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FIFTY YEARS OF THE DEPARTMENT OF OTORHINOLARYNGOLOGY OF THE FACULTY OF MEDICINE, UNIVERSITY OF NOVI SAD

50 GODINA ORL KATEDRE MEDICINSKOG FAKULTETA UNIVERZITETA U NOVOM SADU

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SADRŽAJ

University of Novi Sad, Faculty of Medicine
Clinical Center of Vojvodina, Novi Sad, Serbia
Department of Ear, Nose and Throat Diseases

UDK 378.6:616.2(497.113 Novi Sad)(091)

HISTORY OF THE DEPARTMENT OF OTORHINOLARYNGOLOGY OF THE FACULTY OF MEDICINE IN NOVI SAD

ISTORIJAT KATEDRE ZA OTORINOLARINGOLOGIJU MEDICINSKOG FAKULTETA U NOVOM SADU

Zoran KOMAZEC

The Department of Otorhinolaryngology of the Faculty of Medicine, Novi Sad was founded in 1964 and since then the Department has provided graduate studies to the students of medicine. Since the establishment of the Department of Dentistry affiliated to the Faculty of Medicine, Novi Sad in 1976, professors and associate professors from the Department of Otorhinolaryngology have been giving lectures to the students of dentistry as well. Lectures in medicine and dentistry have been organized in English as well since the academic year 1997-98.

Theoretical instructions provide students with up-to-date knowledge of anatomy, physiology, ear, nose and throat diseases as well as contemporary approaches to the treatment of these diseases. Special emphasis has been placed on practical exercises and the Department has never stopped to insist on them.

Work in small groups provides training which enables each student to perform appropriate otorhinolaryngological examination and to conduct interventions in general practice. The establishment of a study program Special Rehabilitation brought a significant change and the increase in number of classes. As a part of this study program on Modules Multiple Disability and Inclusive Education, teachers and associates have been teaching subjects such as medical basics of surdology and medical basics of voice and speech disorders since 2010. With new accreditation granted to the Faculty of Medicine in 2014, there are new subjects to be taught by the Department members in addition to the existing ones. Special rehabilitation study program (speech pathology module) will include audiology, surdology with medical basics, clinical surdology, phoniatrics and vocal therapy and rehabilitation. Study program "Academic Studies of Health Care" introduces medical care in otorhinolaryngology as a compulsory subject, while vocational studies of health care will offer otorhinolaryngology and care of ear, nose and throat patients as elective subjects. In order to provide such a wide range of subjects for undergraduate programs, a significant commitment of lecturers from the Department of Otorhinolaryngology is required.

All members of the Department are greatly encouraged and inspired by the fact that the Department of Otorhinolaryngology has been marked as the best in the Faculty of Medicine according to medical students' opinion for the last three years. All members of the Department have so far been rewarded by the student parliament as the best teachers and assistants, thus obliging us to improve our further work.

Members of the Department have participated in writing textbooks, practicums and monographs. The current textbook "Otorhynolaryngology - Head and Neck Surgery" is the best-selling textbook at the Faculty of Medicine in Novi Sad.

Since its establishment, the Department has provided education and training of future specialists of otorhynolaryngology as well as subspecialists of audiology and phoniatrics in addition to undergraduate education. So far, about 100 doctors from Serbia, Montenegro, and the Republic of Srpska have taken their specialist and subspecialist examination at this Department. Residents in emergency medicine, neurology, psychiatry, ophthalmology, pediatrics, general medicine, oral and maxillofacial surgery do a part of their residency at the Department of Otorhinolaryngology within their specialization. Having organized and participated in about 30 courses and symposia within the program of continuing medical education, the faculty of the Department have contributed to the acquisition of contemporary knowledge and practical skills of general practitioners and specialists of various specialties.

Scientific work at the Department is implemented through scientific research within national and international projects and most of the members have so far participated in those. Members of the Department have been mentors or evaluation panel members in a number of undergraduate, master and doctoral theses defended at the Faculty of Medicine in Novi Sad, Belgrade, Podgorica and Foča, Faculty of Special Education and Rehabilitation in Belgrade, Academy of Arts in Novi Sad, Faculty of Technical Sciences in Novi Sad and Faculty of Sciences in Novi Sad.

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Heads of the Department

Professor Dr Đorđe Fišer

The very first appointed Head of the Department was Professor Dr Đorđe Fišer, who was the only lecturer for several years and who laid the foundations of otorhinolaryngology at the Faculty of Medicine, Novi Sad. In 1972, Dr Fišer wrote a habilitation thesis "Implementation of olfactometry and its clinical significance," after which he was elected to the position of professor. Besides participation in undergraduate education for students of medicine and dentistry, during his engagement at the Department Prof Dr Đorđe Fišer made a significant contribution to the professional development of doctors-specialists in otorhinolaryngology. A great number of otolaryngologists of Vojvodina trained under his supervision. Prof Dr Fišer was a member of the commission for the examination of otorhinolaryngology at the Faculty of Medicine in Novi Sad and Belgrade. Dr Fišer was head of the Department until his retirement in 1986.

Professor Dr Radivoj Topolac

Professor Dr Radivoj Topolac was Professor Fišer's associate since the establishment of the Faculty. He was appointed assistant lecturer in the subject of otorhinolaryngology right after the establishment of the Faculty of Medicine in Novi Sad in 1961. He started with practical training three years later. Dr Radivoj Topolac, a contemporary of modern microsurgery of ear - tympanoplasty, introduced this surgical method in the routine work at the Department of Ear, Nose and Throat Disease. His engagement in ear microsurgery resulted in his doctoral dissertation "Using alo, auto and homoplastic material in tympanoplasty" which he defended in 1972, and afterwards he was appointed assistant professor and then professor. Prof Radivoj Topolac took the helm of the Department in 1986 as a very experienced teacher and remained in that position until 1990. Even after his retirement, Prof Topolac remained close with the Department as a member of the commission on professor elections and a reviewer of the first textbook of this Department "Otolaryngology - Head and Neck Surgery." As a member of the Medical Academy of Serbian Doctors' Society Prof. Topolac organized seminars as a part of continuing medical education.

Professor Dr Dušan Milošević

Having passed the Board Examination in 1970, Dr Dušan Milošević got the position in practical training at the Department of Otorhinolaryngology, first as an assistant lecturer and later as an assistant professor. He defended his pioneering doctoral dissertation entitled "Clinical vestibulometry in the diagnosis of head injuries" in 1979 and with it laid the foundation of vestibulology not only in the area of Novi Sad but former Yugoslavia as well. After his doctoral dissertation, Dr Milošević was elected to teaching positions. As Vice Dean of the Medical Faculty in Novi Sad, in the period from 1980 to 1988, Prof Dušan Milošević gave his significant contribution to modernization and development of the teaching process at the Faculty of Medicine in Novi Sad. He was appointed head of the Department of Otorhinolaryngology, Faculty of Medicine in Novi Sad in 1990 and remained at that post until his retirement in 2001. He was also appointed head of the Department at the Faculty in Banja Luka in 1994. At that time Prof Milošević was a mentor for four doctoral dissertations and twelve master theses which made a huge contribution to the academic development of the Department of Otorhinolaryngology and Department of Ear, Nose and Throat Diseases in Novi Sad and Banja Luka. Professor Dušan Milošević was a longtime president of the committee for specialist examination in otolaryngology at the Faculty of Medicine in Novi Sad and a member of numerous committees for post elections and defending of theses.

Professor Dr Rajko Jović

After Prof Milosevic's retirement in 2001, a new head of the Department was Prof Dr Rajko Jović, who nad been elected assistant lecturer in 1989. His doctoral dissertation "The impact of resection of laryngopharyngeal structures in laryngeal malignancy on swallowing act" was the result of his work on ear, nose and throat oncology and the results of dissertation greatly improved the quality of life of laryngectomized patients. After his doctoral dissertation, Dr Jović was elected to teaching positions. During his tenure, Prof Rajko Jović was intensively involved in improving education for physicians specializing in otolaryngology and establishing connections with many European departments of ear, nose and throat diseases. Prof Jovic also held lectures at the Faculty of Medicine in Banja Luka and Podgorica. Prof Jović is the author of several textbooks, including the first book of the Department of Otorhinolaryngology, Faculty of Medicine in Novi Sad "Otolaryngology - Head and Neck Surgery", which he wrote with associates Prof Dr Ljiljana Vlaški, Prof Dr Dragan Dankuc and Prof Dr Zoran Komazec. He organized courses in laryngomicroscopic surgery, head and neck surgery as well as a course in ultrasound diagnostics of the neck. He is a collaborator in three scientific research projects and author of several papers published in internationally acknowledged journals. Prof Dr Rajko Jović is the current president of the board of examiners for a specialist examination in otorhinolaryngology and in phoniatrics. He is a member of the Medical Academy of Serbian Medical Society.

Professor Dr Zoran Komazec

Prof Zoran Komazec, who was appointed assistant lecturer in 1997, has been the head of the Department since 2009. His engagement in the physiol-

ogy and pathology of the inner ear was shown in his doctoral dissertation "Analysis of functional characteristics of medial olivocochlear system." Within his teaching posts, Prof Zoran Komazec has taught at the Faculty of Medicine and Faculty of Technical Sciences in Novi Sad and the Faculty of Special Education and Rehabilitation, University of Belgrade. As a mentor or a member of the commission Prof Zoran Komazec was engaged at the Faculty of Medicine, Nis and Faculty of Medicine, Foca - University of East Sarajevo. Prof Komazec endeavors to modernize education for students of medicine, dentistry and special rehabilitation and education. Prof Zoran Komazec organized several courses in the field of audiology, vestibulology and general otolaryngology. He is an associate in three scientific research projects and a mentor of numerous graduate and master theses as well as a doctoral dissertation. He is a member of the commission for the specialist examination in otolaryngology and the president of the commission for specialization examination in audiology.

Professors and Associates since the Establishment of the Department

Professor Dr Živko Majdevac

Upon his arrival at the Department of Ear, Nose and Throat Diseases in Novi Sad, Dr Živko Majdevac founded Phoniatrics Ward and made a significant contribution to the development of the Serbian phoniatrics. His work on voice and speech resulted in his doctoral dissertation "The human voice influenced by vocational burden on speech", which he defended in 1976 and afterwards, he was elected to teaching positions. Prof Živko Majdevac was the author of the original division of dysphonia and a very conscientious and meticulous educator of students of medicine and dentistry and physicians specialists. He was a member of the Department in 1993, when he retired.

Professor Dr Jelena Udovički

Right after passing her specialist exam in 1967, Prof Jelena Udovički began working with students. She defended her doctoral dissertation "Immunological changes in nasal secretions and serum of patients with nasal polyposis" at the University of Belgrade and was elected to the first teaching position in 1982. Professor Jelena Udovički was a responsible and devoted teacher of the Department and she conscientiously held student exercises until her retirement in 1994. During her work at the Department, Prof Jelena Udovički published dozens of papers and books primarily in the field of allergology and rhinopharyngology.

Assistant Professor Dr Slavka Radić

Assist Prof Dr Slavka Radic started working at the Department as a research assistant in 1977 when she also began with student practice. She was elected to the position of assistant professor after defending her doctoral thesis "Evaluation of olfactory and respiratory functions of the nose after rhinoplasty" in 1988. Assist Prof Radic was a member of the Department until she moved to private practice in 1994.

Assistant Dr Dragana Levi

After being elected assistant lecturer in 1987, Dr Dragana Levi began her work at the Department of Otorhinolaryngology. Among other things, Dr Dragana Levi worked on the development of modern audiological methods. She defended her master thesis "Evaluation of auditory and vestibular function in relation to the duration of diabetes" in 1988.

Professor Dr Ljiljana Vlaški

After being elected assistant in 1995, Dr Ljiljana Vlaški began working at the Department of Otorhinolaryngology; however, she actively participated in practical training of students of medicine and dentistry even before the election. After her doctoral thesis "Clinical evaluation of the morphofunctional status of middle ear in surgically treated children with chronic noncholesteatomatous inflammatory processes" in 2001, she was elected to teaching positions. Prof Dr Ljiljana Vlaški has participated in two scientific research projects and has written several papers in the field of pediatric otolaryngology and otology. She has been a mentor of graduate and master theses and a doctoral dissertation. She is a member of the committee for specialist examination in otorhinolaryngology and subspecialist exam in audiology.

Professor Dr Gordana Mumović

Dr Gordana Mumović has been engaged at the Department of Otorhinolaryngology since 1995. She was elected assistant professor after defending her doctoral dissertation "Therapy of the dysphonia after partial laryngectomy using larynx compression" in 2008. As a part of continual medical education, Prof Dr Gordana Mumović has held five courses in the field of diagnostic and therapeutic methods of voice and speech pathology. She has established cooperation with the Academy of Art, University of Novi Sad, where she was a mentor of a doctoral dissertation. She is a member of the commission for the specialist examination in otolaryngology and sub-specialization in phoniatrics.

Professor Dr Dragan Dankuc

After being elected assistant in 1997, Dr Dragan Dankuc began working at the Department of Otorhinolaryngology. He defended his doctoral thesis "The significance of tympanoplasty mobile bridge in surgical treatment of chronic middle ear diseases" in 2001 after which he was elected to teaching positions. So far, Prof Dragan Dankuc has held seven courses of continuing medical education dedicated to the dissection of the temporal bone and five courses devoted to microsurgery of ear. In addition,

he was the organizer of the Summer School of Otology. He is head of the Department of Ear, Nose and Throat Diseases of the Clinical Center of Vojvodina and a member of the Medical Academy of Serbian Medical Society. He is a member of the committee for specialist examination in otolaryngology at the Faculty of Medicine in Novi Sad.

Professor Dr Slobodan Savović

Dr Slobodan Savović has been employed at the Department since 1997. After defending his doctoral thesis "Influence of septoplastics on the course of chronic rhinosinusitis" in 2008, he was elected to teaching positions. As a part of continual medical education, he organized two courses devoted to diseases of the nose and paranasal sinuses. He was a member of the commission for position election of the Faculty of Medicine of Military Medical Academy (VMA), University of Defence in Belgrade. He participated in a scientific research project and mentored undergraduate papers and master theses, as well as a doctoral dissertation. He is a member of the commission for the specialist examination in otolaryngology.

Professor Dr Slobodan Mitrović

Dr Slobodan Mitrovic was appointed assistant of the Department of Otorhinolaryngology in 1999. He defended his first doctoral dissertation entitled "Estimation of the opera singers` voice`s character with the morphoanthropometric parameters` analysis" in 2007, after which he was elected to teaching positions and has established close collaboration with the Faculty of Techincal Sciences in Novi Sad, where he implemented a scientific research project. As a part of continual medical education, he organized two symposia and a very successful course devoted to hereditary angioedema, larygopharyngeal reflux and cough. He is the author of the first textbook for the course "Introduction to Clinical Practice I". He is a member of the commission for the specialist examination in otolaryngology and sub specialization in phoniatrics.

Assistant Professor Dr Vladimir Kljajić

Dr Vladimir Kljajić was appointed assistant lecturer in 1997. After defending his doctoral dissertation "The link of respiratory function and anthropometric characteristics of the nose and the face before and after rhinoseptoplasty" in 2011, he was appointed assistant professor. He has been a mentor of defended graduate thesis. He is the author of several papers in the field of laryngology and rhinology as well as of three chapters in books published by Springer.

Assistant Professor Dr Slobodanka Lemajić Komazec

Dr Slobodanka Lemajić Komazec was elected assistant lecturer in 1997. She defended her doctoral thesis entitled "Evaluation of the auditory and vestibular system in patients with multiple sclerosis" in 2012, after which she was appointed assistant professor. She has participated in a scientific research project of the Ministry of Science, Republic of Serbia as well as in the courses and symposia in the field of audiology and vestibulology. She has been a mentor of defended graduate thesis. She is a member of the commission for subspecialist examination in audiology.

