremor which became more pronounced by intention before reaching the goal of the movement. They had gait instability, bradykinesia and typical small step slow walking with brisk reflexes. The patients with diabetes mellitus type 2, due to the diabetic neuropathy, had a diabetic tremor which occurred when they were tired and the tremor was predominantly action tremor. Tremor was presented in all our 36 patients (Table 1). All of 36 patients at the beginning were treated with standard antiparkinsonian therapy for tremor, but because of failed response to therapy, 77% of the patients with vascular tremor were treated with antiepileptic therapy later on and responded well. The tremor had specificity according to the involved area and tremor was predominantly atherosclerotic vascular tremor, cerebellar, dystonic and diabetic tremor.

DISCUSSION

Vascular Parkinsonism developed later in the post-stroke period had a polymorphic clinical picture presented with Parkinsonian symptoms usually on the lower limbs and also sometimes with pyramidal and cerebellar signs. In our atherosclerotic patients the Parkinsonian symptoms were mainly present and we also found that the tremor at rest can occur, although rarely present; however it is not a typical pill rolling tremor. We also revealed that vascular tremor can developed in patients with larger cerebral infarctions as well. Vascular Parkinsonism presents as lower body Parkinsonism and the condition is the result of the development of the white matter lesions and lacunes in the brain (5).

Cerebrovascular disorders can lead to many cardiovascular events as a consequence of the stroke, as well such as elevated blood hypertension, cardiac tachycardia or arrhythmia, cardiomipathy etc. Cardiac arrhythmia can be the factor leading to the occurrence of cardial embolia and then occlusion of the brain arteries and development of the brain embolic infarctionion. As the result of the involvement of the basal ganglia, cerebellum and other brain structures, different types of tremor can occur in cerebrovascular disorders mostly in atherosclerosis, multiple brain lacunar infarctions and sometimes in large cerebral infarctions.

Diabetes mellitus can be the risk factor that can lead to development of atherosclerosis and consequently later on to the development of vascular Parkinso-

nism. In our 28% of the patients with diabetes mellitus type 2 and with a highly unregulated chronic level of glucose atherosclerosis and diabetic neuropathy lead to the occurrence of diabetic tremor. This type of tremor is mostly action tremor that is more pronounced when patients are tired. In hyperglycemia, tremor can occur similar to the coarse flapping tremor of asterixis, jerking and disorders of muscle tone have been described. With aging, diabetes can worsen rigidity and gait in elderly patients, but not in regard to change in bradykinesia and tremor (6). Arvanitakis Z. et al. in their study in 2004 reported that the presence of stroke reduced the association of diabetes with gait (7). Also, in our patients with atherosclerosis and diabetic tremor, with atherosclerotic vascular Parkinsonism, occurred at the later stage of the disease and was irregular postural or mostly action tremor with high frequency and low amplitude, and was refractory to antiparkinsonian therapy; however 77% of the patients responded well to antiepileptic therapy later on. Three of our patients with large cerebral infarctions had irregular postural tremor; in two of them the tremor was on the legs which became more pronounced by walking and when the muscles became tired with a low frequency. Two cases were presented with the myoclonic tremor caused by parietal cortical lesions manifesting tremulous finger movement provoked by action and posture. The tremor responded well to valproate and clonazepam (8).

In 2011 Andreas Puschmann et al. reported that progress was achieved in understanding the patophysiology of tremor and that available options for the treatment of tremor in patients have increased. There is a more effective treatment for most forms of tremor and the underlying neurologic disorders that cause tremor (9). In accordance with this article, in our patients with atherosclerotic vascular Parkinsonism there was a good response of decreasing the tremor by antiepileptic therapy. In 2000, Deuschl G. reported that 25% of patients with cerebellar dysfunction had moderate to severe kinetic tremor with features of classical intention tremor. They concluded that intention tremor is a feature of essential tremor and that the cerebellum played the major role of its development (10).

Cerebellar tremor in our two patients occurred on the same side with the cerebellar infarction. Cerebellar tremor by its characteristics was an intention tremor in our patients, but it was also kinetic and postural tremor similar to the results of the mentioned author above. Classic cerebelar tremor presents as a low frequency, slow intention or postural tremor and is typically caused by multiple sclerosis with cerebellar plaques, stroke or brain stem tumors. Dystonic tremor is a rare tremor usually irregular and jerky and a certain arm position can extinguish the tremor (11).

In 2012 Netravathi M et al. reported that the underlying etiologies of pure dystonia, dystonia plus, tremor, tremor with dystonia, myoclonus and chorea in approximately 60% of patients was vascular, infections and space-occupying lesions (12). In 1997 Ghika-Schmid F. et al. concluded that hemihorea, hemiballism and hemidystonia were associated with stroke involving basal ganglia and adjacent white matter (13). In our study we also present three patients with infarction of the globus palidus, subthalamic nucleus and putamen and our results are similar to the results of the citied authors. One of the characteristics of the vascular types of tremor and other movement disorders is that they can worsen over the time after stroke and many of this abnormal movement disorders can have a certain good response to antiepileptic therapy. Dystonic tremor is very similar to essential tremor but it differentiates from it by its irregularity; it mostly presents in the head or jaw as an oromandibular dystonic tremor, such as in our patient, and the patient was relived from the tremor when touching the chin. The dystonic tremor can be produced by dystonic muscle contraction or the tremor associated with dystonia is the tremor positioned in one and dystonia in the other body part. Both forms of tremor in dystonia frequently resemble essential tremor or another pure tremor syndrome. New classification, primary tremor, is proposed and would be used for any disorder in which tremor is the sole or principal abnormality with no identifiable etiology (14). EEG findings in stroke patients and with atherosclerosis usually present with sharp irritative background activity associated with slow waves in the posterior areas of billateraly and unilateral tetha waves. The reason of the occurrence of slow waves is brain hypoxia as the result of atherosclerosis. Neuromorphological findings (CT and MRI scabs) showed in our patients cerebrovascular insult, lacunar infarctions, atherosclerotic ischemic changes and infarctions in the basal ganglia.

CONCLUSION

Our study highlights the spectrum of different types of tremor and their correlation with different cerebrovascular and cardiovascular etiologies. In this study we determined specifics of certain types of tremor, certain clinical characteristics and way of manifestations, depending on the type and localization of cerebrovascular disease, especially specifics of abnormal movements in patients with cerebrovascular basal ganglia lesions. We also determined the specifics of diabetic tremor.

This study opens the need for further research that could offer more effective treatments for different

types of tremor and a better understanding of diseases and neurologic disorders that cause tremor.

Conflict of interest

The authors declare that there are no conflicts of interest.

Abbreviations

CT — Computerized tomography of brain
EEG — Electroencephalography
MRI — Magnetic resonance imaging
ECG — Electrocardiography

Sažetak

VRSTE TREMORA KOD BOLESNIKA SA CEREBROVASKULARNIM OBOLJENJIMA I KARDIOVASKULARNIM INCIDENTIMA

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Uvod: Tremor može da se pojavi kao deo kliničke slike cerebrovaskularnih oboljenja. Mnogi bolesnici sa moždanim udarom imaju kardiovaskularna oboljenja kao komorbiditet ili je moždani udar njihova komplikacija; kardiovaskularni incidenti mogu ponekad da uzrokuju pojavu emboličnih moždanih udara.

Cilj: Cilj ispitivanja je da se prikažu vrste tremora: kod bolesnika sa cerebrovaskularnim i kardiovaskularnim obolenjima, bolesnika sa dijabetes melitusom tipa 2. Da se prikažu i kliničke karakteristike tremora i primenjena ispitivanja.

Materijal i metode: Naše ispitivanje je obuhvatilo 36 bolesnika (24 muškaraca i 12 žena) koji su ispitivani i praćeni 3 godine, 2012-2015. Kod svih bolesnika primenjena su sledeća ispitivanja: neurološki pregled, laboratorijske analize, kompjuterizovana tomografija mozga, magnetna rezonanca i elektroencefalografija. Kod bolesnika sa kardiovaskularnim oboljenjima izvršili smo sledeća ispitivanja: Dopler sonografiju karotidnih arterija, elektrokardiografiju i kardiološki ultrazvuk. Ispitivanje i lečenje ovih bolesnika su sproveli kardiolozi.

Rezultati: Od svih bolesnika 22% su imali moždani udar, 41% aterosklerozu, 36% multipli lakunarni infarkt, a 28% dijabetes mellitus tip 2. Tri bolesnika sa moždanim udarom su imali horeu, hemibalizam, distoniju i distonični tremor, 3 su imala posturalni tremor, a 2 cereberalni intencioni tremor. Aterosklerozni bolesnici su imali aterosklerozni akcioni tremor, dok su bolesnici sa dijabetesom u većini slučajeva pokazivali akcioni tip tremora. Nalazi elektroencefalografije (EEG) registrovali su osnovne aktivnosti sa slabim talasima, dok je stenoza karotidnih arterija dijagnostikovana Doppler sonografijom. Kompjuterizovana tomografija mozga i magnetna rezonanca otkrila je cerebrovaskularna obolenja izvesnih moždanih regiona. Bolesnici sa kardiomiopatijom, poremećajima ritma, povišenim krvnim pritiskom i hiperlipidemijom registrovani su nakon kardiološke obrade.

Zaključak: Kod cerebrovaskularnih oboljenja mogu da se pojave različite vrste tremora koji nastaju kao rezultat oštećenja ekstrapiramidnog sistema.

Ključne reči: tremor, bazalne ganglije, aterosklerozni tremor, kardiovaskularni incidenti.

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SANAMED
2016; 11(1): 35–38
ISSN-1452-662X

DOI: 10.5937/sanamed1601035B
UDK: 616.314-008.64-085.31; 615.31:547.495.2
ID: 222048268
Professional article

REMINERALIZATION POTENTIAL OF A CARBAMIDE BLEACHING AGENT

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Primljen/Received 19. 01. 2016. god. Prihvaćen/Accepted 07. 03. 2016. god.

Abstract: **Background:** Bleaching has gradually became a popular procedure for people searching for aesthetic improvement. The aim of this in vitro study was to investigate the effect of bleaching with 45% carbamide peroxide on the level of mineralization of enamel, using laser fluorescence.

Materials and methods: Sixty extracted human teeth were treated with 45% carbamid peroxide (Opalescence, Ultradent), 4 consecutive days for one hour each day. The effect of the bleaching agent on the level of mineralization of enamel was measured with DIAGNO dent pen. The statistical method we use was descriptive analysis.

Results: The average values, measured before the applications of the carbamid peroxide were 6.33. On the first day they were 5.41, on the second 5.38, on the third 5.11 and 5.35 on the forth.

Conclusion: There was observed a slight remineralization effect due to the incorporated Ca^{2+} and F^{-} ions in the bleaching agent that we have used.

Key words: bleaching, DIAGNO den pent, carbamide peroxide.

INTRODUCTION

During the last decade bleaching has gradually become a popular procedure for people searching aesthetic improvement. Despite of the changes in the composition of the bleaching agents a debate concerning their effect on human enamel still exists. They contain either hydrogen peroxide or carbamide peroxide. The peroxide is decomposed into free radicals, which break down large pigmental molecules, thus altering light absorption and eliminating or reducing stains (1). This, according to some authors leads to such side effects as demineralization of the periphery of enamel prisms, increased enamel porosity, erosion (2, 3). It also affects the organic composition of enamel (4). Different types of mineralizing agents were recommended to be used during the bleaching procedures or afterwards in order to reduce these side effects (5, 6).

There has been used a variety of methods for the determination of the demineralization and remineralization that occur during bleaching – confocal laser microscopy, microhardness tests, microradiography, iodide permeability and surface microhardness, scanning electron microscopy, etc. (3, 6, 7, 8).

AIM

The aim of the presented study was to evaluate in vitro the effect of bleaching with 45% carbamide peroxide on the level of mineralization of enamel, using laser fluorescence.

MATERIAL AND METHODS

Sixty extracted human teeth were treated with 45% carbamide peroxide (Opalescence, Ultradent), 4 consecutive days for one hour each time. The effect of the bleaching agent on the level of mineralization of enamel was measured with DIAGNOdent pen. The protocol of the conducted study was the following:

1. Areas with intact smooth enamel surface with sizes 2 mm/2 mm were selected on each tooth using DIAGNOdent pen.

2. The teeth were covered with acid resistant varnish except for the selected areas.

3. DIAGNOdent pen was used to register the values of the enamel surfaces left uncovered with the varnish before the bleaching.

4. The enamel was treated with 45% carbamide peroxide (Opalescence, Ultradent), four consecutive days for one hour each time. The changes in the level of mineralization of the selected areas were measured after each bleaching period.

The statistical method we use was descriptive analysis.