Assistant Professor Dr Maja Buljčik Čupić

Dr Maja Buljčik Čupić was elected assistant lecturer in 2003 and after defending her doctoral dissertation on "Determination of the effects of different therapeutic approaches in the treatment of sinonasal polyposis" she was elected assistant professor in 2012. In addition to her engagement at the Department of Otorhinolaryngology, Assist Professor Dr Maja Buljčik Čupić gives theoretical and practical lectures at the Department of Clinical Immunology. She is a member of the commission for subspecialist examination in allergology.

Assistant Professor Dr Ljiljana Jovančević

Dr Ljiljana Jovančević was elected assistant at the Department of Otorhinolaryngology in 2004. She defended her doctoral thesis "Nasal nitric oxide concentration in diagnostics of inflammatory disorders of the nose and paranasal sinuses" in 2013 after which she was elected to the position of assistant professor. She has given numerous lectures and workshops in the field of rhinology at national and international conferences.

Assistant Professor Dr Danijela Dragičević

Dr Danijela Dragičević was elected associate teacher in 2007. Having defended her dissertation "Speech rehabilitation of totally laryngectomized patients with voice prosthesis insertion" in 2013, she was elected to the position of assistant professor. She has participated in national and international conferences on topics of laryngology and oncology.

Visiting Professors

Professor Dr Irena Hočevar Boltežar

Dr Irena Hočevar Boltežar has been working at the Department of Otorhinolaryngology and Head and Neck Surgery of the University Clinical Centre in Ljubljana since 1987. In 1998, she defended her doctoral thesis entitled "Voice quality after irradiation for early glottic cancer". Since 1992, she has been engaged at the Department of Otorhinolaryngology of Medical Faculty of Ljubljana and the Faculty of Education of Lubljana. She is the President of the Association of Otolaryngologists of Slovenia and the author of numerous works in otorhinolaryngology and phoniatrics. Prof Dr Irena Hočevar Boltežar is a visiting professor at the Department of Otorhinolaryngology, Faculty of Medicine in Novi Sad, she teaches students of medicine and dentistry and actively participates in the implementation of courses and seminars in the field of phoniatrics.

Professor Dr Mihael Podvinec

After habilitation in 1983, Dr Podvinec was appointed assistant professor. He has been a professor at the University of Medicine in Basel since 1995. He was a chief of the Ear, Nose and Throat Clinic in Aarau from 1983 to 2011. He is a co-founder of the Association for knowledge transfer of various European Ear, Nose and Throat clinics – ORL-BAL, which has organized 29 visits of doctors from Serbia to Europe or the United States, 32 courses and seminars in Serbia, two summer schools and 56 visits of foreign experts in Serbia since 2002. He has been a member of the Association of Basle physicians for International Cooperation since 2003. He was elected a visiting professor of the Department of Otorhinolaryngology, Faculty of Medicine in Novi Sad in 2009 and since then has given numerous lectures to the students of medicine and dentistry. He has been an honorary member of the Medical Academy of Serbian Medical Society since 2010.

Associates of the Department

The Department of Otorhinolaryngology has engaged teachers from other faculties and long-term cooperation has been achieved with the following professors:

Professor Dr Ksenija Ribarić Jankes

Dr Ksenija Ribarić Jankes defended her doctoral dissertation "Functional organization of auditory afferent connections in healthy and deaf" at the Faculty of Medicine at the University of Zagreb in 1986, where she was elected to the position of professor in 1986. She became a full-time professor at the Faculty of Medicine in Belgrade in 1996. She has published over 140 papers, is a co-author of two books published in the United States and six books published in ex-Yugoslavia. In the period from 1997 to 2001, Prof Ksenija Ribarić Jankes was in charge of the entire theoretical teaching of otolaryngology to the students of medicine in English at our Department.

Professor Dr Svetlana Slavnić

Dr Svetlana Slavnić is employed at the Faculty of Special Education and Rehabilitation, University of Belgrade. After her doctoral dissertation "Early rehabilitation of the handicapped", she was elected to teaching positions. A significant part of her work has so far been devoted to the phenomenon of hearing loss by focusing on the problem of rhythm and voice dynamics in children with different modes of amplification, to the psychomotoric organization and re-education of children with disabilities and the problem of integration and inclusive education of people with hearing impairments. Prof Dr Svetlana Slavnić has actively participated in teaching the subject medical basics of surdology since 2011 and is highly appreciated as a favorite teacher.

Professor Dr Slavica Golubović

Dr Slavica Golubović has worked as a professor at the Faculty of Special Education and Rehabilitation at the University of Belgrade. After defending her doctoral dissertation "The incidence of aphasia in cerebrovascular etiology of hospitalized patients" in 1986, she was appointed assistant professor. Dr. Slavica Golubović is the author of 27 books and hundreds of articles. She has been invited to speak at numerous congresses. Professor Golubović has been a member of Russian Academy of Natural Science since 2007 and Yugoslav expert in the field of logopedics. She has been the head of the Department of Logopedics at the Faculty of Special Education and Rehabilitation for 13 years. During this period, Dr Golubović has been promoting teaching programs for students of logopedy. Prof Dr Slavica Golubović has actively participated in teaching medical basics of voice and speech disorders.

Professor Dr Vlado Delić

After graduating from the Faculty of Technical Sciences, Vlado Delic was employed by the same faculty as an assistant. He received his PhD title in 1997 on "A new concept of scrambling speech based on Ademar transformation." Prof Dr Vlado Delić is extensively engaged in speech technologies, acoustics and audio signal processing. Within the course "Medical Basics of Surdology" he regularly gives lecture on physical acoustics to the students of Special Rehabilitation and Education. He has participated in numerous national and international projects and has written numerous papers. Prof Vlado Delić has been repeatedly awarded on the suggestion of his students.

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TRANSMANDIBULAR AND TRANSCERVICAL SURGICAL APPROACH IN TREATMENT OF TONGUE BASE CANCERS – TEN-YEAR RESULTS

TRANSMANDIBULARNI I TRANSCERVIKALNI HIRURŠKI PRISTUP TRETMANU KARCINOMA BAZE JEZIKA – REZULTATI DESETOGODIŠNJEG PERIODA

Rajko M. JOVIĆ[1], Danijela DRAGIČEVIĆ[1], Karol ČANJI[1], Jugoslav GAŠIĆ[2] and Maša ĐOZIĆ[1]

Summary

Introduction. The aim of this study was to present oncological and functional results of surgical treatment of the base of tongue cancer by analyzing retrospectively 115 patients treated during a ten-year period. During this period, 150 patients with cancer of the base of tongue were diagnosed, which accounts for 5.6% of all diagnosed head and neck cancers and 24.1% of all oropharyngeal cancers. In 111 patients (96.5%), planocellular carcinoma with various degrees of differentiation was pathohistologically verified. Neck metastases were found in 88 (76.5%) patients. Advanced III and IV stages of disease were verified in 92.9% of patients (stage III in 23.4%, IV A in 59.1%, IV % B in 10.4%). Transmandibular approach was performed in 5.2% of patients, while 94.8% of patients were approached through pharynx The defects were covered by primary reconstruction; the *pectoralis major* myocutaneous *flap* was used in 4 patients . During immediate postoperative period, 17 (14.7%) patients developed complications: bleeding occurred in 7 patients (6%), fistula and wound infection developed in 5 (4.3%) and 11 (9.5%) patients, respectively. Postoperatively, 61 (53%) patients were treated by radiation therapy. Swallowing function was resumed in all patients except in three, who underwent gastrostomy due to the lesion of both hypoglossal nerves. Gasrostoma was closed after six months when swallowing was resumed. Local and regional recurrence developed in 13 (11.3%) and 24 (20.8%) patients, respectively, and distant metastases developed in 4 (3.5%) patients. Second primary cancer was diagnosed in 9 (7.8%) patients Disease-specific 3-year survival rate (according to the T category) was 73%, 60%, 45% and 21% in patients with T1, T2, T3 and T4, respectively. Disease-specific 3-year survival rate (according to category N) was 68% in N0 and 32%) in N +. The overall 3-year survival rate was 42%.

Key words: Tongue Neoplasms; Surgical Procedures, Operative; Deglutition; Diagnosis; Treatment Outcome; Carcinoma, Squamous Cell

Sažetak

Uvod. Cilj rada bio je da se retrospektivnom analizom desetogodišnjeg perioda (2001−2011. godine) 115 operisanih pacijenata prikažu onkološki i funkcionalni rezultati hirurškog tretmana karcinoma baze jezika. U posmatranom periodu dijagnostikovano je 150 karcinoma baze jezika, što čini 5,6% svih dijagnostikovanih karcinoma glave i vrata i 24,1% karcinoma orofarinksa. Kod 111 (96,5%) histološki je potvrđen planocelularni karcinom, različitog stepena diferentovanosti. Metastatski proces u vratu verifikovan je kod 88 (76,5%) pacijenata. Odmakao III i IV stadijum bolesti potvrđen je kod 92,9%, i to III kod 23,4%, IV A kod 59,1% i IV B kod 10,4% pacijenata. Transmandibularni pristup rađen je kod 5,2%, a svi ostali (94,8%) operisani su transfaringealnim pristupom. Defekti su zatvarani primarnom rekonstrukcijom, a kod četvoro pacijenata korišćen je pektoralis major miokutani režanj. U neposrednom postoperativnom periodu, komplikacije su se javile kod 17 (14,7%) pacijenata; u vidu krvarenja kod 7 (6%) pacijenata, fistule kod 5 (4,3%), i kod 11 (9,5%) infekcija rane. Postoperativno je 61 pacijent primio terapiju zračenjem (53%). Kod svih pacijenata je uspostavljena funkcija gutanja, osim kod troje koji su zbog lezije oba hipoglosusa hranjeni do 6 meseci preko gastrostome, a potom je uspostavljeno gutanje, a gastrostoma zatvorena. Lokalni recidiv javio se kod 13 (11,3%), regionalni recidiv kod 24 (20,8%) a udaljene metastaze kod 4 (3,5%). Drugi primarni karcinom dijagnostikovan je kod 9 (7,8%). *Disease* specifično trogodišnje preživljavanje prema T-kategoriji karcinoma je kod T1 73%, T2 60%, T3 (45%) i T4 (21%). *Diasease* specifično preživljavanje u odnosu na N-kategoriju je N0 (68%) i N+(32%). Ukupno trogodišnje preživljavanje iznosilo je 42%.

Ključne reči: Karcinomi jezika; Operativne hirurške procedure; Gutanje; Dijagnoza; Ishod lečenja; Planocelularni karcinom

Introduction

The problem of treatment of the base of tongue cancer is the aggressiveness of the approach itself on one hand and on the other hand, there is the importance of the act of swallowing, chewing and speech, which are the functions closely connected to the tongue.

Trauma of tissue through which the access to this region is granted, as well as the resection of carcinoma of the base of tongue inevitably lead to disruption of these functions, which greatly affect the quality of life of patients [1]. This is largely the

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Abbreviations

CT – computed tomography
MG – magnetic resonance
TNM – tumor, nodes and metastases

reason for seeking different modalities which will give better or at least the same response to oncological demands, while preserving the important functions. An alternative to surgical approach is organ preservation [2]. It includes the use of chemoradiotherapy, which leaves the structure of the organ intact, meaning that functions should be preserved [3]. Although oncological and surgical treatment results are equal, functional results are not encouraging, considering the effects of early and late toxicity [4]. Advanced surgical techniques, particularly the use of flaps for the reconstruction of created defects, visibly improve the functional results of surgery and place surgery again in the spotlight of treatment of the base of tongue cancer [5].

That is why we have accepted the primary surgical approach in the treatment of the base of tongue cancer. The aim of this study was to show the oncological and functional results of surgical treatment of the base of tongue cancer through retrospective analysis of treated patients.

Material and Methods

This is a retrospective analysis of 115 patients operated during 2001-2011 at the Department of Ear, Nose and Throat Diseases, Clinical Center of Vojvodina, which is a tertiary health institution in the country and a reference institution for the treatment of this pathology in the province of Vojodina. Thirteen women (11.3%) and 102 men (88.7%) underwent surgery, the ration being 8:1. Their age ranged between 38 and 80 years (mean age being 57.7 years). Verification of the diagnosis of malignancy was done by patohistological analyses. Biopsies were performed under local epimucose anesthesia using a curved handle, and a smaller number of patients were subjected to general endotracheal anesthesia. In some patients, the primary origin of tumor was found during general examination, without clinically visible tumor, but with clinically evident metastatic neck lymph nodes. Patients were then prepared according to the standard protocols in order to obtain complete information about locoregional prevalence of disease and the possible existence of distant metastases. In addition to blood tests and laboratory analyses, coagulation status, computed tomography (CT) or magnetic resonance (MR) scan of the head and neck, X-rays of the chest and an abdominal ultrasound were performed. In patients with suspected lung deposits, consultation with pulmonologist, CT scan of chest and bronchological analyses were performed. A fully prepared patient was then presented to the Oncological Consilium, consisting of an internist oncologist, radiotherapist and, if necessary a pathohistologist, along with an otorhinolaryngologist. The decision of surgical treatment was made after the complete evaluation of available data. Patients without contraindications for surgery, without distant metastasis, metachronous or synchronous malignancy were selected for surgical treatment, as the primary treatment protocol.

Surgical approach in treatment of the base of tongue cancer was transcervical and transmandibular and it depended on the localization of cancer in the area of the base of tongue. Indications for surgical treatment were epithelial malignancies of the base of tongue, which did not exceed the level of the papilla circumvallate on both sides, towards the middle third of the tongue; in cancer of the lateral side of the base of tongue and pharyngeal wall, if infiltration of the mandible was not more than 5 mm and if cancer did not cross the midline of the tongue; in carcinomas that originated from salivary gland, larger carcinomas were also operated, but not if total glossectomy was required.

Infrahyoid approach, including the resection of one part (epiglotectomy, supraglottic laryngectomy) or the entire larynx, was used within transcervical approach to carcinomas of the base of tongue that spread to the laryngeal structures.

Transhyoid and suprahyoid approach was performed in cancers that did not reach valleculae. For primary reconstruction of defect, pexy to hyoid or thyroid cartilage was performed. Cancers of the lateral side of the tongue with the expansion to the mandible were operated using the so-called "swing" technique of mandibulotomy or with composite resection. "Swing" technique included paramedial or lateral mandibulotomy to approach malignancies which had not invaded the mandibule, and at the end of resection with or without reconstruction with flap, osteosynthesis was performed. In composite or "commando" operations, resection of one part of the mandible or hemiresection of invaded mandible with the base of tongue cancer was performed. The reconstruction was done with pedicled pectoralis major musculocutaneous flap.

In order to improve pathohistological preparation, tumor was fixed in styrofoam, and additional tissue borders were taken and sent to pathohistological analysis. In extensive malignancies with unclear boundaries, borderline tissue was taken during surgery for ex tempore biopsies. In the case of positive borders, additional resection of tissue was done.

Neck dissection was performed in all patients. Unilateral selective neck dissection was done in early T1 and T2 cancers of the base of tongue, which did not cross the midline, whereas in cancers that have crossed the midline, or had multiple or more metastatic nodes, bilateral neck dissection was performed (for N+ modified radical or radical dissection and for N- selective neck dissection). The obtained samples were sent to pathohystological analysis, fixed on a large styrofoam with marked groups of lymph nodes.