RESULTS

The average values, measured before the applications of the carbamide peroxide were 6.33. Average values of 5.41 were registered after bleaching of the unprotected enamel surfaces on the first day. Decrease in the measured data was registered for thirty-seven of the enamel surfaces, increased – for eight and with no change – for fifteen. On the second day forty-two teeth had decreased values, two – increased and sixteen - no changes. The average value for the investigated surfaces was 5.38. For the last two days of our experiment the number of the teeth with decreased values became even higher. They were forty-eight on the third day and forty-five on the fourth day. Only one tooth on the third day and five teeth on the fourth day had increased values. The number of teeth without changes was eleven and ten respectively. The average values, measured on the third day were 5.11 and 5.35 on the forth (Table 1 and Table 2).

DISCUSSION

DIAGNOdent is a 655 nm diode laser, allowing detection of non-cavitated, occlusal pit and fissure tooth decay and smooth surface caries in an early stage. It measures the laser fluorescence of the mineral structure of the tooth. At the specific wavelength that DIAGNOdent laser operates, healthy tooth structure exhibits little or no fluorescence, resulting in very low scale readings on the display. However, decayed tooth tissue exhibits fluorescence, proportional to the degree of the lost tooth structure, resulting in elevated scale readings on the display of the DIAGNOdent. According to one of the theories concerning the way the device operates, when infrared light reaches porosities due to demineralization in tooth structures, a fluorescent light of different wavelength is stimulated. The other explanation of the way of action of DIAGNOdent is that the products of the bacterial metabolism lead to changes in the fluorescence of tooth structures (9). In the conducted study the observed changes in the measured values is due only to the influence of the bleaching agent on the level of mineralization and not to the presence of bacterial products.

DIAGNOdent pen is a device that according to different authors could be used in studies evaluating the level of mineralization of tooth tissues (10, 11, 12, 13).

There are also some studies that found out that demineralization of enamel did not affect the DIAGNOdent measurements and changes in measurements are due to bacteria, but they are dependent on bacterial metabolites rather than the type of bacteria (14).

Concerning the treatment planning, according to the manufacturer, values between 10–15 require no active care or treatment, values between 15–30 require preventative or operative care, depending on the patient's caries risk and values of 30+ require both operative and preventative care. So the bleaching agent did not lead to changes in the enamel that could need preventive treatment.

The bleaching agent that was used in the presented study (Opalescence Boost PF 40%, Ultradental) contains potassium nitrate and fluoride. Potassium nitrate is added in order to reduce sensitivity. Fluoride is added to help remineralization and strengthen enamel. According to some studies on the effect of bleaching

Table 1. *Number of exanimated teeth*

Bleaching day	No of teeth with decreased values	No of teeth with increased values	No of teeth with no change
1	37	8	15
2	42	2	16
3	48	1	11
4	45	5	10

Table 2. *Average values measured with DIAGNOdent pen before and after bleaching*

Before bleaching	First day bleaching	Second day bleaching	Third day bleaching	Forth day bleaching
6.33	5.41	5.38	5.11	5.38

agents the addition of fluoride does not affect the gel's whitening efficacy (15), but it could eventually provide remineralization properties to the gel (16, 17). Despite of the treatment with the bleaching agent the level of mineralization of sound enamel increased in 60.18% of the teeth on the first day and reached 70.5% of the teeth on the fourth day. This demonstrates that the addition of agents restoring the mineral content of tooth tissues into the bleaching agents is effective and could eventually lead to a satisfactory reduce of the post-bleaching side effects.

CONCLUSIONS

Based on the results, obtained from the presented study it may be concluded that the studied bleaching agent has a slight remineralization effect due to the incorporated fluoride ions. No demineralization was observed.

Conflict of interests

The authors declare there is no conflict of interests.

Sažetak

REMINERALIZIRAJUĆI POTENCIJAL KARBAMIDA KAO AGENSA ZA IZBELJIVANJE ZUBA

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Uvod: Izbeljivanje zuba je danas popularna estetska procedura. Cilj ove in vitro studije je ispitati efekat izbeljivanja 45% karbamid-peroksida u odnosu na mineralizaciju gleđi upotrebom lasera.

Materijal i metode: Šezdeset izvađenih ljudskih zuba tretirano je 45% karbamid-peroksidom (Opalescence, Ultradent) tokom četiri uzastopna dana, po sat vremena dnevno. Efekat izbeljivanja na nivou minerelizacije gleđi je meren DIAGNO denta penom. Statistički su podaci obrađeni deskriptivnom analizom.

Rezultati: Prosečne vrednosti, merene pre aplikacije karbamid-peroksidom, su bile 6,33. Prvog dana nakon aplikacije bile su 5,41, drugog dana 5,38, trećeg dana 5,11 i 5,35 četvrtog dana.

Zaključak: Uočen je blag remineralizirajući efekat usled inkorporiranih Ca^{2+} i F^- jona agensa za izbeljivanje koji smo koristili.

Ključne reči: izbeljivanje, DIAGNO denta pen, karbamid-peroksid.

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SANAMED
2016; 11(1): 39–45
ISSN-1452-662X

DOI: 10.5937/sanamed1601039D
UDK: 616.728.3-07
ID: 222047500
Professional aricle

COMPARATIVE ANALYSES OF DIAGNOSTIC METHODS IN KNEE INJURIES

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Primljen/Received 20. 01. 2016. god.

Prihvaćen/Accepted 02. 03. 2016. god.

Abstract: **Objective:** This study is analyzing the role and significance of the three diagnostic methods (clinical diagnosis, magnetic resonance imaging (MRI) and arthroscopy), in establishing accurate diagnosis in knee injuries. The goal is to determine the diagnostic accuracy of each diagnostic method, using arthroscopy as gold standard.

Material and Methods: We examined 70 patients with knee injuries. Clinical diagnosis was established using patient's history and positive clinical tests for meniscal lesions, ACL injury and articular cartilage lesions. All patients underwent MRI on a 1.5 T magnet for MRI diagnosis. This was followed by arthroscopy for making the final diagnosis.

Results: We analyzed the results of clinical tests for meniscal, ligamentous and articular cartilage injuries of the patients in both groups. Validity of the clinical tests was compared to the results got from MRI and arthroscopy. Accuracy of clinical diagnosis versus MRI diagnosis for medial(69.6% vs. 68.5%) and lateral (84% vs. 82.6%) meniscal lesions was almost identical. Accuracy of clinical diagnosis compared with the accuracy of MRI diagnosis for ACL injuries was higher (91.3% vs. 81.4%). Accuracy (85.5% vs. 72.8%) of clinical diagnosis versus MRI diagnosis for articular cartilage lesions was better.

Conclusion: Affirmation of clinical diagnosis in this study is a result of usage of standard clinical signs and tests which are fundamental in establishing clinical diagnosis of knee injuries. MRI is a diagnostic method which enriches the diagnostic process. Arthroscopy is defined as superior diagnostic method, also a gold standard for comparison of the other two diagnostic methods.

Key words: knee injuries, clinical examination, MRI, arthroscopy.

INTRODUCTION

Diagnosis of knee injuries is established using clinical examinations and magnetic resonance imaging (MRI) of the injuried knee. Both methods are used for obtaining necessary data in order to decide whether to perform arthroscopy or not.

Patient's history gives information on the mechanism of the injury, localization of the pain, swelling, limitations etc. Several clinical tests are used for diferentiation if there are a meniscal, ligamentous or cartilage injuries (1, 2, 3, 4, 5, 6, 7, 8). Knee injuries are common. They often can be combined and sometimes is difficult to establish a precise clinical diagnosis of the injuried tissue (9, 10, 11, 12, 13, 14). MRI is an additional diagnostic method since it offers useful data in the final decision on performing arthroscopy (9). Positive clinical and MRI diagnosis for knee injuries gives us an indication for arthroscopy. Arthroscopy is a gold standard for diagnosis and at the same time it is an operative method used for minimal invasive treatment of the injured knee (10, 15, 16, 17, 18).

AIM

The aim of this study was to determine the accuracy of clinical and MRI diagnosis in comparison to arthroscopy for detecting knee injuries. It was also our aim to found out whether MRI diagnosis has an impact on the surgeon's decision for the choice of treatment.

MATERIAL AND METHODS

We have examined 70 patients with knee injuries, 50 (71.4%) of them were male and 20 (28.6%) female, with avarage age of 35 ± 15 years. Patients with meniscal, ACL or cartilage injury were analysed in this

study. Inclusion criteria were as follows: patients with established clinical diagnosis of knee injury, MRI of the injuried knee and arthroscopy.

Patients with acute knee injury, intra-articular fractures, loose bodies, disecant osteochondritis, degenerative osteoarthritis and inflamations were excluded from the study.

Clinical diagnosis was established using patient's history and positive clinical tests for meniscal injuries (McMurray and Apley), ACL injury (anterior drawer test, Lachman test and pivot shift test) and articular cartilage injuries (McMurray test for medial and lateral condyl, patella tests). All patients underwent MRI on a 1.5 T magnet for MRI diagnosis. This was followed by arthroscopy for making the final diagnosis. The same surgeon has performed clinical as well as arthroscopic diagnosis of the injured knee.

Clinical and MRI diagnoses were correlated with arthroscopic diagnosis which was used as a gold standard. To determine the credibility of the clinical examinations and MRI, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy were assessed. We were using statistical programSPSSforWindows for analyzing the data.

RESULTS

From 70 patients with knee injuries, 55 were with clinical diagnosis of meniscal lesions, 26 were with clinical diagnosis of ACL injury and51 were with clinical diagnosis of articular cartilage lesion.

Meniscal lesions

Among 55 patients with clinically diagnosed meniscal lesion 44 were with medial meniscal lesion and 11 with lateral meniscal lesion. Arthroscopy confirmed accuracy of clinical diagnosis in 32 patients (72%) or (44 vs. 32) with medial meniscal lesion, and 8 patients (72.7%) or (11 vs. 8) with lateral meniscal lesion. From 56 patients with medial meniscal lesion on MRI, arthroscopy confirmed the diagnosis in 34 patients (60.7%) or (56 vs. 34) and from 10 patients with lateral meniscal lesion arthroscopy confirmed the diagnosis in 6 patients (60%) or (10 vs. 6).

The sensitivity of clinical diagnosis versus MRI diagnosis for medial meniscus (79.9% vs. 79.5%) was identical. The specificity of clinical diagnosis was better in comparison to MRI (58.1% vs 38.1%). Positive predictive values (69.8%vs. 69.6%) and negative predictive values (69.2% vs. 69.2%) for medial menuscus were the same (Table 1).

The sensitivity of clinical diagnosis versus MRI diagnosis for lateral meniscus (50% vs. 40%) was better. The specificity of clinical diagnosis in comparison to MRI (92.7% vs. 92.7%) was identical. Positive predictive values (63.6% vs. 60%) and negative predictive values (87.9% vs. 85.5%) for lateral menuscus were the same.

Diagnostic accuracy of clinical diagnosis was higher in comparison to MRI diagnosisfor medial meniscal lesion (69.6% vs. 68.5%) and for lateral meniscal lesion (84% vs. 82.6%) (Table 2).

ACL injury

ACL injury was clinically diagnosed in 26 patients.Arthroscopy confirmed the clinical diagnosis in 25 patients (96.15%). From 26 patients with ACL injury on MRI, arthroscopy confirmed the diagnosis in 22 patients (84.61%).

The sensitivity (83.3% vs. 71%), specificity (97.4% vs. 89.7%), positive predictive values (96.2% vs. 84.6%)

Table 1. *Statistical methods for medial meniscal lesions*

Medial meniscus	McMurray	Apley	ClinicalDg	MRI
Sensitivity (95%CI)	82% (66.6-90.8)	63.1% (49.9-78.8)	79.9% (63.7-88.9)	79.5% (65.9-85.8)
Specificity (95%CI)	58.1% (40.8-73.6%)	62.5% (46.9-78.9)	58.1% (40.8-73,6)	38.1% (25.6-55.4)
PPV (95%CI)	70.5% (55.8-81.8)	66.7% (53.1-82)	69.8% (54.9-81.4)	69.6% (56.7-81.4)
NPV (95%CI)	72% (52.4-85.7%)	60.6% (43.7-75.3)	69.2% (50-83.5)	69.2% (42.4-87.3)
LR+	1.9	1.8	1.9	1.2
LR-	0.3	0.5	0.4	0.4
Diagnostic accuracy	71%	64%	69.6%	68.5%
Area Under Roc curve (95%CI)	0.7 0.6-0.8	0.6 0.5-0.7	0.7 06-0,8	0.7 0.5-0.8

Table 2. *Statistical methods for lateral meniscal lesions*

Lateral meniscus	McMurray	Apley	ClinicalDg	MRI
Sensitivity (95%CI)	53.3% (30.1-75.2)	50% (26.8-73.2)	50% (26.8-73.2)	40% (19.8-64.3)
Specificity (95%CI)	94.4% (84.9-98.1)	96.4% (87.7-99)	92.7% (82.7-97.1)	92.7% (82.7-97.1)
PPV (95%CI)	72.7% (43.4-90.3)	77.8% (45.3-93.7)	63.6% (35.4-84.8)	60% (33.3-83.2)
NPV (95%CI)	87.9% (77.1-94)	88.3% (77.8-94.2)	87.9% (77.1-94)	85.5% (73.9-91.9)
LR+	9.6	13.7	6.9	5.5
LR-	0.5	0.5	0.5	0.6
Diagnostic accuracy	85.5%	86.9%	84%	82.6%
Area Under Roc curve (95%CI)	0.8 (0.7-0,9)	0.8 (0.6-0,9)	0.8 (0.6-0.9)	0.7 0.5-0.9

Legend: PPV (positive predictive values); NPV (negative predictive values); LR+ (likelihood ratio positive); LR- (likelihood ratio negative); AUC (area under the curve)

Table 3. *Statistical methods in LCA injuries*

LCA	Anterior drawer test	Lachman	Pivot shift	Clinical Dg	MRI
Sensitivity (95%CI)	83.3% (66.4-92.7)	69.4% (51.8-82.7)	56.5% (39.3-72.2)	83.3% (66.4-92.7)	71% (53.4-83.9)
Specificity (95%CI)	97.4% (86.8-99.5)	98.8% (89.1-99.9)	98.8% (89.1-99.9)	97.4% (86.8-99.5)	89.7% (76,4-95.9)
PPV (95%CI)	96.2% (81.1-99.3)	97.7% (81.5-99.8)	97.2% (78.1-99.7)	96.2% (81.1-99.3)	84.6% (66.5-93.8)
NPV (95%CI)	88.4% (75.5-94.9)	80.6% (67.5-89.3)	74.5% (61.4-84.3)	88.4% (75.5-94.9)	79.5% (65.5-88.8)
LR+	32.5	55.5	45.1	32.5	6.9
LR-	0.2	0.3	0.4	0.2	0.3
Diagnostic accuracy	91.3%	86.9%	81.2%	91.3%	81.4%

Legend: PPV (positive predictive values); NPV (negative predictive values); LR+ (likelihood ratio positive); LR- (likelihood ratio negative); AUC (area under the curve)

and negative predictive values (88.4% vs. 79.5%) of clinical diagnosis versus MRI diagnosis for ACL tears were better. Same results were also found for clinical tests (anterior drawer test, Lachman test, pivot shift test). In our study anterior drawer test was superior against the other two tests in diagnosing LCA tears (Table 3).

Diagnostic accuracy of clinical diagnosis was higher in comparison to MRI diagnosis for ACL injuries (91.3% vs. 81.4%) as depicted in Table 3.

Articular cartilage lesions

We had 51 patients with clinically diagnosed articular cartilage injury. Arthroscopy confirmed the clinical diagnosis in 45 patients (88.23%). From 48 patients with articular cartilage injury on MRI, arthroscopy confirmed the diagnosis in 39 patients (81.25%).

The sensitivity (91.8% vs. 79.6%), specificity (70% vs. 57.1%), positive predictive values (88.2% vs. 81.3%) and negative predictive values (77.8% vs. 54.5%) of clinical diagnosis versus MRI for cartilage lesions were better. Diagnostic accuracy of clinical diagnosis was higher in comparison to MRI diagnosis for articular cartilage injuries (85.5% vs. 72.8%) as depicted in Table 4.

DISCUSSION

Analyzis of the results in this study coresponds with the results from similar studies exploring this feeld. The conclusions were identical. Authors point out

Table 4. *Statistical methods in articular cartilage injuries*

Articular cartilage	Clinical Dg	MRI
Sensitivity (95%CI)	91.8% (80.8-96.8)	79.6% (66.4-88.5)
Specificity (95%CI)	70% (48.1-85.5)	57.1% (36.5-75.5)
PPV (95%CI)	88.2% (54.8-94.5)	81.3% 68.1-89.8)
NPV (95%CI)	77.8% (54.8-91)	54.5% (34.7-73.1)
LR+	3.1	1.8
LR-	0.1	0.4
Diagnostic accuracy	85.5%	72.8%
AUC (95%CI)	0.8 (0.7-0.9)	0.7 (0.5-0.8)

Legend: PPV (positive predictive values); NPV (negative predictive values); LR+ (likelihood ratio positive); LR- (likelihood ratio negative); AUC (area under the curve)

that clinical examination is more reliable in diagnosing meniscal lesions, ACL tears and articular cartilage lesions, altought previously it was asumed that MRI was essential in establishing accurate diagnosis.

In our study sensitivity (79.9% vs. 79.5%), specificity (58.1% vs. 38.1%), PPV (63.6% vs. 60%), NPV (87.9% vs. 85.5%) and accuracy (69.6% vs. 68.5%) of clinical diagnosis versus MRI for medial meniscal lesions were almost identical. Sensitivity (50% vs. 40%), specificity (92.7% vs. 92.7%), PPV (69.8% vs. 69.6%), NPV (69.2% vs. 69.2%) and accuracy (84% vs. 82.6%) of clinical diagnosis versus MRI for lateral meniscal lesions were the same. Rayan et al. analyzed 87 patients with meniscal lesions. They conclude that clinical examination had better sensitivity (86% vs. 76%), specificity (73% vs. 52%) and diagnostic accuracy (79% vs. 63%) in comparison to MRI for diagnosis medial meniscal lesions. In lateral meniscal lesions sensitivity (56% vs. 61%), specificity (95% vs. 92%) and diagnostic accuracy (85% vs. 85%) were almost the same (19).

Rose et al. refer similar results in accuracy between clinical examination and MRI. Diagnostic accuracy for medial meniscal lesions was 82% vs.75%, and for lateral meniscal lesions 76% vs. 69% (20). Kocabey et al. and Bohnsack et al. stated that clinical examination is as accurate as MRI in the skilled orthopedic surgeon's hands and MRI should be reserved for more complicated and confusing cases (21, 22).

Mohan et al. reported accuracy of clinical diagnosis of 88% for medial meniscal lesions and 92% accuracy for lateral meniscal lesions (23).

Dutka J et al. reported of 113 patients who had better sensitivity of MRI in comparison to clinical examination for medial meniscal tears (88% vs. 65%) and for lateral meniscal tears (44% vs. 38%) (24).

Hardy et al. refer sensitivity, specificity and accuracy of MRI diagnosis (90%, 59%, 76%) in comparison to clinical diagnosis (93%, 55%, 73%) (25).

Miller stated that accuracy of clinical diagnosis of meniscal lesions was 80.7% in comparison with accuracy of MRI diagnosis 73.7% (26).

Some authors analyze only the accuracy of MRI in comparison to arthroscopy. Their results were as follows: Aydingoz et al. report 90% sensitivity of MRI in detection of bucket handle lesions of meniscus. Cellar et al. refer of high sensitivity of MRI (92%) for medial meniscal lesions and 70% sensitivity of MRI for lateral meniscal lesions (27, 28).

In our study the accuracy of clinical diagnosis compared with the accuracy of MRI diagnosis for ACL injuries were higher (91.3% vs. 81.4%). Sensitivity, specificity and accuracy were 83.3%, 97.4%, 91.3% of the anterior drawer test, 69.4%, 98.8%, 86.95% of the Lachman test and 56.5%, 98.8%, 81.16% of the pivot shift test.

Dutka et al. found better sensitivity values of clinical examination for injuries of the anterior cruciate ligament (86%) versus MR sensitivity (80%) (24).

Esmaili Jah et al. reported that clinical examination was accurate in 91.4%, and MRI in 88.5% of anterior cruciate ligament injuries (29).

Analysis of the clinical tests for ACL rupture was made by van Eck CF et al. Sensitivity was 38% and specificity 81% of the anteriordrawertest; sensitivity of the Lachman test was 81% and the specificity 81% and sensitivity of the pivot shift test was 28% and the specificity 81%. The authors concluded that the Lachman test had the highest sensitivity for diagnosing an acute, complete ACL rupture (30).

Jain et al. presented the sensitivity of the anterior drawer test, the Lachman test and the pivot shift test and the results were 89.3%, 78.6% and 75%, respectively (31).

In the study of Kim SJ, Kim HK comprising 147 patients, the anterior drawer test was positive in 79.6%, the Lachman test was positive in 98.6%, and the pivot shift test was positive in 89.8% of patients (32).

Some authors had equal or better results using MRI for diagnosis ACL injuries in comparison with clinical examinations.

Rose et al. obtained similar results in accuracy between clinical examination and MRI. Diagnostic accuracy for ACL tears was 99% vs. 98% (20).

Kocabey et al. stated that the accuracy of the clinical examination and MRI evaluation was equal in diagnosing ACL ruptures (21).

Rayan et al. analyzed 26 patients with ACL injuries. They concluded that clinical examination versus MRI had almost the same sensitivity (77% vs. 81%, respectively), specificity (100% vs. 96%), positive predictive value (100% vs. 81%), negative predictive value (95% vs. 95%), and diagnostic accuracy (93% vs. 96%) (19).

The study of Laoruengthana et al. analyzing 50 patients showed that sensitivity, specificity, accuracy and negative predictive value (NPV) of MRI in detecting the complete tear of the ACL injury were 90.9%, 84.6%, 88.6% and 84.6%, respectively (33).

Ruth Crawford found MRI to be highly accurate in diagnosing anterior cruciate ligament (ACL) tears. It is the most appropriate screening tool before therapeutic arthroscopy. It is preferable to diagnostic arthroscopy in most patients because it avoids the surgical risks of arthroscopy (9).

In our study the sensitivity (83.3% vs. 71%), specificity (97.4% vs. 89.7%), positive predictive values (96.2% vs. 84.6%) and negative predictive values (88.4% vs. 79.5%) of clinical diagnosis of ACL tears were better in comparison to MRI diagnosis. Diagnostic accuracy of clinical diagnosis was higher in comparison to MRI for ACL injuries (91.3% vs. 81.4%) (10).

We have better results for sensitivity (91.8% vs. 79.6%), specificity (70% vs. 57.1%), PPV (88.2% vs 81.3%), NPV (77.8% vs 54.5%) and accuracy (85.5% vs. 72.8%) of clinical diagnosis versus MRI for articular cartilage lesions.

Gelb et al. evaluated articular surface damage. They said that the predictive value of positive tests was 100% for clinical assessment and 33% for the magnetic resonance imaging. They conclude that magnetic resonance imaging is overused in the evaluation of knee disorders and not a cost-effective method for evaluating injuries when compared with a skilled examiner (34).

Dutka et al. refer better sensitivity (51% vs. 32%) and specificity (100% vs. 97%) values of clinical examination for chondral injuries versus MRI (24).

Cellar et al. reported that sensitivity, specificity and accuracy of MRI in detecting articular chondral lesions, were 45%.87% and 60% (28).

In our study sensitivity (91.8% vs. 79.6%), specificity (70% vs. 57.1%) and accuracy (85.5% vs. 72.8%) of clinical diagnosis versus MRI for cartilage lesions were better. Duc et al. reported MRI sensitivity, specificity, and accuracy for the two readers and the two evaluations ranged from 56% to 66%, 78% to 93% and 71% to 75%, respectively (35).

Friemert et al. said that the role of MRI for the diagnosis of chondral lesions of the knee joint is still unclear. The sensitivity of the method ranges from 15% to 96%. They concluded that MRI is suitable for the exclusion of cartilage lesions (36).

Munk et al. concluded that the clinical relevance of MRI in cartilage lesions was more doubtful. Because of that the combination of clinical and MRI findings would reduce the number of blank arthroscopies to 5%. MRI is a valuable diagnostic tool, but arthroscopy still remains the gold standard for definitive diagnosis (37).

D'Erme et al. reported 81% sensitivity and 61% specificity of MRI diagnosis for cartilage lesions (38).

Kijwski et al. said that sensitivity, specificity, and accuracy of MR imaging for detecting cartilage lesions were 69.3%, 78.0%, and 74.5% (39).

In our study, we have better results for sensitivity (91.8% vs 79.6%), specificity (70% vs 57.1%), PPV (88.2% vs 81.3%), NPV (77.8% vs 54.5%) and accuracy (85.5% vs 72.8%) of clinical diagnosis versus MRI for articular cartilage lesions.

Diagnosis of intraarticular lesions of the knee is a complex process, which includes clinical examination and MRI of the injured knee. Sometimes MRI is used more frequently because it is a very precise method for visualization of the soft tissue. Nevertheless, MRI does not diminish the importance of orthopedic clinical examination as an indication for arthroscopy.