Table 1. TN classification of tongue base cancer
Tabela 1. *TN klasifikacija karcinoma baze jezika*

TN	N0	N1	N2a	N2b	N2c	N3	Total/*Ukupno*
T1	2	4	0	0	1	2	9
T2	6	2	2	11	4	4	29
T3	14	7	1	6	15	3	46
T4	5	3	2	7	11	3	31
Total/*Ukupno*	27	16	5	24	31	12	115

All patients underwent tracheostomy, and a nasogastric tube was used until the recovery of swallowing.

Upon completion of the collected materials by pathohistologists, radiotherapy was recommended in patients with following indications for radiation: metastasis in more than two nodes, extracapsular expansion of cancer, advanced stages of cancer, and the positive tissue borders.

After completion of therapy, the patients were regularly followed up, every two months during the first year, every three months during the second year, and twice a year to the end of the fifth year. At each examination, ultrasound of the neck was performed. After 5 years, checkup was done once a year.

Statistical data were analyzed using means, standard deviations, Fisher's t test and Kaplan Meyer analysis.

Results

In the analyzed period of ten years, 2638 patients with newly discovered malignant tumor in the head and neck region were diagnosed and treated at the Department. Out of 622 (23.5%) cancers of the oropharynx included in the study sample, 150 were diagnosed as cancers of the base of tongue, thus accounting for 5.6% of all diagnosed head and neck cancers and 24.1% of cancers of the oropharynx. One hundred and fifteen patients were treated primarily surgically. In 111 (96.5%) patients, planocellular carcinoma was diagnosed with various degrees of differentiation, one (0.8%) adenocarcinoma, two (1.7%) adenoid cystic carcinoma and one (0.8%) mucoepidermoid carcinoma. Metastatic lymph nodes (N +) were discovered in 88 (76.5%) patients, and 27 (23.5%) patients were not found to have metastatic processes in the neck (N-) after pathohistological treatment.

The patients were divided into groups according to the tumor, nodes and metastases (TNM) classification (**Table 1).**

According to the stage of the disease, the majority of patients (59.1%) were in IV A stage of disease **(Table 2)**.

Operations were performed by transcervical and transmandibular approach and the resection of laryngeal or other structures within the resection of the base of tongue cancer was done depending on the degree of involvement of these structures (**Table 3**).

The first two categories, transhyoid and infrahyoid pharyngotomy, as well as mandibulotomy, indicate the type of surgical approach to the base of tongue cancer, while other categories indicate the extent of

Table 2. Stage of the disease in patients diagnosed to have tongue base cancer
Tabela 2. *Stadijum bolesti dijagnostikovanih pacijenata sa karcinomom baze jezika*

S	T	N	M	N	%
0	Tis	N0	M0		0%
I	T1	N0	M0	2	1.7%
II	T2	N0	M0	6	5.2%
III	T3	N0	M0	27	23.4%
	T1	N1	M0		
	T2	N1	M0		
	T3	N1	M0		
IVA	T4a	N0	M0	68	59.1%
	T4a	N1, N2	M0		
	T1	N2	M0		
	T2	N2	M0		
	T3	N2	M0		
IVB	T Any	N3	M0	12	10.4%
	T4b	N Any	M0		
IVC	T Any	N Any	M1	0	

Table 3. Approach to the base of tongue cancer resection and the extent of resection of surrounding tissues
Tabela 3. *Pristup resekciji kancera baze jezika i obim resekcije okolnog tkiva*

Approach and extent of resection/Pristup i obim resekcije	N	%
Transhyoid pharyngotomy/*Transhioidna faringotomija**	35	30.4
Infrahyoid pharyngotomy/*Infrahioidna faringotomija**	43	37.4
Near-total laryngectomy/*"Skoro" totalna laringektomija*	2	1.7
Horizontal supraglottic laryngectomy/*Horizontalna supraglotisna laringektomija*	13	11.3
Total larynectomy/*Totalna laringektomija*	12	10.4
Tonsillectomy, the soft palate resection/*Tonzilektomija, resekcija mekog nepca*	2	1.7
Mandibulotomy/*Mandibulotomija**	4	3.5
Composite resection (segmental resection of the mandible) *Kompozitna resekcija (segmentalna resekcija mandibule)*	2	1.7
Partial pharyngotomy/*Parcijalna faringektomija*	2	1.7
Total/*Ukupno*	115	100

Table 4. Type of neck dissection done during the primary base of tongue cancer surgery
Tabela 4. *Vrsta disekcije vrata vršene tokom primarne hirurgije karcinoma baze jezika*

Type of neck dissection/*Vrsta disekcije vrata*	Unilateral/*Jednostrana*	Bilateral/*Obostrana*	Total/*Ukupno*
Selective neck dissection *Selektivna disekcija vrata*	11	27	38
Modified radical neck dissection (MRND) *Modifikovana radikalna disekcija MRDV*	11	4	15
Radical neck dissection (RND) *Radikalna diskecija vrata RDV*	5	0	5
Select/MRND/*Selekt/MRDV*	-	40	40
Select/RND/*Selekt/RDV*	-	6	6
MRND/RND/*MRDV/RDV*	-	5	5
Total/*Ukupno*	27	82	109

resection of the surrounding structures. Defect reconstruction was performed using the pedicled pectoralis major musculocutaneous flap in two patients with tumor spreading to the mandible and in 2 patients where the floor of mouth and lateral pharyngeal wall were infected by tumor.

The operation of the primary base of tongue cancer also included the neck dissection (**Table 4**).

All patients were fed through the nasogastric tube immediately after operation for 1 to 40 days (6.7 days on average). Due to difficult rehabilitation of swallowing and chewing, three patients had to undergo percutaneous gastrostomy, which was used up to 6 months. Permanent gastrostoma remained in none of the patients.

Tracheostomy was performed in all patients and it was closed after 7 to 36 days (7.4 days on average). In the immediate postoperative period, 17 (14.7%) patients had complications in the form of bleeding, fistula and wound infection, which developed in 7 (6%), 5 (4.3%), and 11 (9.5%) patients, respectively.

No fatal outcomes occurred during the period of hospitalization. After operation, 61 (53%) patients were treated by irradiation therapy.

Checkups of patients were performed every two months during the first year, every three months during the second year, and twice a year to the end of the fifth year. At each examination, ultrasound of the neck was performed. After 5 years, the checkup was done once a year.

Local and regional recurrence developed in 13 (11.3%) and 24 (20.8%) patients, respectively and distant metastases developed in 4 (3.5%) patients. Second primary cancer was diagnosed in 9 (7.8%) patients.

Disease-specific 3-year survival rate (according to T category of cancer) was 73%, 60%, 45% and 21% for T1, T2, T3 and T4, respectively **(Graph 1 a)**.

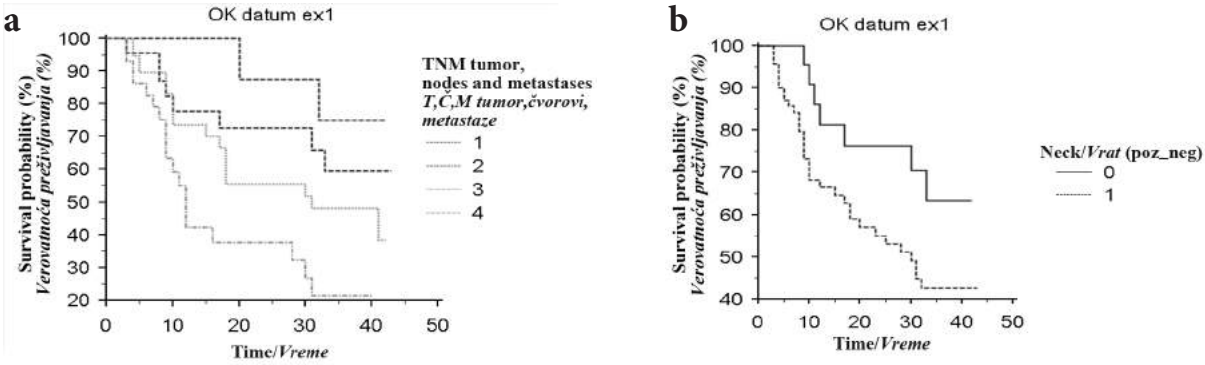
Kaplan Meier survival analysis revealed a significant $p = 0.0052$ difference in 3- year survival rate between groups in T category.

Disease-specific survival rate (according to N category) was N0 (68%) and N + (32%) **(Graph 1 b)**.

Kaplan Meier analysis showed a significant $p = 0.0492$ difference in 3-year survival rate for patients with negative neck lymph nodes compared to those with positive ones. Overall 3-year survival rate was 42% **(Graph 2)**.

Discussion

The base of tongue is built of histologically different tissues, so malignancies of different histological characteristics occur in this region. A malig-



Graph 1 a and b. Disease-specific survival by T stage (a) and N stage (b) (Kaplan Meier method)
Grafikon 1 a i b. *Preživljavanje specifično za bolest za T stadijum (a) i N stadijum (b) (metoda po Kaplan Majeru)*

nant tumor of epithelial origin is most common, and in this study, it accounted for 96.5% of all diagnosed malignancies. Malignant epithelial tumor of other histological structures is rare and mostly related to the salivary glands, with better prognosis.

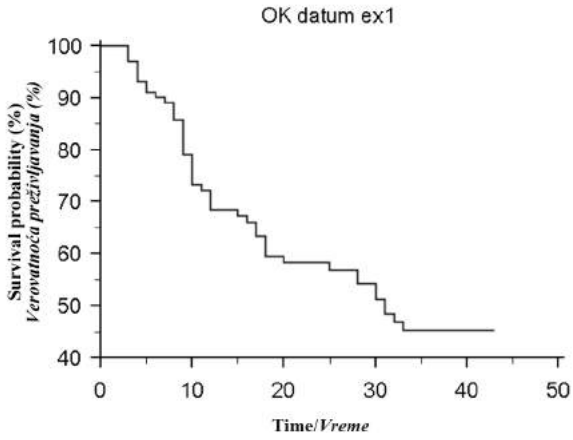
Base of tongue cancer is an aggressive disease with the progressive spreading. Although the tongue is a richly innervated area, which would indicate an early onset of symptoms, a good number of patients are diagnosed in advanced stages of the disease, in stages III and IV (92.9% of patients). Rich drainage of lymphatic system contributed to the presence of metastases in 88/115 (76.5%) of patients at the time of diagnosis. High incidence of metastasis in patients has been reported by other authors, including Gourin and Johnson [6], who found them in 84% of patients in their series.

Advanced clinical stages of disease and metastases contribute to a poor prognosis and it is difficult to select treatment protocols.

Since 1991, when the use of chemoradiotherapy protocol in the treatment of head and neck cancers was initiated [2], many institutions have been implementing this protocol in order to avoid mutilant operations, and have achieved the preservation of organ and seemingly better functional results. However, cancer of the tongue base is often at an advanced stage at the time of diagnosis; therefore, it is difficult to be controlled by radiotherapy and after radiotherapy has failed, salvage surgery is rarely performed [7]. The primary surgical treatment with subsequent radiotherapy in certain cases is an alternative to chemoradiotherapy protocol. Regardless of the degree of mutilation done by surgery in this region due to the complicated approach to the base of tongue, advanced reconstructive surgery leads to better oncological and functional results. This has reconciled the two basic principles of treatment of malignancies of the base of tongue in some way, because each of them has its good and bad sides.

Classic transmandibular approach is now rare, because it leaves more functional problems, some of which are malocclusion, impaired swallowing, and difficulty in speech. Cosmetic effect should not be neglected, either. Huet described transhyoid approach to base of tongue cancers in 1946 [8], and this method has been adopted because it shows an easier and closer approach to the base of tongue with good visibility of structures. The technique was improved by Moore and Calcaterra [9] and others, and an increasing number of authors [10] promote its advantages, and one of the most important is that the neurovascular bundle remains far away, so lesions are rare, visibility is excellent and larger tongue tumors are also approachable for dissection, along with epiglottis and the lateral wall of the pharynx. Transcervical approach to the base of tongue cancer was the basic approach (94.8%) in patients treated in this series. After cancer resection, suspension of larynx to the rest of the tongue was performed. The flap was not used to close the defect in any one because resection did not exceed the level of the papilla circumvalata.

None of the patients with carcinoma of the base of tongue underwent endoscopic transoral surgery because the visibility and possibility to control he-



Graph 2. Overal survival (Kaplan Meier method)
Grafikon 2. *Ukupno preživljavanje po metodi Kaplan Majera*

mostasis was poor, although some authors apply this approach using the laser technique [11].

Another approach used to operate the base of tongue cancer in this series of patients was the transmandibular approach. In the "swing" technique, after the resection of cancer, the defect was filled with pedicled pectoralis major flap in two patients, and osteosynthesis was done afterwards. Segmental resection of the tumor-invaded mandibule was done in two patients, then the defect was also covered with the pectoralis major flap. No patient underwent "near" total or total glossectomy. Total glossectomy includes total laryngectomy because of a swallowing disorder that occurs, although recent studies show that this is not necessary. Tiwari et al. performed total glossectomy with suspension of the larynx and achieved excellent functional results [12]. Chien et al. [13] closed the defect created after total or near total glossectomy with vascular free flaps. A good and understandable speech was achieved in 89.7%, and the patients had difficulty in speaking because of the gap between the soft palate and the flap. Dziegielewski et al. [14] also used the free vascular flaps for reconstruction of defects; however, they achieved worse results regarding swallowing since only 24% of patients achieved good swallowing function.

We believe that transpharyngeal rather than transmandibular approach leads to better functional results, which is also the opinion of other authors [15].

An integral part of primary cancer surgery of the base of tongue is neck dissection. It includes groups II and III of lymph nodes at least, because they are located on the drainage path of this region [16]. Because of the high incidence of metastasis in the region, neck dissection was performed in 109/115 (94.7%) patients. A high percentage of metastases found (76.5%) indicates a very early cancer metastasis in the neck lymphatics. The most common dissection performed was bilateral neck dissection (75.2%), followed by the modified radical one, which was second according to the extent of dissection and it was done in 60/109 (55%), while the radical and selective dissection was performed in 11/109 (10.1%) and 38/109 (34.8%) patients, respectively. None of dissections resulted in major complications.

Tracheostomy was performed in all patients due to a swallowing disorder and consequent aspiration of saliva. Trachoestoma was closed after the wound had healed and swallowing function had been resumed in all patients with the exception of 14 patients who had undergone total and near total laryngectomy. Feeding began with nasogastric tube until swallowing function was resumed. The process of rehabilitation began as soon as the conditions related to wound healing, solving complications and the total recovery of the patient were met. Rehabilitation was done with professional help and always started with thick porridge. Three patients underwent gastrostomy because the rehabilitation was difficult and long. All three patients had lesions of both hypoglossal nerves so swallowing orally was virtually impossible. In later period, one or both hypoglossal nerves recovered, swallowing was resumed and gastrostoma was closed in all three patients. After 6 months, all patients had good swallowing results. In further follow-up period, no patients from this study needed any support in swallowing.

O Connell et al. [17] achieved good functional results in swallowing (95%) after surgery and reconstruction of the base of tongue defects with vascular flaps. The wide application of flaps in this region has significantly contributed to better functional results in treatment of advanced carcinoma of the base of tongue. Swallowing was assessed by penetration-aspiration scale, aspiration implying each penetration of bolus below the vocal cords.

The advantages of chemoradiotherapeutic protocol should mean better functional results than those achieved by primary surgery. However, examination of swallowing function in this group of patients suggests that these patients have difficulties. In their study, Logmen et al. [18] found the reduction of retraction of the base of tongue in 89% and the tongue strength in 51%, as well as slowed or delayed closure of vestibular larynx in 31%, in 53 patients treated with chemoradiotherapy three months after radiation. The effect of radiation was a delayed triggering of the pharyngeal swallowing, reduction of tongue retraction and reduced rise of the larynx. Xerostomia was present in all patients after radiation. As many as 21/53 (40%) patients had a gastrostomy or jejunostomy 3 months after chemoradiation. It seems that organ preservation is not a functional preservation as well.

Rieger et al. [19] showed that swallowing had been resumed in 29 (90.6%) patients after reconstruction of defect with antebrachial flap, whereas three (9.4%) patients needed enteral nutrition.

The most common postoperative complication was wound infection in 11 (9.5%) patients, that percent going up to 17% [6]. The low social status of these patients and very poor oral hygiene put these patients at high risk for the occurrence of inflammation of wound, although carious teeth had been extracted before operation. Bleeding was the second most common (7.6%) complication. Mostly alcoholics with poor liver function showed a greater tendency to bleed in comparison with the normal population. Within the preoperative treatment, all parameters of hemostasis were within normal range, but in spite of that, traumatic shock of ensuing surgical procedure of these proportions led to bleeding in a small number of patients. Revision of wound and ligation of the arterial blood vessels was performed in one patient only. In others, bleeding stopped spontaneously after the cannula with cuff had been placed and fresh frozen plasma administered. Complications of extensive surgical interventions affect the recovery and prolong hospital

stay. They are related to the primary surgery of malignancies but also to the reconstruction by using flaps. Session et al. [20] reported severe complications in 45% of patients.

Locoregional recurrence developed in 37 (32.1%) treated patients, that is in the tongue and pharyngeal wall in 13 patients (11.3%) and regional recurrence in 24 (20.8%) patients. Great biological potency of planocelulanr cancer, lack of natural barriers that slow down the progression of cancer, a rich network of blood vessels and lymphatics allow the tumor to spread quickly and easily through the structure of tongue and regional lymph nodes. This is the reason of high percentage of local and regional recurrence, and difficult intraoperative diagnosis. A high percentage of recurrence was reported by Gourin and Johnson; local relapse occurred in 5.7%, and regional relapse occurred in 13.8% of patients [6]. Sessions et al. [20] reported local recurrence in 12.2% of patients, regional positive lymph nodes in 8.8%, and both local and regional recurrence in 5.3% of patients. In 89% of patients, recurrences developed within four years after the primary treatment.

According to the protocol, patients with positive marginal tissue after definite patohistological analyses were referred to radiation. Sessions et al. [20] found that 41% of surgically treated patients had positive borders in this region. Although all patients were subjected to radiotherapy, they have concluded that the positive tissue borders reduce survival rate and that additional radiation does not improve survival.

Distant metastases were diagnosed in 4 (3.5%) patients in this study, that being significantly less than 25.3% and 16% as recorded by Gourin and Johnson [6] and Sessions et al. [20], respectively. Second primary cancer was diagnosed in 9 (7.8%), and Sessions et al. [20] found it in 20% of patients.

T and N categories have the greatest influence on the survival rate of patients. The survival rate becomes lower with the more advanced stage of tumor and the greater number of metastases. It is therefore expected that patients with T1 tumors have the best survival rate (73%), then those with T2 (60%), and T3 (45%) and patients with T4 (21%) have the worst survival rate. There are significant statistical differences among the categories. Another important criterion for survival is regional spread of the disease. With positive neck lymph nodes, the disease-specific survival rate according to N category is N0 (68%) and significantly worse in N + (32%). The overall 3-year survival rate was 42%. It is very difficult to compare the survival of patients from different series, because of the differences in protocols, the structure of patients, length of follow-up, method of reconstruction, surgeon's skill - therefore the data are only seemingly comparable.

Gurin and Johnson reported the overall survival rate to be 49% [6]. Chien et al. [13] found the total 4-year survival to be 63.8%, for tongue cancer and 42.9% for the base of tongue cancer.

The overall 3-year survival was 46% in the study conducted by Mahtay et al. [21], whereas it was 57% with radiation therapy as reported by Robertson et al. [22].

The overall survival rate of patients after the applied primary surgical protocol did not differ significantly from the survival rate shown in the series of other authors or in comparison with other therapeutic protocols applied.

Conclusion

Cancer of the base of tongue is a silent, progressive, very aggressive disease which is discovered at an advanced stage, although it creates regional and distant metastases early. From the oncological aspect, surgical treatment does not provide significant improvement of survival rate; however, resection all the way to the healthy tissue with good reconstruction yields excellent functional results. Transpharyngeal approach has the advantage over the transmandibular one because it enables an easy access to the base of tongue, good visibility, and the suspension after resection of the tongue base is possible for the larynx through the thyroid cartilage if the epiglottis/supraglotis is removed, or via the thyrohyoid membrane when the epiglottis is preserved. The resumed function of swallowing indicates that a good surgical technique and quality reconstruction have been performed. As the base of tongue cancer increases in younger population, in relation to human immunodeficiency virus infection, the surgical treatment becomes a matter of choice.

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MASTOIDITIS IN CHILDREN – A RETROSPECTIVE ANALYSIS OF CLINICAL CHARACTERISTICS

MASTOIDITIS KOD DECE – RETROSPEKTIVNA ANALIZA KLINIČKIH KARAKTERISTIKA

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Summary

Introduction. Acute mastoiditis is the most common otogenic complication among infants and young children and is always considered a serious complication. In addition to determining the age at which mastoiditis usually occurred in children, the time of onset of clinical signs in relation to the onset of symptoms of middle ear inflammation, as well as the most common clinical signs of mastoiditis, the study has been aimed at finding out whether mastoiditis is of seasonal character. **Material and Methods.** A retrospective study of children surgically treated for mastoiditis was conducted at the Department of Ear, Nose and Throat Disease of the Clinical Center of Vojvodina in Novi Sad in the period January 1, 2002 – December 31, 2011. The sample included 56 children (30 boys - 53.57%, and 26 girls - 46.42%), up to 17 years of age. The obtained results were statistically analyzed and presented using Microfsot EXCEL for statistical analysis. **Results.** Mastoiditis is most common in children up to 2 years of age, 39/56 (69.82%). It has a seasonal character, with the peak season in the autumn-winter period, with a statistically significant difference compared to the spring-summer period ($p = 0.0449$, i.e. $p<0.05$). In 25 children (44.64%), the middle ear symptoms lasted up to three weeks before operation. Otomicroscopic findings showed that the tympanic membrane was thickened and stiff in 41 children (73.21%) and 9 children (16.07%) presented with thickened tympanic membrane and lowering of the posterior wall of the external auditory canal. **Conclusion.** Mastoiditis in children is most common among children up to 24 months of age. It has a seasonal tendency. In nearly half of the cases, clinical manifestations of mastoiditis appear 3 weeks after the onset of the first symptoms of middle ear inflammation, whereas the key otomicroscopic finding is stiffness and thickening of the tympanic membrane.

Key Words: Mastoiditis; Infant; Child Preschool; Child; Adolescent; Male; Female; Otitis Media + complications; Signs and Symptoms; Diagnosis; Seasons; Otoscopy; Otorhinolaryngologic Surgical Procedures

Sažetak

Uvod. Akutni mastoiditis je najčešća otogena komplikacija u ranom dečjem uzrastu i uvek se smatra ozbiljnom komplikacijom. Cilj rada bio je da se utvrdi u kom uzrastu se mastoiditis najčešće javlja kod dece, da li pokazuje sezonski karakter; da se utvrdi vreme pojave kliničkih znakova mastoiditisa u odnosu na vreme pojave prvih simptoma upalnog procesa srednjeg uva i odrede najčešći klinički znakovi mastoiditisa. **Materijal i metode.** Sprovedena je retrospektivna studija dece hirurški lečene zbog mastoiditisa na Klinici za bolesti uva, grla i nosa Kliničkog centra Vojvodine u Novom Sadu u periodu 1.1.2002−31.12.2011. godine. Uzorak je činilo 56 dece (30 dečaka, 53,57%, i 26 devojčica, 46,42%), uzrasta do 17. godina. Dobijeni rezultati prikazani su grafički pomoću *Microfsot EXCEL* programa i obrađeni standardnim statističkim metodama. **Rezultati.** Mastoiditis se najčešće javlja u uzrastu do druge godine života, 39/56 (69,82%). Pokazuje sezonski karakter sa najvišim pikom pojave u periodu jesen−zima, sa statistički značajnom razlikom u odnosu na period proleće−leto, ($p = 0,049$). Preoperativna dužina trajanja simptoma bolesnog stanja srednjeg uva kod 25 dece (44,64%) bila je do tri nedelje. Otomikroskopskim pregledom utvrđeno je da je kod 41 deteta (73,21%) bubna opna zadebljala i napeta, a kod devetoro dece (16,07%) bilo je prisutno i spuštanje zadnjeg gornjeg zida spoljašnjeg slušnog hodnika. **Zaključak.** Mastoiditis u dečjem uzrastu najčešće se javlja u populaciji dece do 24 meseca života. Pokazuje sezonski karakter. Klinička slika mastoiditisa se kod gotovo polovine slučajeva razvija do treće nedelje od pojave prvih kliničkih simptoma upalnog procesa srednjeg uva, a dominatnu otomikroskopsku sliku čini napetost i zadebljanje bubne opne.

Ključne reči: Mastoiditis; Odojče; Dete predškolskog uzrasta; Dete; Adolescent; Muško; Žensko; Otitis media + komplikacije; Znaci i simptomi; Otoskopija; Otorinolaringološke hirurške procedure

Introduction

Acute inflammation of the middle ear, acute otitis media (AOM), is the most common bacterial infection among infants and young children. Almost all children experience at least one episode of AOM, and about 30% have two or more episodes by the age of 3 years. The peak incidence of AOM is in children aged 3–18 months, with the most sensitive period between 3 and 11 months.

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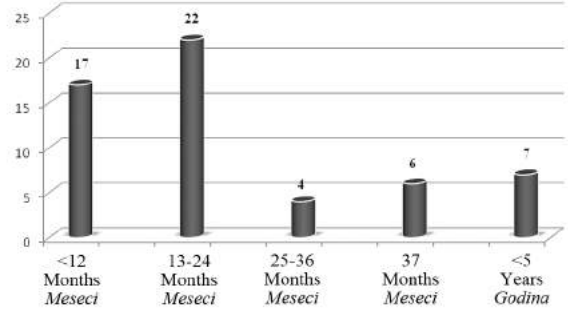
Abbreviations

AOM – acute otitis media
ME – middle ear
TM – tympanic membrane
MP – microperforation
PW – posterior wall
EAC – extrernal auditory canal

In Europe, the overall annual incidence rate of AOM is 268 episodes per 1.000 children [1–4]. Today, otitis media is considered a multifactorial, dynamic and continuous inflammatory process of the tubotympanomastoid complex which may have one or more clinical manifestations. Bearing in mind the dynamics and progression of the middle ear (ME) inflammation, classification of ME diseases has a didactic importance primarily because the transition borderlines from one clinical form to another are often unclear [5–7].

Otogenic complications are most common in recurrent acute bacterial otitis and exacerbation of chronic inflammatory processes of the middle ear. They are related to disturbed balance between local and general immune defense mechanisms, severe pathogen virulence and/or adequate, but untimely treatment. Sometimes they can be the first sign of inflammation of the middle ear. Infection spreads from the middle ear either towards intracranial or extracranial structures. The most common otogenic complication in children with acute inflammation of the middle ear is mastoiditis [8]. In the initial stage, the pathoanatomical substrate of mastoiditis includes mucosal edema in the mastoid area, dilation of blood vessels, and seromucous secretions in the cellular space. The stage of coalescence is dominated by purulent discharge from the mastoid cells, which causes local hypoxia, ischemia, and local acidosis under increased pressure, resulting in the osteoclastic dissolution of the pneumatic cell walls, formation of larger spaces filled with purulent exudate and granulations, whereas the final stage is the stage of exteriorizing mastoiditis [6]. Acute mastoiditis in early childhood is always considered a serious complication. It is associated with significant morbidity with potential spread of infection outside the mastoid system with consequent extracranial and intracranial complications, as well as possible hearing impairment. There are three clinical types of mastoiditis: acute mastoiditis with exteriorization, acute mastoiditis without exteriorization, and latent (subclinical, masked) mastoiditis.



Graph 1. The age structure of children with mastoiditis
Grafikon 1. *Uzrasna struktura dece sa mastoiditisom*

Material and Methods

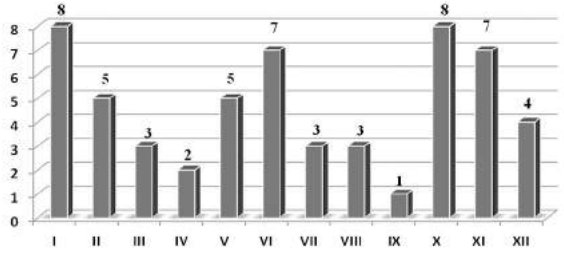
A retrospective study of children surgically treated for mastoiditis was conducted at the Department of Ear, Nose and Throat Diseases of the Clinical Center of Vojvodina in Novi Sad in the period January 1, 2002 – December 31, 2011. The sample included 56 children (30 boys - 53.57%, and 26 girls - 46.42%), aged to 17 years. Relevant data from case histories and surgical procedures were analyzed for all studied children. The initial prehospital treatment included antibiotics or antibiotics and paracentesis, without favorable clinical results, thus mastoidectomy was required. The obtained results were statistically analyzed and presented using Microfsot EXCEL for statistical analysis.

Results

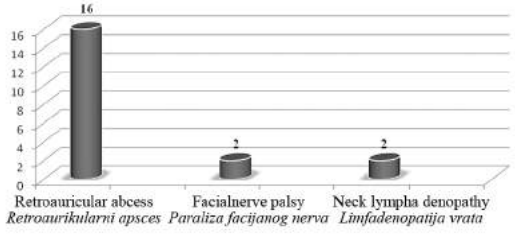
In the analyzed sample, the incidence of mastoiditis was highest in early childhood: in children up to 36 months of age (43/56 children - 76.78%), infants up to 12 months of age (17/56 - 30.35%), and 13–24 months of age (22/56 - 39.28%). Mastoiditis developed in 13 children (23.22%) over 36 months of age (**Graph 1**).

Seasonal incidence peaks of mastoiditis were in the autumn-winter period, accounting for 62.5% of children (**Graph 2**).

Of 56 children diagnosed with mastoiditis in the studied period, 16 children (28.57%) had a retroauricular abscess, 2 (3.57%) had facial nerve paresis, and 2 children (3.57%) had neck lymphadenopathy (**Graph 3**). Before mastoidectomy, 34 children (60.71%) out of 56 children were treated with prolonged multiple antibiotic therapy, while 22 children (39.28%) underwent paracentesis and antibiotic therapy, before or after admission. Right-sided mastoiditis was found in 30 children (53.57%), left-sided in 20 (35.71%), and bilateral in 6 children (10.71%).



Graph 2. Incidence of mastoiditis by months
Grafikon 2. *Incidencija mastoiditisa prema mesecima*



Graph 3. The clinical picture of children with mastoiditis on admission
Grafikon 3. *Klinička slika na prijemu dece sa mastoiditisom*

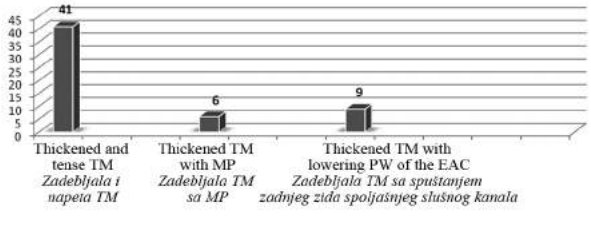
Otomicroscopic findings showed that the tympanic membrane was thickened and stiff in 41 children (73.21%), it was thickened with microperforation in 6 children (10.71%), and 9 children (16.07%) presented with thickened tympanic membrane and lowering of the posterior wall of the external auditory canal (**Graph 4**).