The study of Trieshmann et al. shows that MRI of the knee is a valuable tool for augmenting the diagnostic process. It is a cost-effective technique for avoiding unnecessary surgery and affects patient outcome by improving surgical decision (40).

CONCLUSION

In conclusion, carefully performed clinical examination can give better diagnosis of knee injuries in comparison to MRI diagnosis. Any experienced orthopedic surgeon can trust his/her clinical diagnosis as an indication for arthroscopy followed by surgical treatment. When the clinical diagnosis is established, without any doubts due to positivity of the clinical tests, the MRI is not essential. In suspected cases where there is a dilemma, MRI is very helpful in making decision for arthroscopy.

Diagnostic accuracy of clinical and MRI diagnosis in knee injuries is high. Their reliabilities in diagnosis of meniscal lesions, ACL tears and articular cartilage lesions are evident.

Abbreviations

MRI — magnetic resonance imaging
ACL — anterior cruciate ligament
PPV — positive predictive value
NPV — negative predictive value
LR+— likelihood ratio positive
LR- — likelihood ratio negative
AUC — area under the curve

Sažetak

KOMPARATIVNE ANALIZE DIJAGNOSTIČKIH METODA KORIŠĆENIH KOD PACIJENATA SA POVREDOM KOLENA

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Uvod: Ova studija analizira ulogu i značaj tri dijagnostičke metode (klinička dijagnoza, magnetna rezonanca (MR) i artroskopija), u postavljanju tačne dijagnoze povrede kolena. Cilj ove studije bio je utvrđivanje tačnosti pojedinačnog dijagnostičkog metoda, koristeći artroskopiju kao zlatni standard.

Materijal i metode: Ispitivali smo 70 pacijenata sa povredom kolena. Klinička dijagnoza je postavljena na osnovu istorije bolesti pacijenta i pozitivnih kliničkih testova na povrede meniskusa, ACL i artikularne hrskavice. Svi pacijenti su podvrgnuti MR snimanju na 1.5 T magnetu za MR dijagnozu. Ovo je praćeno artroskopijom, za postavljanje finalne dijagnoze.

Rezultati: Analizirali smo rezultate kliničkih testova povreda meniskusa, ligamenata i artikularne hrskavice pacijenata u obe grupe. Validnost kliničkih testova bila je poređena sa rezultatima dobijenim sa MR i artroskopijom. Tačnost kliničke dijagnoze poređena sa MR dijagnozom za povrede medijalnog lemniskusa (69.6% vs. 68.5%) i lateralnog (84% vs. 82.6%) bila je skoro identična. Tačnost kliničke dijagnoze poređena sa tačnosti MR dijagnoze za ACL povrede bila je viša (91.3% vs. 81.4%). Tačnost kliničke dijagnoze prema MR dijagnozi povrede artikularne hrskavice (85.5% vs. 72.8%) išla je korist kliničkom postavljanju dijagnoze.

Zaključak: Potvrđivanje validnosti i značaja kliničke dijagnoze u ovoj studiji je rezultat korišćenja standardnih kliničkih znaka i testova, koji su fundamentalni u postavljanju kliničke dijagnoze povrede kolena. MR je dijagnostička procedura, koja obogaćuje dijagnostički proces. Artroskopija je definisana kao superiorni dijagnostički metod, kao i za zlatni standard, korišćen za upoređivanje tačnosti druga dva dijagnostička metoda.

Ključne reči: povreda kolena, kliničko ispitivanje, magnetna rezonanca, artroskopija.

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SANAMED
2016; 11(1): 47–52
ISSN-1452-662X

DOI: 10.5937/sanamed1601047G
UDK: 616.717.7/.9-007.2-073; 616.717.7/.9-089
ID: 222046732
Professional article

COMPARATIVE RADIOGRAPHIC ANALYSIS OF THE RESULTS OF TREATMENT OF HALLUX VALGUS DEFORMITY ACCORDING TO MITCHELL AND KELLER OPERATIVE METHODS

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Primljen/Received 25. 01. 2016. god. Prihvaćen/Accepted 28. 02. 2016. god.

Abstract: **Introduction:** Hallux valgus represents a complex progressive deformity of the front part of the foot, with the most distinguished malformation as lateral deviation of the toe. Radiography is extremely important in the decision of the surgical procedure for the best correction of this deformity. **Aim:** The aim of this work is to show the significance of radiographic examinations in operated patients with Hallux Valgus deformityaccording to Mitchell and Keller techniques. **Material and methods:** The study included 70 patients having hallux valgus deformity of the foot, and they were divided to two groups. The patients were grouped according their sex, age, the degree of deformity (moderate or severe degree of deformity) and according to radiographic findings. The first group (Group 1) was composed of 35 patients who were treated by osteotomy of the I metatarsal bone according to Mitchell, while the second group (Group 2) was also composed of 35 patients who were treated by resectional arthroplasty according to Keller. Radiographic examinations (Method of Hardy and Clapham, Piggott classification, presence and absence of the secondary arthritic and reactive changes of the first metatarsophalangeal joint) were analyzed comparatively during the evaluation. The analyses of the radiographic results were performed pre-operatively and post-operatively for the two groups. **Results:** According to their sex, the patients were 5 men and 65 women. The average age of the patients in group 1 was 42 years, while for group 2 it was 56 years. There is no significant difference ($p > 0.05$) in the patients of the two groups concerning the pre-operative mean dimension values of the I metatarsophalangeal angle and I intermetatarsal angle. However, the radiographic analysis of the same angles in both groups, one year post-operatively, showed a high statistically significant difference ($p < 0.001$). The patients operated by Mitchell's technique, according to Piggott classification, have deviation significantly more often on the I metatarsophalangeal joint of 51.43% as a result of their hallux valgus deformity. Significantly more often, there is a subluxation of 77.14% on the I metatarsophalangeal joint in the patients treated by Keller's technique. The radiographic analysis of the I metatarsophalangeal joint (presence and absence of the secondary arthritic and reactive changes) in both groups, pre-operatively ($p < 0.01$) and one year post-operatively ($p < 0.001$), showed a high statistically significant difference.

Conclusion: Radiographic analyses were of enormous benefit as in the choice of the decision on the type of the operative procedure and also for the evaluation of the postoperative results.

Key words: radiographic analysis, Mitchell, Keller, hallux valgus.

INTRODUCTION

The first thorough description of hallux valgus deformity was published in 1871 by Carl Hueter. Hallux valgus deformity characterized with valgus position of the big toe, enlarged of the I intermetatarsal angle, appearance of pseudoegsostosis or bursitis in the area of the medial side of the head of the I metatarsal bone, as well as with an inside rotation of the big toe in more severe cases.

Since no muscles insert into the metatarsal head, it is vulnerable to extrinsic factors. Furthermore, the I metatarsophalangeal joint plays a major role in the transmission of body weight during locomotion, and if

there is abnormal stress placed on the joint it may become deformed. Static deformities such as hallux valgus have a tendency to affect this joint and may require surgical intervention (1, 2).

A physical examination demonstrates that the affected joint is tender. Motion of the joint often causes discomfort. Bony proliferation around the margin of the affected joint can be palpated and is frequently visible. On the basis of radiographic analysis of the foot with hallux valgus gets systematic tracking and adequate treatment of this deformity. A radiographic examination demonstrates a grade of deformity according to values of I metatarsophalangeal and first intermetatarsal angle, evaluation of the condition of the first metatarsophalangeal joint and secondary arthritic and reactive changes in the same joint (3, 4, 5, 6).

The treatment of hallux valgus is surgical. More than 150 surgical procedures have been describes for the correction of this deformity. The numerous operative procedures and modifications point to the fact that none of them can make a correction on every hallux valgus deformity. The essence of these surgical procedures is to correct the deformity, to make an effort to eliminate the anatomic potential for the origination of the deformity, and to create a normal position, direction and physiologically antagonistic function of the muscles which are not balanced (7, 8, 9). The main parameters in the selection of the surgical procedure are by the type of deformity, the degree of deformity, clinical, radiographic findings, patient age, comorbidities and the expectations of patients from the surgery itself. In this paper, emphasis is set on comparative preoperative and postoperative radiographic analysis in patients operated according to the methods of Mitchell and Keller.

AIM

The aim of this work is to show the importance of radiographic examinations in preoperative and postoperative period in patients with hallux valgus deformity operated by the methods of Mitchell and Keller.

MATERIAL AND METHODS

The study was carried out at the University Orthopaedic Surgery Clinic, Faculty of Medicine in Skopje, in the period from 2008 to 2012 year. The material for the research consisted of 70 patients having hallux valgus deformity. The patients were divided to two groups of 35 patients each. They were treated by operative procedures according to the methods of Mitchell (first group), and of Keller (second group). The study included patients with only static hallux valgus deformity. Of the study were excluded young patients up to 20 years of age, congenital, inflammatory and post-traumatic hallux valgus deformity.

The patients were grouped according to their sex, age (in 2 groups: from 20 to 50 and over 50 years of age), the degree of deformity (moderate or severe degree of deformity), and according to the clinical and radiographic findings. Grouping of patients was done by orthopedic surgeons who be conducted by both operational intervention. The operative procedures in both groups were performed under regional spinal anesthesia.

Radiographic examinations were done by the method of Hardy and Clapham (the dimensions of the I metatarsophalangeal and the I intermetatarsal angle are determined by this method), Piggott method (according to this method the I metatarsophalangeal joint can be congruent, in deviation, and with subluxation). A radiographic examination in the first metatarsophalangeal joint demonstrated sclerotic joint margins, proliferative bone about the periphery of the joint (osteophytes), and subchondral cyst formation. In accordance with the radiographic findings, in our study, patients with moderate degree of deformity were selected in the first, Mitchell group, while patients with severe degree of deformity were included in the second, Keller group.

Radiographic examinations were done pre-operatively and post-operatively. Radiographic measurements were made strictly from within orthopedic surgeons who conducted the appropriate surgical intervention.

For statistical analysis of data obtained in the study was made based in statistical program SPSS 13.0 for Windows. Moreover, during the computer analysis were used the following statistical methodologies: t-test for independent samples, Kolmogorov-Smirnov two sample test, and Chi-square Pearson test with and without correction.

RESULTS

According to sex, the first group consisted of 3 (8.57%) male patients and 32 (91.43%) female patients, while the second group consisted of 2 (5.71%) males and 33 (94.29%) female patients. The difference between the two groups is statistically highly significant ($p < 0.001$).

The average age of the patients in group 1 was 41.94 ± 16.5 years, while for group 2 it was 56.29 ± 12.5 years. The difference in the mean age between the two groups is statistically highly significant ($p < 0.001$).

An average dimension of the I metatarsophalangeal angle of 40.31 ± 7.6 degrees was measured in the group of patients treated by the method of Mitchell, before the operation, and it is not significantly greater ($p > 0.05$) than the average dimension of the same angle in the group of patients treated by the method of Keller,

where its value is 37.49 ± 9.7 degrees (Table 1). The dimension of the I metatarsophalangeal angle in all patients was measured post-operatively during the control examinations, namely 3 months and 1 year after the intervention. The average dimension of the I metatarsophalangeal angle in the patients operated by the method of Mitchell after 3 months was 16.97 ± 3.8 degrees, after operation while in the patients operated by the method of Keller this average dimension was smaller and was 15.0 ± 1.7 degrees. This difference tested by the t test for independent samples was statistically high significant ($p < 0.01$). During the second control examination, 1 year post-operatively, average dimension of the 1st metatarsophalangeal angle in the patients of the first group was 18.66 ± 4.0 and 15.83 ± 1.9 degrees in the patients of the second group. This difference was statistically high significant ($p < 0.001$), (Table 2).

There is a non-significant difference in the pre-operative average values in the dimensions of the 1st intermetatarsal angle in the patients of both groups. Its value was 15.26 ± 3.9 degrees in the patients treated by the method of Mitchell and 14.97 ± 4.0 degrees in the patients treated by the method of Keller (Table 1). The average dimension of the 1st intermetatarsal angle, 3 months after the operation was 10.83 ± 2.4 degrees (Mitchell), and it is significantly less ($p < 0.001$) than the average dimension of this angle treated by the method of Keller, which was 14.97 ± 4.0 degrees. This statistically significant difference ($p < 0.001$) in the average dimension of the Iintermetatarsal angle between the two groups was confirmed 1 year after the operation, too (Table 3).

The patients operated by Mitchell's technique, according to Piggott classification, have deviation significantly more often on the 1st metatarsophalangeal joint of 51.43% as a result of their hallux valgus deformity. Significantly more often, there is a subluxation of 77.14% on the 1st metatarsophalangeal joint in the patients treated by Keller's technique (Table 4). Piggot classification was useful for Mitchell group (Table 5), but it was not possible to use post-operatively in patients from the second group since it was made resection arthroplasty by the method of Keller.