The preoperative middle ear symptoms lasted up to three weeks in 25 children (44.64%), between one and three months in 21 children (37.5%), and over three months in 10 children (17.85%) (**Graph 5**).

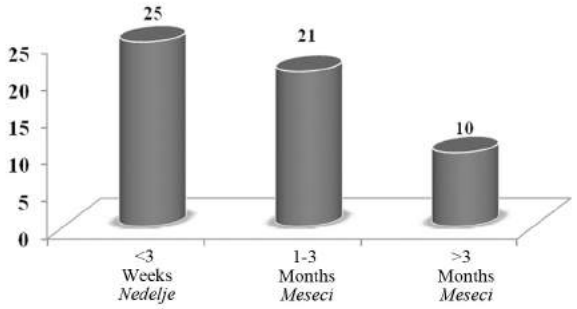
Laboratory findings revealed leukocytosis in 29 children (51.78%) (10–15x10^9 g/l), 23 children (41.07%) had leukocytes exceeding 15x10^9 g/l, while 4 children (7.14%) had 10x10^9 g/l. The sedimentation rate was over 61 in 20 children (35.71%), between 41 and 60 in 8 children (14.28%), between 21–40 in 15 children (26.78%), and less than 20 in 4 children (7.14%). Hematocrit was less than 0.29 g/l in 21.42% out of 56 children, and hemoglobin was below 109 g/l in 42.85% of cases.

Intraoperative findings showed that 20 children (35.71%) had severe hyperplasia of the mucosa and granulation, 10 children (17.85%) had osteitis and granulation, 22 children (39.28%) presented with mucosal hyperplasia and mucopurulent discharge, and 4 children (7.14%) had mucosal hyperplasia and denudation of the dura mater of the middle cranial fossa (**Graph 6**).

Mastoidectomy was performed in 56 children, intraoperative swabs were not obtained from 36 of



Graph 4. Intraoperative otomicroscopic findings (TM-tympanic membrane, MP-microperforation, PW-posterior wall, EAC-Extrernal Auditory Canal)
Grafikon 4. *Intraoperativni otomikroskopski nalaz (TM-timpanična membrane, MP-mikroperforacija, PW-zadnji zid, EAC-spoljašnji slušni hodnik)*

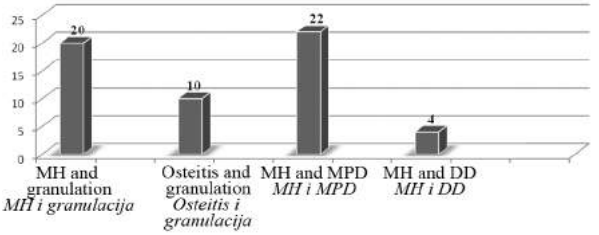


Graph 5. The preoperative duration of middle ear symptoms
Grafikon 5. *Preoperativna dužina simptoma bolesnog stanja srednjeg uva*

them (64.28%), *Streptococcus pneumoniae* and *Coagulase-negative staphylococci* were isolated in 3 (5.35%) and 2 children (3.57%), respectively and swabs were negative in 15 children (26.78%).

Discussion

Inflammation of the middle ear is a common condition in early childhood. It clinically manifests as sporadic, recurrent or chronic inflammation. Although the introduction of antibiotics has reduced the incidence of mastoiditis, a rising tendency has been observed in recent years [9, 10]. This phenomenon may be due to the development of bacterial resistance to antibiotics. However, the initial treatment of otitis media may be ineffective (dose- and duration-wise), or inadequate, which leads to additional development of complications, particularly acute mastoiditis. Defence against pathogenic microorganisms is lowest in infants and young children. Diagnosing children with acute otitis media is difficult, mainly due to the characteristics of the external auditory canal, specific position and quality of the tympanic membrane. In the examined sample, the incidence of mastoiditis was highest in children under two years of age, 22 (39.28%). The age distribution in this study is in agreement with available literature data [11, 12].



Graph 6. Intraoperative mastoid findings (MH-mucosal hyperplasia, MPD-mucopurulent discharge, DD-dura denudation)
Grafikon 6. *Intraoperativni nalaz mastoida (MH-hiperplazija mukoze, MPD-mukopurulentan sadržaj, DD-denudacija dure)*

With regard to gender distribution, mastoiditis is somewhat more common in boys than in girls, 1.15:1. Higher incidence of mastoiditis among boys was also reported by other authors, Serrao-Neto et al., Spratley J. et al., Baljošević I. et al. [13–15], while Paterson et al. reported a lower percentage of boys treated for mastoiditis compared to girls [16].

A seasonal mastoiditis incidence analysis showed that most children (62.5%) were admitted during the autumn-winter period (October to March), as opposed to 37.5% of children admitted in the spring-summer period (April to September), showing a statistically significantly higher incidence of mastoiditis in the autumn-winter period compared to the spring-summer period ($p = 0.0449$, i.e., $p<0.05$). Regular seasonal peaks that may confirm the association between mastoiditis and inflammation of the upper respiratory tract were also reported by other authors [16].

The duration of symptoms of the middle ear inflammation in children with mastoiditis differed, so the symptoms lasted less than three weeks, between one and three months and over three months in 44.64% of children with acute mastoiditis, 37.5% with subacute course and in 17.85% of children with chronic mastoiditis, respectively. According to literature data, the average duration of illness before admission is under 7 days [8, 17].

The clinical picture of the studied children was typical. Of 56 children, 16 children (28.57%) had a retroauricular abscess, 2 (3.57%) had facial nerve paresis, and 2 children (3.57%) had neck lymphadenopathy. Otomicroscopic findings showed that 73.21% of children had stiff and thickened tympanic membrane, in 10.71% it was thickened with microperforation, and 16.07% of children presented with thickened tympanic membrane and lowering of the posterior wall of the external auditory canal, corresponding with pathological findings in 89% of children who underwent mastoidectomy [18].

In the diagnosis of mastoiditis, laboratory tests are an integral part of the diagnostic process: increased erythrocyte sedimentation rate, leukocyte count, and red blood cell count (hemoglobin - HGB, hematocrit - HCT). In our sample, 76.78% of children had an elevated sedimentation rate (higher than 21), and 92.85% had leukocytosis > $10x10^9$ g/L, but it was very significant that in 42.85% the level of hemoglobin was less than 109 g/l, whereas in 21 children (42%) the hematocrit was less than 0.29 g/l. In their sample of patients undergoing mastoidectomy (60% with exteriorizing mastoiditis), Lautermann J. et al. [18] found elevated sedimentation rate in 95% of patients, that being the best laboratory indicator, but no analysis or comparison was made for the red blood cell count (hemoglobin, hematocrit).

Streptococcus A β-haemolyticus, Streptococcus pneumoniae, Coagulase-negative staphylococci and *Haemophilus influenzae* are the most common organisms recovered in acute mastoiditis [15, 19, 20]. Results of our study show that intraoperative swabs were not obtained from 36 children (64.28%), in 15 cases (26.78%) swabs were negative, *Streptococcus pneumoniae* and *Coagulase-negative staphylococci* were isolated in 3 cases (5.35%) and 2 cases (3.57%), respectively. Failure to collect swabs can be explained by the assessment of the ENT surgeon that taking intraoperative swab would be inappropriate due to preoperative, often prolonged multiple antibiotic treatment, which was confirmed by negative findings of swabs taken under these conditions.

Without appropriate treatment, mastoiditis may rapidly progress to severe extracranial and intracranial complications. So far, there are no clearly defined criteria for performing mastoidectomy in children. Indications for mastoidectomy include elevated white blood cell count, retroauricular abscess and fever. According to the clinical practice at the Department of the Ear, Nose and Throat Diseases of the Clinical Center of Vojvodina in Novi Sad, indications for cortical mastoidectomy in childhood include: acute coalescent (purulent) mastoiditis with subperiosteal abscess or other forms of exteriorization, purulent otomastoiditis without exteriorization, and latent mastoiditis with positive otomicroscopic findings, prolonged clinical course with or without positive laboratory markers for active purulent infection.

Conclusion

Mastoiditis in children is most common among children up to 24 months of age. It has a seasonal tendency with the highest peak during the autumn-winter period, with a statistically significant difference compared to the spring-summer period ($p = 0.049$). In nearly half of the cases, clinical manifestations of mastoiditis appear three weeks after the onset of the first symptoms of middle ear inflammation, whereas the key otomicroscopic finding for all three types of mastoiditis is stiffness and thickening of the tympanic membrane.

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COCHLEAR IMPLANT SURGERY AT THE CLINICAL CENTER OF VOJVODINA – TEN-YEAR EXPERIENCE

KOHLEARNA IMPLANTACIJA U KLINIČKOM CENTRU VOJVODINE – DESETOGODIŠNJE ISKUSTVO

Dragan DANKUC, Darja ŠEGAN, Zoran KOMAZEC, Ljiljana VLAŠKI, Slobodanka LEMAJIĆ KOMAZEC and Ivana SOKOLOVAC

Summary

Introduction. The first cochlear implant surgery was performed at the Center for Cochlear Implantation of the Department of Ear, Nose and Throat Diseases, Clinical Center of Vojvodina in 2002 after long preparations and that was the first successful cochlear implantation in Serbia. **Material and Methods.** Over the period from November 2002 to November 2013, 99 patients underwent surgical procedures and 100 cochlear implants were placed. **Results.** The analysis encompassed 99 patients, the youngest and the oldest one being 1 year and 61 years old, respectively. Prelingual and postlingual deafness developed in 84 (84.9%) and in 15 (15.1%), respectively. Postlingual deafness was observed in all 11 adult patients. The prelingual deafness was diagnosed in 84 (95.4%) children, whereas in four (4.6%) children it occurred after the development of speech between 6 and 8 years of age. Progressive hearing loss was observed in 11 patients - seven adults and four children. The majority of our patients, i.e. 74 (74.75%) manifested idiopathic deafness of unknown cause. A range of usually reported hearing loss etiologies included ototoxic medications in seven (7.07%), hereditary factor in six (6.06%), and bacterial meningitis in four (4.04%) patients. Somewhat less common causes were perinatal hypoxia in three (3.03%), premature birth in three (3.03%), Down syndrome in one (1.01%), and chronic otitis media in one (1.01%) patient. **Conclusion.** Both intraoperative and postoperative complications were analyzed in the investigated patient population. The complications developed in 11 patients, i.e. in 10.5% of 105 surgical procedures. The majority of procedures (89.5%) were not accompanied by any post-surgical complications. Unsuccessful implantation in a single-step procedure and transient facial nerve paralysis can be considered most frequent among our patients, whereas cochlear ossification and transient ataxia occurred more rarely. Stimulation of facial nerve, intraoperative perilymph liquid gusher, device failure and late infections were recorded extremely rarely.

Key words: Cochlear Implants; Cochlear Implantation; Risk Factors; Hearing Loss; Deafness; Intraoperative Complications; Postoperative Complications; Infant; Child; Adolescent; Adult; Middle Aged

Sažetak

Uvod. Centar za kohlearnu implantaciju Klinike za bolesti uva, grla i nosa Kliničkog centra Vojvodine započeo je rad nakon višegodišnjih priprema 2002. godine kada je i urađena prva implantacija. U ovom centru, dakle, izvedena je prva uspešna kohlearna implantacija u Srbiji. **Materijal i metode.** U periodu od novembra 2002. do novembra 2013. godine operisano je 99 pacijenata, a pritom je ugrađeno 100 kohlearnih implantata. **Rezultati.** Analizom je obuhvaćeno 99 pacijenata, od kojih je najmlađi pacijent bio star jednu godinu a najstariji 61 godinu. Kod većine pacijenata, njih 84 (84,9%), gluvoća se razvila prelingvalno a kod 15 (15,1%) postlingvalno. Svih 11 odraslih pacijenata imali su gluvoću razvijenu postlingvalno, dok je u grupi dece 84 (95,4%) ogluvelo pre razvoja govora, a njih četvoro (4,6%) nakon razvoja govora, u uzrastu između 6 i 8 godina. Ukupno 11 pacijenata imalo je progresivni tip razvoja nagluvosti, 7 odraslih i 4 dece. Kod najvećeg broja pacijenata gluvoća je *idiopatska*, odnosno nepoznatog uzroka, i to kod 74 pacijenta (74,75%); među ostalim uzrocima najčešće se navode *ototoksični lekovi*, kod 7 pacijenata (7,07%), *nasledni faktor* kod 6 pacijenata (6,06%) i *bakterijski meningitis* kod 4 pacijenta (4,04%). Od ostalih, manje zastupljenih uzroka navode se *perinatalna hipoksija* kod 3 pacijenta (3,03%), *prevremena rođenost* kod 3 pacijenta (3,03%), *Daunov sindrom* kod jednog (1,01%) i *hronična upala srednjeg uva* kod jednog pacijenta (1,01%). **Zaključak.** Intraoperativne i postoperativne komplikacije analizirane su u ispitivanoj grupi pacijenata. Komplikacije su se javile kod 11 pacijenata od 105 (10,5%) izvršenih operacija. Većina operacija, njih 89,5%, prošlo je bez komplikacija. Od češćih komplikacija zabeležene su neuspešna implantacija u prvom aktu i prolazna oduzetost facijalnog živca. Od ređih komplikacija javile su se osifikacija kohlee i prolazna ataksija. Vrlo retke su bile stimulacija facijalnog živca, intraoperativno pojačano isticanje perilimfe, kvar aparata i kasna infekcija.

Ključne reči: Kohlearni implanti; Kohlearna implantacija; Faktori rizika; Gubitak sluha; Gluvoća; Intraoperativne komplikacije; Postoperativne komplikacije; Odojče; Dete; Adolescent; Odrasli; Odrasli, srednjih godina

Introduction

The first cochlear implant surgery was performed at the Center for Cochlear Implantation of the Department of Ear, Nose and Throat Diseases, Clinical Center of Vojvodina in 2002 after long preparations and that was the first successful cochlear implantation in Serbia.

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Abbreviations

ENT – ear, nose and throat
CMV – cytomegalovirus
Cx – connexin
DNA – deoxyribonucleic acid
TEOAE – Transient-Evoked Otoacoustic Emission

The first modern cochlear implant, Nucleus R 24, was placed on November 20th, 2002 in a female patient with postlingual hearing impairment (patient I. J., aged 40). The surgery was performed by Prof. J. Jori, MD, PhD, Prof. J. G. Kiss from the Ear, Nose and Throat (ENT) Clinic Szeged, Hungary and Prof. Dragan Dankuc, MD, PhD from the Department of Ear, Nose and Throat Diseases in Novi Sad.

Subsequently, for the first time in Serbia, Prof. Dragan Dankuc, MD, PhD, assisted by Prof. J. Jori, MD,PhD, performed the first implantation of an artificial inner ear – a cochlear implant Nucleus R 24. Ever since, the cochlear implant surgery in Novi Sad has been exclusively performed by an experienced team led by eminent professors Zoran Komazec, Dragan Dankuc, Ljiljana Vlaški, Slobodanka Lemajić Komazec, surdology specialists Spomenka Nedeljkov, Ivana Sokolovac and Oliver Vajs as well as engineers Tibor Mendrei and Vladimir Mrđanov [1, 2].