The secondary arthritic and reactive changes in the area of 1st metatarsophalangeal joint were registered in 6 (17.1%) patients operated by Mitchell's technique, and in 30 (85.7%) patients operated by Keller' procedure. The tested difference for the presence and absence of the secondary arthritic and reactive changes in the patients treated by the two different operative techniques was verified as statistically highly significant ($p < 0.001$). During the second follow-up examination, 1 year post-operatively, the secondary arthritic and reactive changes in the patients in the first group was 7 (20%) and 31 (88.6%) in the patients in the second group. This difference was statistically highly significant ($p < 0.001$).

Table 1. *I metatarsophalangeal/intermetatarsal angle – pre-operatively*

BEFORE OPERATION	Mean MITCHELL	Standard deviationMITCHELL	Mean KELLER	Standard deviationKELLER	t-value	p
I metatarsophalangeal angle	40.31	7.6	37.49	9.7	1.36	0.18
I intermetatarsal angle	15.26	3.9	14.97	4.0	0.3	0.76

Table 2. *I metatarsophalangeal angle – 3 months/1 year post-operatively*

AFTER OPERATION	Mean MITCHELL	Standard deviationMITCHELL	Mean KELLER	Standard deviationKELLER	t-value	p
I metatarsophalangeal angle – 3 months	16.97	3.78	15.0	1.66	2.82	0.006
I metatarsophalangeal angle – 1 year	18.66	3.99	15.83	1.93	3.77	0.00034

Table 3. *I intermetatarsal angle – 3 months/1 year post-operatively*

AFTER OPERATION	Mean MITCHELL	Standard deviationMITCHELL	Mean KELLER	Standard deviationKELLER	t-value	p
I intermetatarsal angle – 3 months	10.83	2.36	14.97	4.0	-5.27	0.000001
I intermetatarsal angle – 1 year	11.26	2.58	14.97	4.0	-4.61	0.000018

Table 4. *Condition of the I metatarsophalangeal joint between both groups – pre-operatively*

Condition of the Imetatarsophalangeal joint	MITCHELL - group 1		KELLER - group 2	
	Nomber	%	Nomber	%
Congruent	2	5.71	1	2.86
In deviation	18	51.43	6	17.14
With subluxation	15	42.86	27	77.14
Luxation	0	0	1	2.86
Summary	35	100	35	100

Kolmogorov-Smirnov Dmax = –0.38, $p < 0.025$

Table 5. *Condition of the I metatarsophalangeal joint – pre-operatively/post-operatively (Group 1)*

Condition of the Imetatarsophalangeal joint in Mitchell group	Pre-operatively		Post-operatively	
	Nomber	%	Nomber	%
Congruent	2	5.71	30	85.71
In deviation	18	51.43	5	14.29
With subluxation	15	42.86	0	0
Summary	35	100	35	100

DISCUSSION

Patients with hallux valgus deformity of our region were included in this prospective study, the first of its kind in the Republic of Macedonia. From numerous surgical techniques attention about resolving this deformity in this study were processed essentially two completely different procedures. An important place is given to this deformity in the world literature as a complex orthopedic problem. It is a subject of the numerous clinical studies during the past decades. This study resulted from the fact that this deformity is insufficiently elaborated in our environment, and it will contribute either in the orthopedic theory or orthopedic practice.

Hallux valgus is the most frequent deformity of the foot. It presents a complex and progressive deformity which affects the front part of the foot, where the most emphatic change is the lateral deviation of the big toe. Concerning the type of deformity, the static one was the most prevalent in our study, but also it is represented in all scientific studies for this deformity (7, 8, 9).

The world literature data show more frequent incidence of this deformity in women compared to men, which is the case in our study, too (1, 2, 3). The mean age of the patients is 41 and 56 years of age, according to Mitchell and Keller respectively.

In more studies and papers like Joseph TN, Kitson K, Chong N, with collaborators, and many others, the accent was put on the importance of radiographic analysis in the surgical treatment ofhallux valgus deformity (8, 9, 10). Based on the radiographic variables, we can make correct evaluation of the type and degree of the deformity. The angles and distances are manifested variables for studying the deformity degree. Radiographic findings should always be in correlation to clinical findings. Based on the clinical-radiographic analysis of the foot with hallux valgus, systematic following and adequate treatment of this deformity is enabled (11, 12, 13, 14, 15). Our study, too, showed the usefulness of the classification according to Hardy and Clapham for the determination of the hallux valgus deformity degree in respect to the dimension of I metatarsophalangeal angle and I intermetatarsal angle pre- and post-operatively. The mean dimension of I metatarsophalangeal angle and I intermetatarsal angle post-operatively, in both groups, was shown as the significantly high ($p < 0.001$). This study showed that the operational procedure according to Mitchell reduces the value of I metatarsophalangeal angle and I intermetatarsal angle to normal values, while operating procedure Keller does not correct metatarsus primus varus, followed by post-operative I intermetatarsal angle remains unchanged values, while I metatarsophalangeal angle is reduced to normal.

Ferrari J.underlines the importance of congruence of I metatarsophalangeal joint (15). In our study application of Piggott classification showed as very important one in the choice of corresponding surgical procedure in the treatment of hallux valgus deformity. Preoperative respondents operated by Mitchell technique had signifi-

cantly more often deviated I metatarsophalangeal joint, while subjects treated by Keller technique significantly more common are diagnosed subluxation. Postoperatively the method of Mitchell, congruent I metatarsophalangeal joint register with a majority of respondents in this group 85.7%, while the remaining 14.3% registered deviation.Postoperatively the respondents operated by the method of Keller was not possible to use this classification due to performed resection of the proximal half of the proximal phalanx of the thumb.

The changed ratios of the foot can be determined by the help of radiography, and in the later stages secondary arthritic and reactive changes can be also determined (3, 5, 6, 12, 13). The secondary arthritic and reactive changes (osteophytes, subchondral sclerosisand degenerative cysts) in the area of I metatarso-phalangeal joint were not a frequent occurrence in the patients treated by the method of Mitchell, neither pre-operatively nor post-operatively. They were registered in 6 patients pre-operatively and in 7 patients after the intervention. Secondary arthritic and reactive changes in the area of I metatarso-phalangeal joint were diagnosed pre-operatively in 30 (85.7%) patients in the group surgically treated by the method of Keller, and that was the case with 31 patients post-operatively. Tested the difference between respondents in both groups with or without secondary arthritic changes postoperatively showed highly statistically significant ($p < 0.001$), as a result of significantly more often diagnose these changes in the group of subjects treated with the method of Keller. In our study, as well as in the world literature, the operative method by Keller showed as "golden standard" for the patients having arthritic changes.

Numerous surgical procedures for correction of this deformity are described. They can be simple ablations with capsulographies up to complex operations such as arthrodesis, transfer of tendons, resection arthroplasty and different osteotomies of the I metatarsal bone. The operative procedure must protect the integrity of the anatomic structure of the joint (1, 16, 17). Another important deciding factor is the presence or absence of arthrosis in the joint. Especially important as an indication of a surgical procedure is always to have in mind what are the patient's expectations from the operation (3, 17, 18).

CONCLUSION

Radiographic analyses are of special importance in order to make a final decision for the type of operative treatment. Our study, at the same time showed that radiographic analysisis very useful for an excellent evaluation of preoperative, postoperative period and further controls of the patients.

In this study, the operative technique according to Mitchell showed to be an effective procedure for hallux valgus and metatarsus primus varus in young and middle-aged patients. The resectional arthroplasty according to Keller's method is a good procedure for correction of hallux valgus deformity in older patients having arthrotic changes.The results of this research have major implications for the systematic monitoring and planning of activities for adequate surgical treatment of patients with hallux valgusdeformity, but also making its own contribution to contemporary orthopedic practice and science.

Conflict of interest

The authors declare that there are no conflicts of interest.

Sažetak

KOMPARATIVNA ANALIZA RADIOGRAFSKIH REZULTATA NAKON HIRURŠKIH PROCEDURA PO MITCHELL-u i KELLER-u U LEČENJU HALLUX VALGUS DEFORMACIJE

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Uvod: Hallux valgus predstavlja kompleksan progresivan deformitet stopala, sa najviše izraženom lateralnom devijacijom palca. Radiografija zauzima izuzetno važno mesto u donošenju odluke o tipu hirurškog zahvata, koji je najbolji za korekciju ovog deformiteta.

Cilj: Cilj ovog rada bio je da se pokaže značaj radiografskog ispitivanja u operisanih pacijenata sa hallux valgusom, po Mitchell i Keller tehnikama.

Materijal i metode: U studiju je uključeno 70 pacijenata sa hallux valgus deformacijom stopala, koji su

bili podeljeni u dve grupe. Pacijenti su bili podeljeni prema polu, uzrastu, stepenu deformiteta (umereno do ozbiljnog stepena deformiteta) i prema radiološkim nalazima. Prvu grupu (Grupa 1) je činilo 35 pacijenata koji su bili lečeni osteotomijom I metatarzalne kosti, prema Mitchell, dok je drugu grupu (Grupa 2) činilo takođe 35 pacijenata, koji su bili lečeni resekcionom artroplastikom, prema Kelleru. Radiografska ispitivanja (Metoda po Hardy I Clapham, Piggott klasifikacija, prisustvo ili odsustvo sekundarnog artiritisa I reaktivnih promena na zglobu prvog metatarzalnog zgloba) su bili analizirani komparativno tokom evaluacije. Analize radiografskih rezultata su učinjene preoperativno i postoperativno za obe grupe.

Rezultati: Prema polu, bilo je 5 muškaraca i 65 žena. Prosečni uzrast pacijenata u Grupi 1 bio je 42 godine, dok je u Grupi 2 bio 56 godina. Nije bilo statistički značajne razlike ($p < 0,05$) između pacijenata ove dve grupe kada je u pitanju preoperiativna srednja vrednost dimenzija I metatarzofalangealnog ugla i I intermetatarzalnog ugla. Međutim, radiografska analiza istog ugla u obe grupe, godinu dana posle operacije, pokazala je značajnu razliku ($p < 0,001$). Pacijenti operisani po Mitchell zahvatu, po Piggott klasifikaciji, su imali devijaciju prvog metatarzalnog zgloba u 51,43% slučajeva, kao rezultat njihovog hallux valgus deformiteta. Značajno češće se javlja subluksacija na I metatarzofalangealnom zglobu u pacijenata lečenih po Kellerovoj tehnici (77,14%). Radiografska analizana I metatarzofalangealnog zgloba (prisustvo ili odsustvo sekundarnih artitisnih ili reaktivnih promena) u obe grupe, preoperativno (p 0,01) i godinu dana posleo peracije (p 0,001), pokazala je statistički visoku razliku.

Zaključak: Radiografske analize su od značajnog benefita u odlučivanju vrste operacione procedure i za evaluaciju postoperativnih rezultata.

Ključne reči: radiografska analiza, Mitchell, Keller, hallux valgus.

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SANAMED
2016; 11(1): 53–56
ISSN-1452-662X

DOI: 10.5937/sanamed1601053K
UDK: 616.12-008.313
ID: 222046476
Case report

BRUGADA SYNDROME — A CASE REPORT

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Primljen/Received 25. 01. 2016. god. Prihvaćen/Accepted 12. 02. 2016. god.

Abstract: Brugada syndrome is a type of arrhythmia disorder, which is characterised by abnormal electrocardiogram (ECG) findings and an increased risk of sudden cardiac death. The most frequent sign is a persistent ST elevation in the electrocardiographic leads V_1-V_3 with a right bundle branch block (RBBB).We present a case of 12 years old healthy child, without any complains until then. He had 2 episodes of collapse/syncope, which lasted long and spontaneously disappeared. The collapses were provoked by physical activity. On ECG we found sinus rhythm 62 bpm, RBBB (right bundle brunch block) and Brugada signs in V_2 and V_3 channel-ST elevation ≥ 2 mm. The child was sent in electrophysiological centre abroad where the electrophysiological study was performed. They did not found any accessory pathway. The atrioventricular (AV) conduction was normal. Long lasting polymorphic ventricular tachycardia/fibrillation was induced with programed stimulation with 3 extrastimuli in right ventricular outflow tract. Performing one defibrillation the rhythm turned in sinus way. Then they performed ECG with translocation of electrodes $V_{1\text{-}3}$ in 2nd intercostal space and the Brugada I type findings was discovered. After confirming of presence of Brugada type -1 syndrome the implantable cardioverter- defibrillator (ICD) was applied on child heart.

Key words: Brugada syndrome, ventricular fibrillation, sudden cardiac death.

INTRODUCTION

Brugada syndrome is a type of arrhythmia disorder, which is characterised by abnormal electrocardiogram (ECG) findings and an increased risk of sudden cardiac death. It is the major cause of sudden death in adults and most common reason of unexplained death in young men without known underlying cardiac disease (1).

First time was reported in 1989, but in 1992 was for the first time recognized and described as a new clinical entity and named Brugada (by the brothers Paedro and Joseph- Spanish cardiologists). The syndrome is mostly genetic disorder, frequently causes cardiac death due to ventricular fibrillation. A persistent ST elevation (≥ 2 mm) in the electrocardiographic leads V_1-V_3 with a right bundle branch block (RBBB), with or without the terminal S waves in the lateral leads that are associated with a typical RBBB is the most frequent sign of recognitions the Brugada syndrome. This abnormality — called a type 1 Brugada ECG pattern — is detected only by an electrocardiogram (2, 3).

Brugada syndrome is much more common in men. The typical patient with Brugada syndrome is young (under 40 years) male, and otherwise healthy person, with normal general medical and cardiovascular physical examinations. Many people who have Brugada syndrome don't have any symptoms, and so they're unaware of their condition (4).

Brugada-type ECG isn't frequent. It has been identified in the United States in 0.012% and in Canada in 0.07% (5). The prevalence of type 1 ECG in the healthy Asian population is considered to be around 0.15% in adults and 0.005% in children. However, it is considered to be less than 0.02% in the Western population (6, 7).

There are not many reports in the literature data about this syndrome in children.

CASE REPORT

We present a case of 12 years old healthy child, without any complains until then. He had two episodes of collapses/syncope, which lasted long and spontaneously disappeared. The collapses were provoked by physical activity.

Familiar anamnesis was negative; none of the relatives had any medical history of cardiac disease. No data of sudden cardiac death in the family, two generations back.

On physical examination we had a child in very good condition, with normal physical growth and development (weight 42 Kg). Heart rhythm was rhythmical with 60/ beats per minute, normal heart sounds (first and second heart tone), no evidence of murmur, good pulses on 4 extremities, without organ enlargement. The blood pressure was normal 120/70 mm Hg.

The chest X-ray showed normal heart silhouette and normal lung vascularisation.

On ECG we found sinus rhythm 62 bpm, RBBB (right bundle brunch block) and Brugada signs in V_1 and V_2channel- ST segment elevation ≥ 2mm (electrodes positioned in 2^{nd},3^{rd} and 4^{th} intercostal space) (Figure 1).

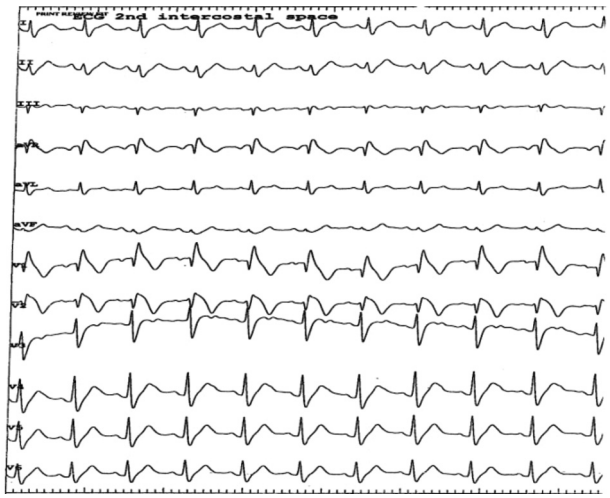

Figure 1. *ECG in a child with Brugada syndrome*

Echocardiogram was normal (normal structure; ejection fraction (EF) = 69% and Fraction shortening (FS) = 39%; normal morphology and function of the AV and semilunar valves, no evidence of septal defects).

Holter 24 hour ECG showed Brugada type findings, but without presence of ventricular tachycardia or fibrillation. On laboratory tests we found normal potassium and calcium levels in the serum, also CK-MB fraction in serum was normal.

The child was sent in electrophysiological centre abroad where the electrophysiological study was performed. They did not found any accessory pathway. The AV conduction was normal. Long lasting polymorphic ventricular tachycardia/fibrillation was induced with programmed stimulation with 3 extras stimuli in right ventricular outflow tract. By performing one defibrillation the rhythm turned in sinus way. Then they performed ECG with translocation of electrodes V_{1-3} in 2^{nd} intercostal space and the Brugada 1. type findings were discovered.

After confirming of presence of Brugada type -1 syndrome the implantable cardioverter- defibrillator was applied on child chest and connected by electrodes on the heart (Figure 2).

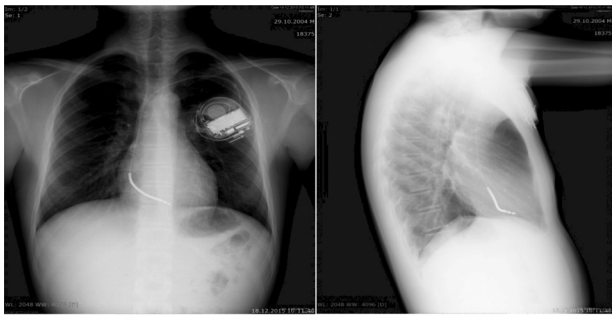

Figure 2. *Xray of the chest – visualisation of intra-cardiac converter/defibrillator*

The child had regularly check-up (according the ESC 2015 guidelines) with ECG, Holter 24 hour ECG and echocardiography 1 month after application of ICD, and every 3 month after that. After three years follow up the child was in very good condition, with normal physical activity, no evidence of infection, three short episodes of tachycardia at home (probable ventricular tachycardia/fibrillation) were stopped with the shocks from the device. On ECG and Holter ECG we did not found ventricular tachycardia/fibrillation. The echocardiography was normal. He is under therapy with Metoprolol retard (Beta blockers therapy).

This is the unique patient-child in our country with confirmed diagnosis of Brugada syndrome, and first and unique child with applied ICD.

DISCUSSION

Three different types of ECG patterns in Brugada syndrome are known. A type 1 ECG pattern is caracterised by pronounced elevation of the J point (arrow), a coved-type ST segment, and an inverted T wave in V1 and V2. A type 2 pattern is with a saddleback ST-segment elevated by >1 mm (usually is seen in healthy subject). A type 3 pattern has either a coved or a saddle back pattern with less than 2 mm J-point elevation and less than 1 mm ST segment elevation (8). Signs and symptoms in patients with Brugada syndrome may include the following:

• Syncope and/or cardiac arrest: Most common clinical manifestations; in many cases, cardiac arrest occurs during sleep at night or rest

• Nightmares or thrashing at night

• Asymptomatic, but routine ECG shows ST-segment elevation in leads V1-V3

• Associated atrial fibrillation (20%)

• Fever: frequently reported to be a trigger or exacerbate clinical manifestations

The lack of a prodrome has been reported to be more common in patients with ventricular fibrillation documented as the cause of syncope in patients with Brugada syndrome (9).

Literature date reports that sudden cardiac death or ventricular fibrillation occurred in 8.2% of patients with Brugada syndrome. A history of syncope, a spontaneously abnormal ECG, and inducibility during programmed electrical stimulation (by one study) significantly increased this risk (10).

All patients with suspected Brugada syndrome need the following: 12- leads standard ECG and electrophysiological study for determination the inducibility of life threatening arrhythmias for risk stratification. In some cases may be performed laboratory test, which may be helpful for the diagnosis such as potassium and calcium levels, CK-MB and troponin levels, and genetic testing for a mutation in SCN5A gene (11).

It is necessary to perform imaging studies - echocardiography and/or magnet resonance imaging primary to excluding other reasons for potential life threatening arrhythmias like arrhythmogenic right ventricular dysplasia, Duchenne muscular dystrophy, acute myocarditis, infarction of the myocardium (12).

Because of genetic origin of the disorder (autosomal dominant inheritance), patient with Brugada syndrome may be genetically tested for a mutation of SCN5A. This mutation affects the cardiac sodium channel subunits or proteins that regulate them. Literature date showed that only in 11-28 % of the population the genetic test of mentioned SCN5A gene is proven (negative genetic test did not exclude the disorder) (13).

Brugada syndrome is 8-10 time more prevalent in men that in women, but there is not difference of carrying mutation in both sex. The penetrance of the mutation is probable higher in man then in women. Brugada syndrome may affect individuals of any age (0-83), but most often the symptoms occur around the age of 40. Brugada syndrome is known as a sudden unexpected nocturnal death syndrome (SUNDS). Also is presented as a sudden infant death syndrome (SIDS), which means death in infant (within first year of life) without any previous cause or disorder (11, 14).

Brugada syndrome treatment depends on the risk of an abnormal heartbeat (arrhythmia). The patients considered at a high risk have:

• A personal history of serious heart rhythm problems

• A personal history of fainting spells

• A personal history of survived sudden cardiac arrest

Treatment may include application of an implantable cardioverter-defibrillator in persons who are at high-risk. The cardioverter defibrillator is a medical device applied on patients' chest and is connected by electrodes located in the heart. It continuously monitors the heart rhythm and if is necessary delivers electrical shocks when abnormal heartbeats (especially ventricular tachycardia or fibrillation) occurs (14).

Beta blockers are effective for patients with unstable ventricular arrhythmias. The role of Qiunidine is reported to have an effect on decreasing of ventricular fibrillation in these patients. Recommendation for treatment of asymptomatic patients is not established yet. Careful observation and performing electrophysiological study in a patient from risk family is recommended in most papers in the literature (13).

CONCLUSION

Brugada syndrome is very rare arrhythmia disorder. The physicians must think of it when repeated syncope and/or nightmare were found in a healthy children and young male persons, and try to find the typical ECG findings. Rapid diagnosis and application of intra-cardiac cardioverter-defibrillator will save the life of the patient.

Conflicts of interest

The authors declare that there are no conflicts of interest.

Abbreviations:

ECG — Electrocardiography

RBBB — right bundle branch block

AV — atrioventricular conduction

EF — ejection fraction

FS — fraction shortening

CK-MB — cardiac enzyme fraction in serum

J point — repolarization phase starts at the junction or j point

ST segment — isoelectric section of the ECG between the end of S wave and beginning of the T wave. It represents the interval between ventricular depolarization and repolarization and it is sign of myocardial ischemia

ICD — intra-cardiac cardioverter defibrillator

SUNDS — sudden unexpected nocturnal death syndrome

SIDS — sudden infant death syndrome

Sažetak

BRUGADA SINDROM — PRIKAZ SLUČAJA

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Brugada sindrom je vrsta aritmije, koja se karakteriše abnormalnim nalazom elektro-kardiograma (EKG) i povećanim rizikom od iznenadne srčane smrti. Najčešći znak na elektrokardiogramu je perzistentna elevacija ST segmenta u V1-V3 odvodima, sa blokom desne grane (RBBB). Mi predstavljamo slučaj dvanaestogodišnjeg zdravog deteta, bez ikakvih komplikacija do tada. Imao je dve epizode kolapsa/sinkope, koje su trajale dugo i spontano iščezle. Kolapsi su bili izazvani fizičkom aktivnošću. Na EKG-u se video sinusni ritam od 62 bpm, RBBB i znaci Brugade u V2 I V3 odvodima, ST elavacija ≥ 2 mm. Dete je poslato u elektrofiziološki centar u inostranstvu gde je izvršeno elektrofiziološko ispitivanje. Nije pronađen nijedan akcesorni put. Atrioventrikularna provodljivost je bila normalna. Dugotrajna polimorfna ventrikularna tahikardija/fibrilacija je indukovana programiranim stimulacijama sa 3 ekstra stimulusa desnog ventrikularnog izlaznog trakta. Jednom defibrilacijom vraćen je sinusni ritam. Nakon toga su izveli EKG sa translokacijom elektroda V1-3 u drugi interkostolarni prostor i pronašli tip 1 Brugada sindroma. Nakon potvrde prisustva Brugada, tipa 1, apliciran je implantabilni kardioverter-defibrilator (ICD) na srcu deteta.

Ključne reči: Brugada sindrom, ventrikularna fibrilacija, iznenadna srčana smrt.

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SANAMED
2016; 11(1): 57–61
ISSN-1452-662X

DOI: 10.5937/sanamed1601057B
UDK: 616.717.4-001.5-06-053.2
ID: 222057228
Case report

VOLKMANN'S CONTRACTURE AS A COMPLICATION OF SUPRACONDYLAR FRACTURE OF HUMERUS IN CHILDREN — CASE REPORT

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Primljen/Received 23. 01. 2016. god. Prihvaćen/Accepted 06. 03. 2016. god.