Material and Methods

Over the period from November 2002 to November 2013, 99 patients underwent surgical procedures and 100 cochlear implants were placed. In four patients, a single-stage surgery was not applicable because of intraoperative complications, thus successful implantation was accomplished in the second procedure. Late postoperative complications required the revision surgery (reimplantation) in one patient, whereas one female patient underwent bilateral cochlear implantation.

Results

The analysis encompassed 99 patients, the youngest and the oldest one being 1 year and 61 years old, respectively. The patient population included 11 (11.1%) adults and 88 (88.9%) children as the major population. The gender ratio was 56 (56.6%) females to 43 (43.4%) males (**Graph 1a**).

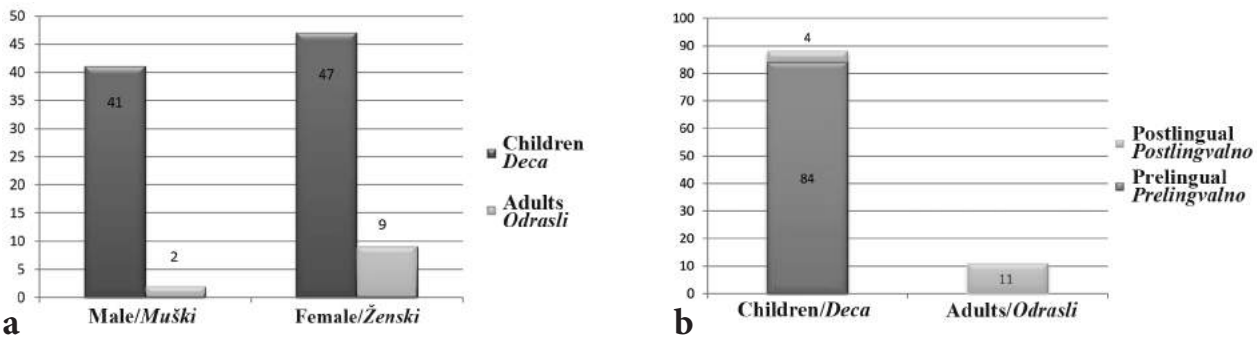
Prelingual and postlingual deafness developed in 84 (84.9%) and in 15 (15.1%), respectively. Postlingual deafness was observed in all 11 adult patients. Prelingual deafness was diagnosed in 84 (95.4%) children, whereas in four (4.6%) children it occurred after the development of speech, between 6 and 8 years of age (**Graph 1b**). Progressive hearing loss was observed in 11 patients - seven adults and four children.

The distribution of patients by the year when implant surgery was performed and their age is presented in (**Graph 2**).

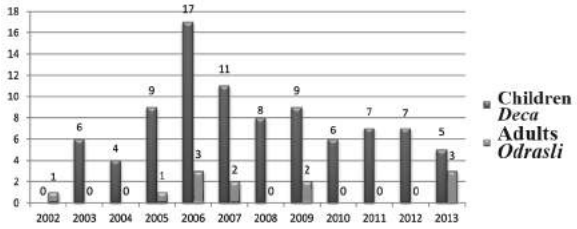
The average number of surgeries performed per year is 8.4, with the largest number of procedures [20] recorded in 2006.

The majority of our patients, i.e. 74 (74.75%) manifested *idiopathic* deafness of unknown cause. A range of usually reported hearing loss etiologies included *ototoxic medications* in seven (7.07%), *hereditary factor* in six (6.06%), and *bacterial meningitis* in four (4.04%) patients. Somewhat less common causes were *perinatal hypoxia* in three (3.03%), *premature birth* in three (3.03%), *Down syndrome* in one (1.01%), and *chronic otitis media* in one (1.01%) patient (**Graph 3**).

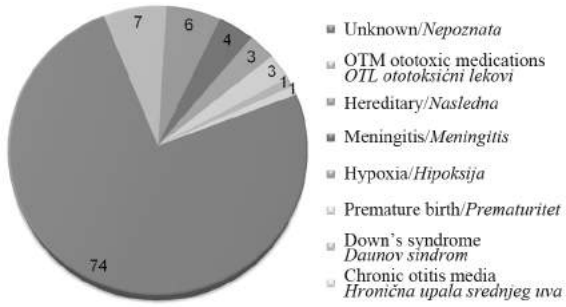
Potential risk factors for deafness recorded in our patients included positive family history of hearing loss in 13 (13.1%), premature birth in 11 (11.1%) patients as well as administration of ototoxic medications from the group of aminoglycosides to the mother during pregnancy or to the child in 10 (10.1%) cases. Significant perinatal hypoxia and postpartum incubation period were recorded in eight (8.08%) patients. History of bacterial meningitis was reported in five (5.05%) patients. Prolonged neonatal jaundice was observed in five (5.05%) children. Examination by a pediatric psychologist revealed symptomatic delay in development in four (4.04%) children. Birth weight under 1500 g was recorded in four (4.04%) newborns. Three (3.03%) patients had history of chronic otitis media, whereas sepsis and neonatal intracranial hemorrhage were recorded in three (3.03%) patients each. Falling-associated head injuries, febrile convulsions and presence of cytomegalovirus (CMV) anti-



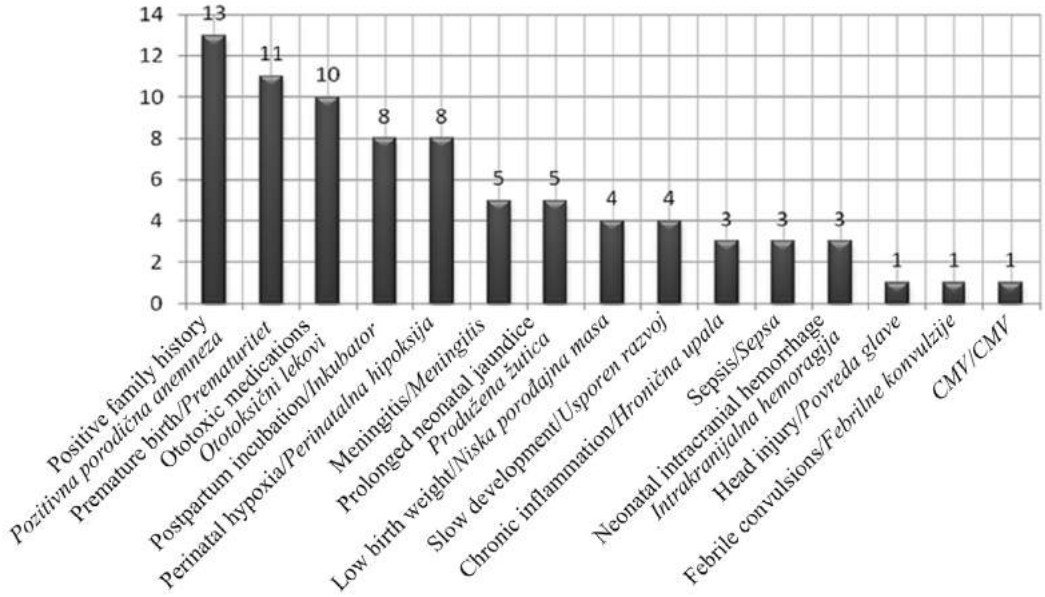
Graph 1a and b. Distribution of patients by gender and age (a) and by the type of deafness (b)
Grafikon 1a i b. *Distribucija pacijenata prema polu i uzrastu (a) i prema vrsti oštećenja sluha (b)*



Graph 2. Number of patients who underwent implant surgery according to age
Grafikon 2. *Broj pacijenata prema uzrastu kada je rađena implantacija*



Graph 3. Etiology of hearing loss
Grafikon 3. *Etiologija gubitka sluha*



Graph 4. Incidence of risk factors for sensorineural hearing impairment
Grafikon 4. *Incidencija faktora rizika za senzorineuralno oštećenje sluha*

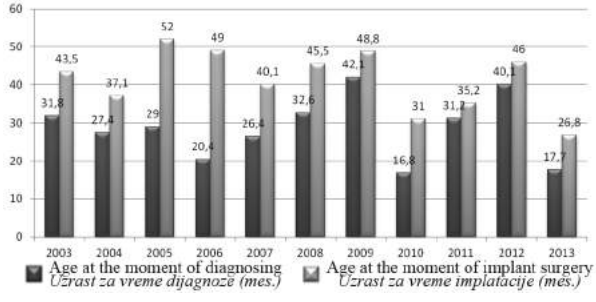
bodies were recorded in one (1.01%) patient each (**Graph 4**).

The analysis of the age at which the hearing impairment had been observed was performed according to heteroanamnesis based on parents' reports. The average age at which the parents reported the suspect hearing impairment or underdevelopment of speech is 13.12 months, ranging from 0 months (parents reported the hearing loss from the very birth) to maximum 36 months, when hearing loss was diagnosed in three (3.4%) children by audiology screening.

The analysis encompassed patients' age at the moment of establishing the diagnosis and at implant surgery, as well as the total time between the diagnosis and implant surgery (**Graph 5**).

As is can be concluded from the graph, deafness was diagnosed before the 4th year of age with subsequent implantation before the 5th year of age in all children. This strongly indicates the tendency towards early diagnosis and implant surgery as well as shortening the period between the confirmation of diagnosis and implantation procedure [3–5].

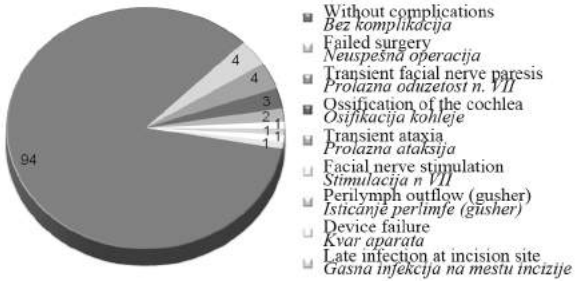
Both intraoperative and postoperative complications were analyzed in the investigated patient population. The complications developed in 11 pati-



Graph 5. Patients' age at the moment of diagnosing and of implant surgery
Grafikon 5. *Uzrast pacijenta u trenutku postavljanja dijagnoze i implantacije*

ents, i.e. in 10.5% of 105 surgical procedures. Implant placement in a single-stage procedure was not possible in four cases because of acute otitis media in one patient (diagnosed during surgery) and the ossification of the cochlea that prevented electrode array placement in the remaining three patients. The second surgery was successfully performed in all four patients, without any subsequent complications. Transient facial nerve paresis was recorded in four (4.04%) patients, which completely subsided two months after surgery and administration of appropriate therapeutic treatment. Transient ataxia was observed in two (2.02%) patients [6].

Some rare complications such as facial nerve stimulation associated with electro stimulation of the cochlea (late complication occurring one year after surgery), device failure identified at tuning and late infection were observed in one (1.01%) patient each. All complications were successfully managed by incision and drainage, while preserving the functionality of the device (**Graph 6**).



Graph 6. Cochlear implant complications
Grafikon 6. *Komplikacije kohlearne implantacije*

Discussion

The youngest patient was only 1 year old (i.e. 14.7 months) at the moment of surgery. In 27 (30.7%) children, the surgery was performed before the age of 3 years, whereas 50 (56.8%) children underwent implantation procedure before the age of 4 years. According to the research of Valencia et al. from the ENT Clinic of Minnesota Medical Center, U.S.A., a completely safe procedure of implant placement can be accomplished even in infants under 12 months of age (their youngest patients was 6.6 months old) provided that there are no medical risks associated with anesthesia at this age. The aims of early implantation are to reduce the hearing deprivation period and to improve the development of auditory performance [7].

In adult patients with postlingual deafness, comprehensive evaluation of the ratio between potential benefit and risks associated with surgery itself and potential comorbidities should be performed. However, the age itself is not the criterion for excluding the patient from implantation procedure unless other risk factors are present [8, 9].

Habilitation process in children who were completely deaf until the moment of implant switch-on implicates the appropriate auditory training aimed at establishing acoustic memory and then, as a second stage, the development of speech [10].

A wide range of etiological factors may be responsible for sensorineural hearing impairment, including intrauterine, perinatal and postnatal ones.

More than 60% of all prelingual hearing impairments are attributed to genetic factors (Vivero et al.) and genetic deafness is either nonsyndromic or syndromic. Nonsyndromic hereditary deafness is mostly attributed to the defect of connexin 26 (Cx26), a structural protein located on the long arm of human chromosome 13. The absence and dysfunction of this protein cause the disturbance of intracellular junctions resulting in the dysfunction of receptor cells of the inner ear and their irreversible loss. Some more rare genetic conditions are usually inherited in a mitochondrial deoxyribonucleic acid (DNA) pattern or are syndrome-related [11–13].

Among the patients included in our study, genetic analysis revealed the mutation in the gene encoding connexin 26 in one patient only. The prevalence of such mutations is believed to be higher; however, genetic analysis aimed at identifying the etiology of hearing impairments are not a part of routine practices in our country. Moreover, the majority of such mutations are inherited through autosomal recessive inheritance pattern that corresponds with the negative family history of hearing disorder, even though more than half of hearing impairments are considered genetically related.

Ototoxic medications were reported as the cause of hearing loss in seven (7.07%) of our patients. In these cases, hearing loss was directly associated with the administration of ototoxic medications, whereas application of drugs from the category of aminoglycosides (predominantly Gentamycin) during the intrauterine or postnatal period was identified as a risk factor in 10 (10.10%) patients. Histopathological studies have demonstrated that outer receptor cells are most susceptible to aminoglycosides ototoxicity, that is, a symmetrical, irreversible, high frequency sensorineural hearing loss occurs as the first stage. Exposure of the child to increased cumulative drug doses rapidly compromises the hearing ability in speech relevant frequencies.

According to numerous authors, timely prevention of adverse effects of aminoglycosides, even in cases when their application is justified and inevitable, could be accomplished through routine application of relevant diagnostic methods, especially Transient-Evoked Otoacoustic Emission (TEOAE), which is a highly sensitive, non-invasive and objective technique. Such monitoring throughout the period of aminoglycoside therapy would enable timely detection of hearing loss in children hospitalized for severe Gram-negative bacterial infections and consequent reduction of drug dosage or further adjustment of treatment regimen [14].

According to the data from the literature, bacterial meningitis has been reported as a risk factor in

6.10% of children (Bielecki et al.). In these patients, the changes of the inner ear are highly progressive involving fibrosis or ossification of the cochlea. In case of prolonged delay of surgical procedure, the insertion of electrode could be compromised due to complete obliteration of membranous labyrinth. Thus, an early implantation procedure is highly advisable within maximum 6 months after meningitis [15–17].

In our study, perinatal hypoxia of newborns was identified as a cause of hearing impairment in three (3.03%) and as a positive risk factor in eight (8.08%) patients. Premature birth was believed to be a cause of hearing loss in three (3.03%) patients. Prematurity, that is, delivery before the 37th gestation week was identified as a positive risk factor in as many as 11 (11.1%) patients from our study sample. According to international reports, prematurity is confirmed as a risk factor for acquired sensorineural hearing disorder; however, it is quite difficult to estimate its incidence since prematurity is commonly associated with a range of comorbidities and risk factors. Premature birth with subsequent period in incubator was observed in eight (8.08%) children, which corresponds to the number of prematurely born children in our case study [18–20].

Down syndrome was identified as a cause of deafness in one (1.01%) patient. According to some authors, some 4–20% of children with Down syndrome manifest sensorineural hearing loss. Since Down syndrome is the most common genetic disorder with an incidence of 1:800 live-born children, the aforementioned percentage is not negligible. In the past, children with Down syndrome were not considered candidates for cochlear implantation and subsequent habilitation because of apparent morphological problems and learning disorders. However, such an approach has recently been abandoned thanks to novel information and positive experiences. Regrettably, the postoperative outcomes of cochlear implantation in a child with Down syndrome were not satisfactory in our case. A number of authors reported very good postoperative outcomes in such children, especially when implanted at an early age [21, 22].