Abstract: The patient T. K, 7 years old, had sustained a supracondylar fracture of the left elbow after the fall on the left hand with elbow extended. She was admitted in local hospital where the clinical examination and X ray were made and they confirmed the diagnosis of supracondylar fracture of the left elbow (Gartland Type III). She was treated with closed reduction (without anaesthesia) and cast immobilization for four weeks. With poor to no function of the left hand she was send to physical therapy for duration of 10 days, but she did not gain her functions of the left hand, almost all active movements of the left hand were impossible and the muscles of the left underarm were hypotonic. Due to loss of left hand function, EMG was made and the EMG result showed acute lesion of the nerves of left forearm caused by possible nerve compression (n. medianus, n. radialis and n. ulnaris). After four months she was admitted in University Clinic for Orthopaedic Surgery in Skopje were we perform operation of the left elbow, with removing callus formation in which we find entrapped median and ulnar nerves. We also have done osteotomy of the humerus for correction of the angular deformity and fixation with K wire. The patient was put in cast immobilisation after the surgery for four weeks. After the removal of the cast and K wire she was sent to intensive rehabilitation. One year after surgery she regains almost all of hand and elbow functions with satisfying range of motion. She is now able to fulfil every day function without any help or support.

Keywords: supracondylar fracture, ORIF, Volkmann's contracture, Gartland classification.

INTRODUCTION

A supracondylar fracture of the distal humerus is one of the most common fractures in children with up to 60% of paediatric elbow fractures and it is often associated with the development of serious complications (1). It requires appropriate assessment and prompt orthopaedic care in order to prevent serious and long-term complications.

This fracture occurs most frequently in children between 5 and 10 years of age, which is the period of maximum ligamentous laxity (2). The boys have a higher incidence of this fracture than girls with left or no dominant side predomination. The mechanism of injury is a fall from a height with an outstretched arm in 70% of all the fractures. Strong action of the triceps muscle produces proximal displacement of the distal fragment. If patient falls on an outstretched supinated arm, the posteromedial periosteum is disrupted first and the fragment is displaced poster-laterally. If patient falls on pronated arm, the distal fragment is displaced posteromedial (3).

Medial displacement of the distal fragment places the radial nerve at risk (4, 5). Lateral displacement of the distal fragment places the median nerve and brachial artery at risk. Nerve injury occurs in at least 7-15% and significant vascular injury in 2% to 12% of cases. The median nerve with 52% and radial nerve with 32% are most frequently injured in the course of the injury (6). Most of injuries are neuropraxias (a contusion or stretch of the nerve) and spontaneously recover function in 2–3 months (7, 8).

Depending upon the displacement of the distal fragment of bone the supracondylar fractures are classified as an extension type (9), which is most common type (95%) of all supracondylar fractures with distal fragment displaced posteriorly and flexion type (5%) with distal fragment displaced anteriorly, relatively to the proximal segment. The most used classification in

practice is Gartland classification system (10), based upon the degree of displacement of the distal fragment (on the lateral x-ray).The Gartland type I is undisplaced fracture, Gartland type II is angulated fracture with intact posterior cortex and Gartland type III is displaced distal fragment posteriorly, no cortical contact divided into posteromedial or poster-lateral.

The most common clinical features are:

- Pain and inability to use the upper extremity after the fall
- Swelling around the elbow within a few hours
- Point tenderness over medial and lateral columns
- Anterior pucker sign or anterior bruising may be present, which occurs when brachialis has been penetrated by proximal fragment and it is a sign of considerable soft tissue damage.

Diagnostic protocol include: clinical examination, neurologic examination and vascular assessment which is essential and radiological examination. Baumann's angle which is formed by a line perpendicular to the axis of the humerus (11), and a line that goes through the physis of the capitellum must be measured. There is a wide range of normal for this value, and it can vary with rotation of the radiograph, but normal range is in between 64 and 81 degrees. Decreased angle is a sign of varus angulation which it is not obscured by elbow flexion or pronation. It is important to notice that the Baumann angle is not equal to the carrying angle of the elbow and any change in 5 degree will result in 2 degree change of clinical carrying angle.

The general management of the supracondylar fractures include:

- Closed reduction
- Traction method
- Surgery

* CRPP (closed reduction and percutaneous pinning)

* ORIF (open reduction and internal fixation)

Complication following this type of fixation include: immediate complications such as a neurological or vascular complications, early as compartment syndrome and Volkmann's ischemia and late as non- union or mal union (cubitus varus/cubitus valgus) (12), Volkmann's ischemic contracture, myositis ossificans, elbow stiffness, pin track infection.

So understanding the anatomy, radiographic findings, management options, and complications associated with this fracture, allow physicians to limit the morbidity associated with this relatively common paediatric injury.

CASE REPORT

The patient T. K, 7 years old, had sustained a supracondylar fracture of the left elbow after the fall on the left hand with elbow extended. She was submitted in local hospital where the clinical examination and X-ray were made and they confirmed the diagnosis of supracondylar fracture of the left elbow (Gartland Type III) (Figure 1). She was treated with closed reduction (without anaesthesia) and cast immobilization (Figure 2). The 3rd day after immobilization she complained of swelling of the arm and the plaster was remodelled. Plaster was removed after 18 days. With poor to no function of the left hand she was send to physical therapy for duration of 10 days, but she did not gain her functions of the left hand, almost all active movements of the left hand were impossible and the muscles of the left underarm were hypotonic. She also had angular deformity of the left elbow because of mal-union of the fracture. Due to loss of left hand function, EMG was made and the EMG result showed acute lesion of the nerves of left forearm caused by possible nerve compression (n. medianus, n. radialis and n.ulnaris). Extensor muscles of the left forearm were active only with electrical stimulation. In that condition, she was sub-

Figure 1. *X-ray of supracondylar fracture-Gartland type III*

Figure 2. *X-ray after closed reposition and cast immobilisation*

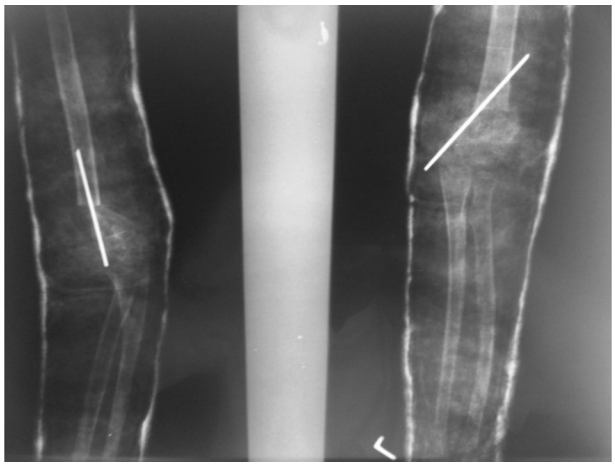

Figure 3. *X ray after ORIF of the supracondylar fracture*

mitted in University clinic for orthopaedic surgery in Skopje, four months after the fracture and previous treatment. Although with clinical presentation of a lot complications, very bad EMG results and statistically poor chances of recovery due to poor result's in clinical examination we perform operation. With anterior approach of cubital fossa, we removed callus formation in which we find entrapped median and ulnar nerves. We make a transposition of the nerves on more suitable position within safety muscle cover. The brachial artery was decompressed. We also have done osteotomy of the humerus for correction of the angular deformity and fixated it with K wire (Figure 3). After the operation a plaster cast was applied for four weeks. After cast removal, she was continued with intense physical therapy and exercise.One year after surgery she regains almost all of hand and elbow functions with satisfying range of motion. EMG result showed complete recovery of the median, radial and ulnar nerve. Range of motion of the elbow was 100 degree flexion, full extension, pronation 70 degree and supination 50 degree. Also function of the hand (pinch and grasp, opposition of the thumb with other fingers) completely recovered. She is now able to fulfil every day function without any help or support.

DISCUSSION AND CONCLUSION

Supracondylar fractures are one of the classical paediatric injuries with very high incidence. They should be treated with high vigilance mostly because they are associated with development of serious complication. For this reason detailed examination and diagnostic protocol should be always followed so exact and proper diagnose can be made. Also the treatment plan must be carefully made according to official recommendations and protocols so we can avoid development of iatrogenic complication and bad outcomes.

According to the X-rays our patient T. K., 7 years old girl, had Gartland type III fracture.

The AAOS recommendations about various type of fracture include: nonsurgical immobilization of the injured limb for patients with acute Gartland Type I or non-displaced paediatric supracondylar fractures of the humerus or posterior fat pad sign and closed reduction with pin fixation for patients with displaced Gartland Type II and III, and displaced flexion paediatric supracondylar fractures of the humerus.

After clinical assessment and diagnosis, the elbow should be splinted in a position of comfort (approximately 20°–30° of flexion) to provisionally stabilize the limb. Splinting in full elbow extension is contraindicated because it stretches the neurovascular bundle over the fracture site in displaced or unstable fractures. The application of a comfortable, well padded, and appropriately applied splint is a critical part of the initial management of these injuries, regardless of their definitive treatment.

Historically, a majority of these fractures were treated with closed reduction and long arm casting with the elbow in a position of greater than 100° of flexion. This flexed posture helped maintain the fracture reduction, but lead to problems with vascular complication and subsequent Volkmann's contracture. An injury of the brachial artery as the cause of the ischemia is leading to the flexion contracture of the hand at the wrist, resulting in a claw-like deformity of the hand and fingers. The most affected are flexor group of muscles of the forearm, especially m. flexor digitorum profundus and m. flexor pollicis longus which becomes fibrotic and short. After a closed reduction, percutaneous pinning maintains fracture reduction without the need for immobilizing the elbow in significant flexion and thus prevents obstructing the circulation of brachial artery (13).

Supracondylar fractures of the distal humerus that creates significant displacement, classified as Gartland Type III are particularly prone to neurovascular compromise so determining the integrity of the neurovascular structures should be a vital component of the physical exam. Vascular examination for presence of the radial and ulnar pulses must be performed at the wrist with palpation. If no pulse is present, then other signs of perfusion must be checked, as the colour of the hand, the warmth, and good capillary refill.

The radial, median, and ulnar nerves should each be tested for both motor and sensory function. Discrete sensory areas of the radial nerve should be checked -dorsal first web space, for medial nerve -palmar index finger, for ulnar nerve -palmar little finger.

Finger, wrist, and thumb extension problems usually correlate with radial nerve injury, index, distal interphalangeal flexion and thumb interphalangeal flexion with anterior interosseus nerve and thenar strength

with median nerve injury. Also, passive finger extension and flexion should be tested and the findings should be accurately recorded. Entire limb should be evaluated for associated forearm fractures. Fractures with displacement treated by closed reduction and casting have a higher incidence of residual deformity that those managed with operative reduction and pinning (14). So after a careful clinical evaluation that finds no neurovascular injury, an operative fracture may be splinted and managed safely in a delayed fashion (within 24 h) while awaiting operative fracture reduction. An open reduction and internal fixation is indicated in cases where the fracture is irreducible by closed methods or if the brachial artery has been compromised and requires exploration. Also ORIF is indicated in open fractures. The should be performed emergently (< 8 hours) or urgently (< 24 h hours), or after swelling has decreased, but not later than 5 days after injury because the possibility of myositis ossificans apparently increases after that time (15, 16). Preoperative arterial insufficiency may be improved by operative reduction and pinning, in that a kinked brachial artery, draped over the distal end of the proximal fragment, may become patent after manipulative reduction of the fracture. Open supracondylar fractures warrant a surgical debridement of the fracture followed by stabilization.

While postoperative protocols vary from surgeon to surgeon, a typical regiment calls for a long arm, ulnar gutter-type splint or a split long arm cast to control elbow motion and forearm rotation for 4 weeks, followed by pin removal and early range of motion or continued splinting for additional 1–2 weeks. If a stable closed reduction and pinning of the fracture is achieved by an experienced paediatric orthopaedic surgeon, follow-up may safely be delayed until the day of pin removal. However, if there is any uncertainty about fracture reduction or stability after pinning, the first follow-up visit should be within 7 days of surgery (17, 18). This early follow-up for unstable fractures allows for a repeat closed manipulation and pinning if there has been a loss of reduction.

The children with these fractures can have easy recovery and good prognosis only if we provide them with proper treatment and rehabilitation protocol, so they can quickly return to their normal activities.

Conflict of interest

The authors declare are no conflict of interest.