Chronic cholesteatomic otitis media has been identified as a cause of deafness in one (1.01%) adult female patient. This is not a very common situation since cholesteatomic inflammations rarely result in complete bilateral deafness.

Besides the aforementioned risk factors, a range of other conditions associated with perinatal period was recorded in our patients: prolonged neonatal jaundice in five (5.05%), extremely low birth weight (below 1500 g) in four (4.04%), perinatal sepsis in three (3.03%), and intracranial hemorrhage in three (3.03%) children. All these factors are regarded as risk factors for hearing loss in the reports of other authors.

A range of further risk factors observed in our patients includes symptomatically retarded psychomotor development in four (4.04%) patients, chronic otitis media in three (3.03%), head injury in one (1.01%), febrile convulsions in one (1.01%), and positive diagnosis to cytomegalovirus associated with progressive hearing loss in one female patient (1.01%).

The average age of children at which the parents suspected hearing disorder was 13.12 months. In 15 children (17.04%), the parents noticed the hearing impairment and reported it to the physician to be diagnosed when their child was two or more years old, which strongly suggests the denial of parents to face the expected diagnosis. In view of the well-established fact that early diagnosis and amplification is crucial for proper development of a child, such a delay represents highly harmful time loss for the child on a long-term basis.

Another possibility of time-loss pertains to the period between the moment of establishing final diagnosis and implantation procedure. As shown in Graph 6, the average period is one year showing decreasing tendency, thus greatly reducing the time-loss and increasing probability of successful outcomes of the procedure [23, 24].

Complications associated with cochlear implantation can be categorized as major of minor ones. Major complications include those resulting in the necessity for revision surgery, explantation, reimplantation, severe disease or even lethal outcomes. Minor complications resolve spontaneously or can be managed by conservative therapy and do not require any prolonged hospitalization of the patient [25, 26].

In our Center for Cochlear Implantation of the Clinical Center of Vojvodina, complications were observed in 11 patients, that is, 10.05% of performed surgical procedures. This incidence corresponds to the incidence rates reported from related centers worldwide, being around 10%. In four (4.04%) patients treated at our Center, the single-stage surgery was not initially possible, thus implantation was postponed and successfully accomplished in the second stage. In one patient, successful implantation using another type of electrode was performed at the same side. In other three patients, the second-stage surgery was performed at the other side with a favorable outcome.

In cases of congenital malformations of the inner ear (two of our pediatric patients), the placement of the electrode into the altered cochlea could not be accomplished in spite of the surgical navigation system.

Transient postoperative peripheral facial nerve paresis was observed in four (4.04%) patients. This condition is considered a minor complication and is explained by transient edema of facial nerve in the fallopian canal induced by the heating of its immediate surrounding structures during lateral tympanotomy. This impairment of nerve function was transient in all our patients. The symptoms resolved completely within the first month after surgery and administration of conservative

corticosteroid therapy without a need for subsequent surgical nerve decompression.

Transient ataxia was noticed in two (2.02%) patients, who presented with symptoms of postoperative instability and nausea. The patients responded well to symptomatic therapy and recovered rapidly without any consequences. This complication might be explained by perilymph and endolymph leakage during formation of cochleostoma. After the surgery, upon reestablishment of the homeostasis of the semicircular canals, ataxia resolves spontaneously without a need for any specific therapy.

Postoperative facial nerve stimulation was observed in one (1.01%) female patient. According to the available literature, this major complication of cochlear implantation occurs in some 0.31-14% cases. Switching-off the electrodes that directly stimulate the nerve might be a possible solution in such cases; however, it can result in reduced sound perception, which was the case in our patient. Thus, implantation of the second ear was performed to accomplish satisfactory overall hearing performance through bilateral stimulation at sub maximal level. Instead of electrode reprogramming, facial nerve stimulation can be managed by botulinum toxin injections; however, this therapeutic option requires repeated administration at 3- to 6-month intervals [27, 28].

Increased intraoperative perilymph gusher was observed in one (1.01%) patient. It is considered a minor complication, which was successfully managed during surgical procedure without affecting the outcome.

Device failure at tuning occurred in one (1.01%) patient. Such failures are considered major complications, as they inevitably require second surgery, which was successfully performed in our patient.

Skin infection in implant region developed as a late complication in one (1.01%) adult patient several months after surgery. Prophylactic perioperative application of antibiotics can greatly reduce such infections, but other authors also reported the occurrence of this complication with the incidence of about 1%. In our patient, the infection was successfully managed by drainage and antibiotic therapy while preserving the functionality and position of the implant.

Complications reported in the literature, such as electrode extrusion, skin necrosis over the implant or meningitis, which is considered to be the most severe postoperative complication, have not been recorded in our Center since the very beginning. Absence of postoperative meningitis in patients treated at our Center can be attributed to timely pneumococcal vaccination of children.

Conclusions

The majority of our patients, i.e. 84 (84.9%) manifested prelingual hearing loss, whereas postlingual disease type was observed in 15 (15.1%) cases.

Deafness of unknown etiology was recorded in 74 (74.75%) patients. Among known causes of hearing loss, administration of ototoxic drugs was the most prevalent one followed by hereditary factors and somewhat fewer cases of meningitis, perinatal hypoxia and premature birth. Down syndrome and chronic otitis media were recorded in only one patient, each.

Positive family history of sensorineural hearing disorder was identified as the most common risk factor. Premature birth, administration of ototoxic drugs, postpartum incubation and perinatal hypoxia were observed more rarely. Other risk factors identified within our patient population included meningitis, prolonged postpartum jaundice, low birth weight, symptomatic developmental disorder, chronic otitis media, sepsis, intracranial hemorrhage, head injury, febrile convulsions, and cytomegalovirus infection.

In all children, the deafness was diagnosed before the 4th year of age, and the implantation was performed before the 5th year of age.

The majority of procedures (89.5%) were not accompanied by any post-surgical complications. Unsuccessful implantation in a single-step procedure and transient facial nerve paralysis can be considered most frequent among our patients, whereas cochlear ossification and transient ataxia occurred more rarely. Stimulation of facial nerve, intraoperative perilymph liquid gusher, device failure and late infections were recorded extremely rarely.

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ACOUSTIC ANALYSIS OF VOICE IN CHILDREN WITH COCHLEAR IMPLANTS

AKUSTIČKA ANALIZA GLASA KOD DECE SA KOHLEARNIM IMPLANTATOM

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Summary

Introduction. The focus of this study was the analysis of objective acoustic characteristics of voice in children with cochlear implants. The objective of this study was to compare acoustic parameters of voice in children with cochlear implants and normal hearing children of the same age, and to determine differences, if there were any. **Material and Methods**. There were 60 children (aged from 6 to 13) included in this prospective study. They were divided into 2 groups: children with cochlear implants (30) and normal hearing children with normal speech development (30). The most stable voice sample was analyzed using a software program *Dr Speech: Vocal Assessment*. Objective acoustic analysis of voice included 13 acoustic parameters. **Results**. Standard deviation of fundamental frequency was significantly (p=0.000) higher in children with cochlear implants, as well as the values of harmonic to noise ratio (p=0.003) and signal to noise ratio (p=0.000) parameters. Values of jitter %, shimmer %, normalized noise energy, fundamental frequency tremor and amplitude tremor showed no significant differences between the two groups. However, the values of parameters that refer to voice frequency (habitual fundamental frequency, mean fundamental frequency, min fundamental frequency and max fundamental frequency) and the mean value of voice intensity (p=0.004), were significantly higher in the boys and the girls with cochlear implants than in the normal hearing children. **Conclusion.** Gender non-related parameters of hoarseness did not show significant differences between the children with cochlear implants and the normal hearing children; the results of cochlear implantation and voice and speech education were therefore positive. However, the children with cochlear implants of both gender showed significantly higher values of voice intensity, voice pitch and insufficient control of voice pitch variation.

Key words: Acoustics; Voice; Voice Quality; Speech Therapy; Child; Adolescent; Cochlear Implants

Sažetak

Uvod. Predmet ovog istraživanja je analiza objektivnih akustičkih karakteristika glasa dece sa kohlearnim implantatom. Postavljen je osnovni cilj istraživanja da se utvrdi eventualno postojanje razlika u objektivnim akustičkim parametrima glasa kod dece sa kohlearnim implantatom i zdrave dece. **Materijal i metode.** Prospektivnom studijom obuhvaćeno je 60 dece uzrasta od 6 do 13 godina. Ispitanici su podeljeni u 2 grupe: deca sa kohlearnim implantatom (30) i deca urednog sluha sa dobrim govornim razvojem (30). Najstabilniji segment glasovnog uzorka analiziran je pomoću softverskog programa *Dr Speech: Vocal Assessment.* Objektivna akustička analiza glasa obuhvatala je 13 akustičkih parametara. **Rezultati.** Standardna devijacija fundamentalne frekvencije statistički je značajno veća kod dece sa kohlearnim implantatom (p = 0,000), kao i vrednosti parametara HNR (p = 0,003) i SNR (p = 0,000). Vrednosti parametara *jitter* %, *shimmer* %, NNE, tremor fundamentalne frekvencije i tremor amplitude statistički se značajno ne razlikuju između dve grupe. Međutim, vrednosti akustičkih parametara koje se odnose na visinu glasa (habitualna fundamentalna frekvencija, srednja vrednost fundamentalne frekvencije, minimalna fundamentalna frekvencija i maksimalna fundamentalna frekvencija), kao i prosečna vrednost intenziteta glasa (p = 0,004), statistički su značajno veće kod dečaka i devojčica sa kohleranim implantatom nego kod dece urednog sluha. **Zaključak.** Vrednosti polno nezavisnih akustičkih parametara promuklosti (*jitter* %, *shimmer* %, NNE, tremor fundamentalne frekvencije i tremor amplitude) ne razlikuju se značajno kod dece sa kohlearnim implantatom u odnosu na decu urednog sluha, te su u tom smislu rezultati implantacije i edukacije glasa i govora kod dece sa kohlearnim implantatom pozitivni. Međutim, prosečne vrednosti intenziteta glasa i parametara koji se odnose na visinu glasa i kontrolu varijacije visine glasa veće su kod dece sa kohlearnim implantatom, što ukazuje na njihovu nedovoljnu slušnu kontrolu.

Ključne reči: Akustika; Glas; Kvalitet glasa; Govorna terapija; Dete; Adolescent; Kohlearni implanti

Introduction

A cochlear implant is a sophisticated electronic device which stimulates the auditory nerve directly, and thus provides a sense of sound to a person who is profoundly deaf or has a severe degree of hearing loss [1]. Hearing has three important functions in children: auditory system development, speech development and personality development [2]. Children with hearing impairment

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Abbreviations

F0 – fundamental frequency
SD – standard deviation
HNR – harmonic to noise ratio
SNR – signal to noise ratio
NNE – normalized noise energy
NH – normal hearing children
CI – children with cochlear implants
Hz – hertz
dB – decibel
HNR – harmonic to noise ratio
SNR – signal to noise ratio
NNE – normalized noise energy

develop without the necessary auditory stimulus. The lack of sound and the lack of positive enviromental impact confuses a deaf child and inhibits him/her to develop speech [3, 4].

It is well known that speech and voice characteristics of deaf people differ signifficantly from those of normal hearing people. Speech of the hearing impaired is characterized by the disorder of syntax, rhythm, resonance and articulation [5]. There are problems with the articulation of vowels and consonants [6, 7], such as failure to differentiate vowels [8, 9] and lack of adequate differentiation between voiced and voiceless consonants [10–12]. Many deaf speakers can produce isolated phonemas correctly, but are still unable to combine them smoothly in connected speech, which results in unintelligible speech [13]. According to Dale, deaf children are likely to have a restricted vocabulary. A normal hearing 5-year old child may have a vocabulary of approximately 2000 words, while the vocabulary of a profoundly deaf child may consist of only 250 words [14].

Auditory feedback is considered important for the control of voice and speech characteristics such as fundamental frequency (F0), intensity and voice quality [15]. Voice of the deaf can be too loud or too soft, or vary irregularly [16, 17]; it is usually described as tense, flat, breathy, harsh, with differences in pitch and intonation [18]. Prelingually deaf people generally have a higher fundamental frequency of voice than normal hearing people [8, 19, 20]. They either vary pitch less than normal hearing speakers, producing a monotone voice [21], or show excessive pitch variation, resulting in abrupt changes [19, 22].

There are a few factors that affect speech perception in children with cochlear implants: the age of onset and the degree of hearing impairment, the duration of hearing impairment, the age of receiving a cochlear implant, the duration of cochlear implant usage, the duration of educational programme, child's characteristics and family involvement [3, 23].

Numerous studies have proved positive effects of cochlear implantation, which enables hearing and leads to a significant improvement in the sound perception; however, studies that focus on the effect of cochlear implantation on the sound structure of voice and speech in hearing disabled children are scarce. The focus of this study was the analysis of objective acoustic characteristics of voice in children with cochlear implants. The objective of this study was to compare acoustic parameters of voice in children with cochlear implants and normal hearing children of the same age, and to determine differences, if there were any.

Material and Methods

This prospective study was conducted during 2012 and 2013 at the Department of Ear, Nose and Throat Diseases of the Clinical Center of Vojvodina, and in the "Kosta Trifković" primary school in Novi Sad. The study included 60 children, aged from 6 to 13, divided into two groups: children with cochlear implants (30) and normal hearing children with normal speech development (30). This was confirmed by examination of experienced speech therapist. The following methods were applied in the study:

1. Patients' history provided data considering the degree of hearing impairment, usage of hearing aids, the age of cochlear implantation and the duration of speech education.
2. The voice sample was obtained in a silent room, with a child sitting in a comfortable position, speaking with the usual voice pitch and intensity. Voice (long vowel A....) was recorded using a microphone positioned 5 cm from the mouth (model *Behringer ultravoice* XM 8500) with a mixette (*Eurorack* UB 520 *ultra low-noise design 5 – input 2 bus mixer*). The most stable voice sample was analyzed using the software program *Dr Speech: Vocal Assessment*. Objective acoustic analysis of voice included 13 acoustic parameters: habitual F0, mean F0, standard deviation (SD) of F0, maximal and minimal F0, mean F0 intensity, jitter %, shimmer %, harmonic to noise ratio (HNR), signal to noise ratio (SNR), normalized noise energy (NNE), F0 tremor and amplitude tremor.
3. The obtained data were statistically processed by the Statistical Package for the Social Sciences *(SPSS) 17* program, and analyzed using a descriptive statistics method and by applying the relevant statistical significance tests: t- test, *Mann Whitney U test*, and *Kruskall Wallis test*.