Abbreviations

EMG — Electromyography
CRPP — closed reduction and percutaneous pinning
ORIF — open reduction and internal fixation
AAOS — American Association of Orthopaedic Surgeon

Sažetak

VOLKMANOVA KONTRAKTURA KAO KOMPLIKACIJA SUPRAKONDILARNE FRAKTURE KOD DECE — PRIKAZ SLUČAJA

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Pacijentkinja T. K, stara sedam godina, zadobila je suprakondilarnu frakturu levog lakta posle pada na levu ruku, sa laktom u ekstenziji. Primljena je u lokalnu bolnicu gde su urađeni klinički pregled i radiografija leve ruke, i potvrđena je suprakondilarna fraktura levog lakta (Gartland Type III). Izvedena je zatvorena repozicija (bez anestezije) i imobilizacija gipsom u toku četiri nedelje. Posle toga, pacijentkinja je, gotovo bez ikakve funkcije leve šake, upućena na fizikalnu terapiju u trajanju od 10 dana, ali nije vraćena funkcija leve šake. Gotovo svi aktivni pokreti leve šake su bili nemogući i mišići leve podlaktice su bili hipotonični. Zbog gubitka funkcije leve ruke urađen je EMG koji je pokazao akutnu leziju nerava leve podlaktice nastalu najverovatnije zbog kompresije nerava (n. medianus, n. ulnaris i n. radialis). Posle četiri meseca pacijentkinja je upućena na Univerzitetsku Kliniku za Ortopedsku hirurgiju u Skoplju gde je izvedena operacija levog lakta sa uklanjanjem kalusa u kojem su nađeni uklješteni n. medianus i n. ulnaris. Izvedena je i osteotomija humerusa radi korekcije angularnog deformiteta i fiksacija K žicom. Ruka je nakon hirurškog tretmana imobilisana gipsom tokom četiri nedelje. Nakon sklanjanja gipsa i K žice, pacijentkinja je upućena na intenzivnu fizikalnu rehabilitaciju. Nakon godinu dana povratila je gotovo u potpunosti funkciju lakta i leve ruke sa zadovoljavajućim opsegom pokreta. Danas je u mogućnosti da obavlja svakodnevne aktivnosti bez ikakve pomoći.

Ključne reči: suprakondilarna fraktura, ORIF, Volkmanova kontraktura, Gartlandova klasifikacija.

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Naslovna strana. Naslovna strana sadrži naslov rada, kratak naslov rada (do 50 slovnih mesta), puna prezimena i imena svih autora, naziv i mesto institucije u kojoj je rad izvršen, zahvalnost za pomoć u izvršenju rada (ako je ima), objašnjenje skraćenica koje su korišćene u tekstu (ako ih je bilo) i u donjem desnom uglu ime i adresu autora sa kojim će se obavljati korespondencija.

Naslov rada treba da bude sažet, ali informativan.

Ako je potrebno, može se dodati i podnaslov.

Kratak naslov treba da sadrži najbitnije informacije iz punog naslova rada, ali ne sme biti duži od 50 slovnih mesta.

Ako je bilo materijalne ili neke druge pomoći u izradi rada, onda se može sažeto izreći zahvalnost osobama ili institucijama koje su tu pomoć pružile.

Treba otkucati listu svih skraćenica upotrebljenih u tekstu. Lista mora biti uređena po abecednom redu pri čemu svaku skraćenicu sledi objašnjenje. Uopšte, skraćenice treba izbegavati, ako nisu neophodne.

U donjem desnom uglu naslovne strane treba otkucati ime i prezime, telefonski broj, broj faksa i tačnu adresu autora sa kojim ce se obavljati korespodencija.

Stranica sa sažetkom. Sažetak mora imati do 350 reči. Treba koncizno da iskaže cilj, rezultate i zaključak rada koji je opisan u rukopisu. Sažetak ne može sadržati skraćenice, fusnote i reference.

Ključne reči. Ispod sažetka treba navesti 3 do 8 ključnih reči koje su potrebne za indeksiranje rada. U izboru ključnih reči koristiti Medical Subject Headings — MeSH.

Stranica sa sažetkom na engleskom jeziku. Treba da sadrži pun naslov rada na engleskom jeziku, kratak naslov rada na engleskom jeziku, naziv institucije gde je rad urađen na engleskom jeziku, tekst sažetka na engleskom jeziku i ključne reči na engleskom jeziku.

Struktura rada. Svi podnaslovi se pišu velikim slovima i boldovano.

Originalni rad treba da ima sledeće podnaslove: uvod, cilj rada, metod rada, rezultati, diskusija, zaključak, literatura.

Prikaz bolesnika čine: uvod, prikaz bolesnika, diskusija, literatura.

Pregled iz literature čine: uvod, odgovarajući podnaslovi, zaključak, literatura.

Bolesnici i metode/materijal i metode. Treba opisati izbor bolesnika ili eksperimentalnih životinja, uključujući kontrolu. Imena bolesnika i brojeve istorija ne treba koristiti.

Metode rada treba opisati sa dovoljno detalja kako bi drugi istraživači mogli proceniti i ponoviti rad.

Kada se piše o eksperimentima na ljudima, treba priložiti pismenu izjavu u kojoj se tvrdi da su eksperimenti obavljeni u skladu sa moralnim standardima Komiteta za eksperimente na ljudima institucije u kojoj su autori radili, kao i prema uslovima Helsinške deklaracije. Rizične procedure ili hemikalije koje su upotrebljene se moraju opisati do detalja, uključujući sve mere predostrožnosti. Takođe, ako je rađeno na životinjama, treba priložiti izjavu da se sa njima postupalo u skladu sa prihvaćenim standardima.

Treba navesti statističke metode koje su korišćene u obradi rezultata.

Rezultati. Rezultati treba da budu jasni i sažeti, sa minimalnim brojem tabela i slika neophodnih za dobru prezentaciju.

Diskusija. Ne treba činiti obiman pregled literature. Treba diskutovati glavne rezultate u vezi sa rezultatima objavljenim u drugim radovima. Pokušati da se objasne razlike između dobijenih rezultata i rezultata drugih autora. Hipoteze i spekulativne zaključke treba jasno izdvojiti. Diskusija ne treba da bude ponovo iznošenje zaključaka.

Literatura. Reference numerisati rednim arapskim brojevima prema redosledu navođenja u tekstu. Broj referenci ne bi trebalo da bude veći od 30, osim u pregledu literature, u kojem je dozvoljeno da ih bude do 50.

Izbegavati korišćenje apstrakta kao reference, a apstrakte starije od dve godine ne citirati.

Reference se citiraju prema tzv. Vankuverskim pravilima, koja su zasnovana na formatima koja koriste *National Library of Medicine* i *Index Medicus*.

Primeri:

1. **Članak:** (svi autori se navode ako ih je šest i manje, ako ih je više navode se samo prva tri i dodaje se *"et al."*)

Spates ST, Mellette JR, Fitzpatrick J. Metastatic basal cell carcinoma. J Dermatol Surg 2003; 29: 650–652.

2. **Knjiga:**

Sherlock S. Disease of the liver and biliary system. 8th ed. Oxford: Blackwell Sc Publ, 1989.

3. **Poglavlje ili članak u knjizi:**

Latković Z. Tumori očnih kapaka. U: Litričin O i sar. Tumori oka. 1. izd. Beograd: Zavod za udžbenike i nastavna sredstva, 1998: 18–23.

Tabele. Tabele se označavaju arapskim brojevima po redosledu navođenja u tekstu, sa nazivom tabele iznad. Svaku tabelu odštampati na posebnom listu papira i dostaviti po jedan primerak uz svaku kopiju rada.

Slike. Sve ilustracije (fotografije, grafici, crteži) se smatraju slikama i označavaju se arapskim brojevima u tekstu i na legendama, prema redosledu pojavljivanja. Treba koristiti minimalni broj slika koje su zaista neophodne za razumevanje rada. Slike nemaju nazive. Slova, brojevi i simboli moraju biti jasni, proporcionalni, i dovoljno veliki da se mogu reprodukovati. Pri izboru veličine grafika treba voditi računa da prilikom njihovog smanjivanja na širinu jednog stupca teksta neće doći do gubitka čitljivosti. Legende za slike se moraju dati na posebnim listovima, nikako na samoj slici.

Ako je uveličanje značajno (fotomikrografije) ono treba da bude naznačeno kalibracionom linijom na samoj slici. Dužina kalibracione linije se unosi u legendu slike.

Treba poslati dva kompleta slika, u dva odvojena koverta, zaštićene tvrdim kartonom. Na pozadini slika treba napisati običnom olovkom prezime prvog autora, broj slike i strelicu koja pokazuje vrh slike.

Uz fotografije na kojima se bolesnici mogu prepoznati treba poslati pismenu saglasnost bolesnika da se one objave.

Za slike koje su ranije već objavljivane treba navesti tačan izvor, treba se zahvaliti autoru, i treba prilo-

žiti pismeni pristanak nosioca izdavačkog prava da se slike ponovo objave.

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Propratno pismo. Uz rukopis obavezno priložiti pismo koje su potpisali svi autori, a koje treba da sadrži: izjavu da rad prethodno nije publikovan i da nije istovremeno podnet za objavljivanje u nekom drugom časopisu, te izjavu da su rukopis pročitali i odobrili svi autori koji ispunjavaju merila autorstva. Takođe je potrebno dostaviti kopije svih dozvola za: reprodukovanje prethodno objavljenog materijala, upotrebu ilustracija i objavljivanje informacija o poznatim ljudima ili imenovanje ljudi koji su doprineli izradi rada.

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The manuscript should be submitted in triplicate, typed on one side of A4 white paper. Text of the paper should be typed in a word processing program *Word*, written in Latin, double-spaced, only in *Times New Roman* font size 12 points. All margins should be set at 25 mm, and the text should be typed with the left alignment and paragraph indentations of 10 mm, without dividing the words.

The manuscript should be arranged as following: title page, abstract, key words, introduction, patients and methods/material and methods, results, discussion, conclusion, references, tables, figure legends and figures.

Each manuscript component (title page, etc.) begins on a separate page. All pages are numbered consecutively beginning with the title page. The first author's last name is typed at the top right corner of each page.

References in the text are designated with Arabic numerals in parentheses, and the order in which they appear in the text.

Manuscript volume. The complete manuscript, which includes title page, short abstract, text of the article, literature, all figures and permisions for them and legends (tables, images, graphs, diagrams, drawings), title page and abstract in English, can have the length up to 5000 words for original paper, report, paper on the history of medicine and literature overview, while for patient presentation, practice paper, educative article it can be up to 3000 words, and other papers can be up to 1500 words.

The word count check in a document can be done in *Word* processor program in submenu *Tools Word Count* or *File Properties Statistics*.

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Title page. The title page contains the title, short title, full names of all the authors, names and full location of the department and institution where work was performed, acknowledgments, abbreviations used, and name of the corresponding author. The title of the article is concise but informative, and it includes animal species if appropriate. A subtitle can be added if necessary.

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Original work should have the following headings: introduction, aim, methods, results, discussion, conclusion, references.

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Review of the literature include: an introduction, subheadings, conclusion, references.

Patients and methods/Material and methods. The selection of patients or experimental animals, including controls is described. Patients' names and hospital numbers are not used.

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Statistical methods used, are outlined.

Results. Results are clear and concise, and include a minimum number of tables and figures necessary for proper presentation.

Discussion. An exhaustive review of literature is not necessary. The major findings should be discussed in relation to other published works. Attempts should be made to explain differences between results of the present study and those of the others. The hypothesis and speculative statements should be clearly identified. The discussion section should not be a restatement of results, and new results should not be introduced in the discussion.

References. References are identified in the text by Arabic numerals in parentheses. They are numbered consecutively in the order in which they appear in the text. Number of references should not exceed 30, except in the literature review, which is allowed to be to 50.

Avoid using abstracts as references and abstract older than two years are not cited.

References are cited by the so-called Vancouver rules, which are based on formats that use the National Library of Medicine and Index Medicus. The following are examples:

1. **Article:** (all authors are listed if there are six or fewer, otherwise only the first three are listed followed by *"et al."*)

Spates ST, Mellette JR, Fitzpatrick J. Metastatic basal cell carcinoma. J Dermatol Surg 2003; 29: 650–652.

2. **Book:**

Sherlock S. Disease of the liver and biliary system. 8th ed. Oxford: Blackwell Sc Publ, 1989.

3. **Chapter or article in a book:**

Trier JJ. Celiac sprue. In: Sleisenger MH, Fordtran J5, eds. Gastro-intestinal disease. 4 th ed. Philadelphia: WB Saunders Co, 1989: 1134–52.

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Народна библиотека Србије, Београд

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SANAMED / glavni i odgovorni urednik Avdo Ćeranić. — God. 1, br. 1 (2006)– . — Novi Pazar : Udruženje lekara Sanamed, 2006– (Novi Pazar : ProGraphico). — 30 cm

Tri puta godišnje. — Drugo izdanje na drugom medijumu: Sanamed (Online) = ISSN 2217-8171

ISSN 1452-662X = Sanamed

COBISS.SR-ID 135154444

ISSN 1452-662X