Results

The group of normal hearing children consisted of 16 boys (54%), their average age being 8, and 14 girls (46%), their average age being 7.93. The group of children with cochlear implants consisted of 15 boys (50%), whose average age was 9.73, and 15 girls (50%), whose average age was 10.73. The average degree of hearing impairment in this group was 98.17 dB. Prior to cochlear implantation, 80% of children used hearing aids for an average period of 21.13 months. The age of co-

Table 1. The average values of gender non-related acoustic parameters
Tabela 1. *Prosečne vrednosti polnonezavisnih akustičkih parametara kod kojih nema statističke značajnosti*

		N	$\bar{X}$	SD	Minimum	Maximum	t	p
Jitter	NH	30	0.2793	0.09716	0.14	0.49		
	CI	30	0.3747	0.38177	0.15	2.16	-1.325	0.190
	Total/*Ukupno*	60	0.3270	0.28034	0.14	2.16		
Shimmer	NH	30	3.6677	1.33219	1.57	6.38		
	CI	30	2.6560	2.49943	0.07	9.83	1.956	0.055
	Total/*Ukupno*	60	3.1618	2.05016	0.07	9.83		
F0 Tremor	NH	30	4.1300	3.78780	1.12	14.33		
	CI	30	3.7047	4.01716	1.00	14.61	0.422	0.675
	Total/*Ukupno*	60	3.9173	3.87687	1.00	14.61		
NNE	NH	30	-14.9907	3.57226	-23.40	-10.21		
	CI	30	-14.3683	5.52759	-23.14	-1.65	-0.518	0.606
	Total/*Ukupno*	60	-14.6795	4.62483	-23.40	-1.65		
Amp Tremor	NH	30	4.0280	3.03566	1.03	12.30		
	CI	30	3.3040	2.75810	1.00	12.68	0.967	0.338
	Total/*Ukupno*	60	3.6660	2.89860	1.00	12.68		

jitter – varijabilnost frekvencije; shimmer – varijabilnost intenziteta; FO – fundamental frequency – *visina govornog glasa;* NH – osobe sa normalnim sluhom; HNR – harmonic to noise ratio/*odnos harmonijskih i šumnih elemenata glasa*; SNR – signal to noise ratio/*odnos zvučnih i šumnih komponenti glasa*; NNE – normalized noise energy/*magnituda energije šuma u glasu*

chlear implantation was on average 3.27 years in the boys, and 4.90 years in the girls. In the boys, the education of speech started on average 66.33 days after cochlear implantation and in the girls after 50 days. The average duration of speech education was 46.40 months in the boys and 36.80 months in the girls.

The values of gender non-related acoustic parameters (jitter %, shimmer %, NNE, F0 tremor and amplitude tremor) showed no significant differences between the two groups (p=0.675 – 0.055). Apart from slightly higher values of shimmer parameter in the normal hearing children, the average values of these acoustic parameters were within the normal range (**Table 1**).

Significantly higher values of SD F0 (p=0.000), HNR (p=0.003) and SNR (p=0.000) parameters were found in the children with cochlear implants (**Table 2**).

All gender related acoustic parameters that refer to voice frequency (habitual F0, mean F0, min F0 and max F0) showed statistically significant differences; all these parameters were higher in the boys and the girls with cochlear implants than in the normal hearing children.

A significant difference was found in the values of parameters: habitual F0 (p=0.011), mean F0 (p=0.011), min F0 (p=0.024) and max F0 (p=0.010). These values were higher in the boys with cochlear implants than in the normal hearing boys (**Table 3**).

A significant difference was found in the values of parameters: habitual F0 (p=0.005), mean F0 (p=0.006), min F0 (p=0.015) and max F0 (p=0.003). These values were higher in the girls with cochlear implants than in the normal hearing girls (**Table 4**).

The mean value of voice intensity was significantly (p=0.004) higher in the children with cochlear implants compared to the normal hearing children (**Table 5**).

Discussion

The values of gender non-related acoustic parameters (jitter %, shimmer %, NNE, F0 tremor and amplitude tremor) showed no significant differences between the two groups. Apart from slightly

Table 2. Statistically significant gender non-related acoustic parameters
Tabela 2. *Statistički značajni polnonezavisni akustički parametri*

		N	$\bar{X}$	SD	Minimum	Maximum	t	p
SDF0	NH	30	2.3420	.73031	1.25	5.14		
	CI	30	5.3487	3.26176	2.11	17.44	-4.927	0.000
	Total/*Ukupno*	60	3.8453	2.79103	1.25	17.44		
HNR	NH	30	15.0107	5.01344	7.59	26.79		
	CI	30	19.6283	6.50978	2.69	31.81	-3.078	0.003
	Total/*Ukupno*	60	17.3195	6.21328	2.69	31.81		
SNR	NH	30	14.3640	4.85531	7.63	25.78		
	CI	30	19.3813	5.40721	10.65	29.93	-3.782	0.000
	Total/*Ukupno*	60	16.8727	5.68845	7.63	29.93		

Table 3. The average values of gender related acoustic parameters in boys
Tabela 3. *Prosečne vrednosti polno zavisnih parametara kod ispitanika muškog pola*

		N	$\bar{X}$	SD	Minimum	Maximum	t	p
Hab F0	NH	16	237.52	21.11211	207.16	286.46	-2.721	0.011
	CI	15	275.78	51.88274	210.68	408.07		
	Total/*Ukupno*	31	256.03	43.08916	207.16	408.07		
Mean F0	NH	16	237.32	21.28874	205.81	286.84	-2.728	0.011
	CI	15	275.46	51.47042	209.19	407.08		
	Total/*Ukupno*	31	255.78	42.87497	205.81	407.08		
Max F0	NH	16	246.63	22.46078	209.00	294.00	-2.762	0.010
	CI	15	287.77	54.93935	213.04	416.04		
	Total/*Ukupno*	31	266.54	45.80044	209.00	416.04		
Min F0	NH	16	231.39	21.09092	202.29	280.89	-2.373	0.024
	CI	15	264.22	50.90472	199.55	397.30		
	Total/*Ukupno*	31	247.28	41.34965	199.55	397.30		

Hab–habitual/*uobičajena*

higher values of shimmer parameter in the normal hearing children, the average values of these acoustic parameters were within the normal range. Therefore, these findings suggest positive results of implantation and voice and speech education of children with cochlear implants. However, the literature data are contradictory: Coelho [18] found higher values of jitter and shimmer in the children with cochlear implants, while in Baudonck's study [24], the values of these parameters were higher in normal hearing children.

Considering other gender non-related parameters, significantly (p=0.000) higher values of SD F0 were found in the children with cochlear implants, which indicates insufficient control of voice frequency variation, probably due to insufficient auditory feedback. Coelho [18] reached the same conclusions, while Baudonck [24] did not find a significant difference of SD F0 values between the children with cochlear implants and the normal hearing children.

On the other hand, significantly higher values of HNR (p=0.003) and SNR (p=0.000) parameters in the children with cochlear implants show that, regarding these parameters, the children with cochlear implants are more successful. The abundance of harmonic tones in the voice of children with cochlear implants could probably be a result of successful voice and speech education.

In the boys aged from 5 to 11, normal values of mean F0 are within the range from 210 to 297 Hz (Wilson [25]. In this study, the values of mean F0 were significantly higher in the boys with cochlear implants (275.46) than in the normal hearing boys (237.32) - p=0.011. The same was found for the habitual F0 parameter. Numerous studies have shown that the voice of the prelingually deaf has a higher fundamental frequency [8, 19, 20]. Considering F0 range, the minimum and maximum F0 value was 264.22 and 287.77 Hz, respectively in the boys with cochlear implants. In the normal hearing boys, the minimum and maximum F0 value

Table 4. The average values of gender related acoustic parameters in girls
Tabela 4. *Prosečne vrednosti polnozavisnih parametara kod ispitanika ženskog pola*

		N	$\bar{X}$	SD	Minimum	Maximum	t	p
Hab F0	NH	14	255.3714	28.03299	220.58	310.39	-3.043	0.005
	CI	15	303.6787	52.81420	184.52	386.20		
	Total/*Ukupno*	29	280.3579	48.61114	184.52	386.20		
Mean F0	NH	14	255.8429	28.33261	221.54	312.09	-2.952	0.006
	CI	15	301.6033	51.09788	184.56	381.70		
	Total/*Ukupno*	29	279.5121	47.11425	184.56	381.70		
Max F0	NH	14	261.0864	28.51947	226.15	317.27	-3.208	0.003
	CI	15	313.7213	54.81274	189.27	400.91		
	Total/*Ukupno*	29	288.3114	50.95431	189.27	400.91		
Min F0	NH	14	250.5464	28.66889	217.24	308.39	-2.597	0.015
	CI	15	287.9973	46.27265	179.27	355.65		
	Total/*Ukupno*	29	269.9176	42.60178	179.27	355.65		

Table 5. The average values of voice intensity
Tabela 5. *Prosečne vrednosti intenziteta glasa*

		N	$\bar{X}$	SD	Minimum	Maximum	t	p
Intensity *Intenzitet*	NH	30	67.35	7.741	58	86	-2.990	0.004
	CI	30	73.02	6.915	53	85		
	Total/*Ukupno*	60	70.18	7.818	53	86		

was 231.39 and 246.63 Hz, respectively, so we can conclude that the voice of children with cochlear implants has a normal F0 range, but that the range is wider and within the scope of higher frequencies than in the normal hearing children.

In the girls aged from 5 to 11, normal values of mean F0 are in the range from 221 to 294 Hz [25]. In the normal hearing girls, the value of mean F0 is within the normal range (255.84), while it is higher in the girls with cochlear implants (301.60). The same was found for the habitual F0 parameter, which is in accordance with the results of other studies [19, 20]. Considering F0 range, the minimum F0 value was 287.99 and maximum 313.72 Hz in the girls with cochlear implants. In the normal hearing girls, the minimum F0 value was 250.54 and maximum 261.08 Hz. During voice and speech education of children with cochlear implants, we should strive to lower the voice frequency and match it to the vocal frequency range of normal hearing children.

The available literature does not offer the comparison of these acoustic parameters separately for male and female gender. Similar to this study, Coelho [18] found higher minimum and maximum values of F0 in children with cochlear implants. Baudonck [24] and Monsen [26] did not find any significant differences considering parameter mean F0. Contrary to our findings, Seifert [27] found lower mean F0 values in children with cochlear implants, and he also found that children implanted before the age of 4 showed no significant deviation regarding F0. This conclusion agrees with the results of many other studies [1, 28, 29] claiming that children who receive a cochlear implant at a younger age have better results in controlling voice pitch.

Normal voice intensity in children is 64 - 78 decibel (dB) [30]. We have found that the children with cochlear implants have a higher value of mean voice intensity (73.02 /dB/) than the normal hearing children (67.35 dB). These results are in accordance with those of other studies proving that children with cochlear implants have higher voice intensity than their normal hearing peers [16, 28]. Children with cochlear implants cannot control their voice precisely enough probably due to inadequate sound perception. On the other hand, Baudonck [24] did not find any significant differences in the voice intensity between children with cochlear implants and normal hearing children.

Conclusion

Gender non-related parameters of hoarseness did not show significant differences between the children with cochlear implants and the normal hearing children; the results of cochlear implantation and voice and speech education are thus sufficient.

However, the children with cochlear implants of both gender showed significantly higher value of voice intensity, voice pitch and insufficient control of voice pitch variation.

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VESTIBULAR EVOKED MYOGENIC POTENTIAL

VESTIBULARNO EVOCIRANI MIOGENI POTENCIJAL

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Summary

Introduction. Vestibular evoked myogenic potentials are neurophysiological method for examining of saccular function, the bottom of the vestibular nerve that in nervates the sacculus and central vestibular pathways. Those are inhibitory potentials of the sternocleido mastoid musclein response to ipsilateral acoustic stimulation of the sacculus. Parameters of vestibular evoked myogenic potential testing include threshold, latencies of p1 and n1 wave and interamplitude p13-n23, interaural difference of p13 and n23 latency and interaural amplitude difference ratio. The aim of this study was to compire parameters standardization of vestibular evoked myogenic potentials responses, latency p13 and n23 of waves, the amplitude of responses and interaural differences in the amplitude andto determinewhether there is a difference in values between the sexes. **Material and methods.** This research was meant to be a prospective study which included 30 normal audiovestibular volunteers of both sexes. The group consisted of 53.3% women and 46.7% men. The saccular function testing by vestibular evoked myogenic potentials was performed monoaurally using air-conductive 500 Hz tone burst auditory stimulation. **Results**. The average value of the p13 wave latency in healthy subjects of this study was 15.18 ms (±1.24) while the mean latency of n23 waves in the same subjects was 25.00 ms (±2.23). The average value of the amplitude of the p13-n23 waves was 80.28 (34. ±04) microvolts. **Conclusion.** The difference in the values of the basic parameters of vestibular evoked myogenic potential responses between men and women does not exist. No differences between the right and the left ear in the values of latency and amplitude were observed.

Key words: Vestibular Evoked Myogenic Potentials; Vertigo; Saccule and Utricle; Vestibular Diseases; Vestibular Function Tests; Male; Female

Sažetak

Uvod. Vestibularno evocirani miogeni potencijali predstavljaju neurofiziološku metodu za ispitivanje funkcije sakulusa, donjeg vestibularnog nerva koji inerviše sakulus i centralnih vestibularnih puteva. Oni su inhibitorni potencijali sternokleidomastoidnog mišića kao odgovor na ipsilateralnu akustičku stimulaciju sakulusa. Parametri testa vestibularno evociranog miogenog potencijala su prag latencije p13 i n23 talasa i interamplitude p1-n1, interauralna razlika p13 i n23 latencije i razlika u amplitudama između oba uva. Cilj ove studije bio je da se načini standardizacija parametara vestibularno evociranog miogenog potencijal odgovora, latencija p13 i n23 talasa, amplituda odgovora i interauralna razlika u amplitudi odgovora i da se utvrdi da li postoji razlika u vrednostima između polova. **Materijal i metode.** Istraživanje je načinjeno kao prospektivna studija kojom je obuhvaćeno 30 audiovestibularno zdravih dobrovoljaca, oba pola. Grupu je činilo 53,3% žena i 46,7% muškaraca. Ispitivanje funkcije sakulusa vestibularno evociranim miogenim potencijalima vršeno je unilateralno, vazdušnim provođenjem, *tone burst* 500 Hz zvučnom stimulacijom. **Rezultati.** Prosečna vrednost latencije p13 talasa kod zdravih ispitanika u ovoj studiji bila je 15,18 ms (± 1,24), a srednja vrednost latencije n23 talasa kod njih iznosila je 25 ms (± 2,23). Prosečna vrednost latencije amplitude p13-n23 talasa bila je 80,28 (34 ± 04) mikrovolta. **Zaključak.** Razlika u vrednostima osnovnih parametara vestibularno evociranog miogenog potencijala odgovora između muškaraca i žena ne postoji. Nije konstatovana razlika ni između desnog i levog uva u vrednostima latencija i amplituda kod oba pola.

Ključne reči: Vestibularni evocirani miogeni potencijali; Vertigo; Sakulus i utrikulus; Vestibularna oboljenja; Testovi vestibularne funkcije; Muško; Žensko

Introduction

Sound challenged vestibular symptoms in humans were described in the early work of Tullius back in 1929 [1]. In 1958, when Geisler et al. recorded short-latency responses to auditory click (through the nape of the neck), those responses were believed to originate from the cerebral cortex [2]. For the first time in 1964, Bickford, Jacobson and Cody presented their theory describing characteristic responses to a click sound stimulus originating from the vestibular apparatus [3]. In a study of 30 healthy people they reported the responses to sound stimulation received by "adequate muscle tension" and concluded that their origin was in the vestibular rather than the cochlear part of the inner ear. Later studies of Cody and Bickford in 1969, and Townsend and Cody in 1971 [2] suggested that this response occurred by activation of the vestibular organ, especially the sacculus. Despite these

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Abbreviations

VEMP – vestibular evoked miogenic potential
ms – milisecond
μV – microvolt
dBnHL – decibel above normal adult hearing level
SCDS – semicircular canal dehiscence
MVST – medial vestibulospinal tract

studies, measurement of sound evoked potentials was not found clinically applicable at that time.

It was after the pioneering work of Colebatch, Halmagy, and Skuse in 1994 that the measurement procedure of myogenic potentials evoked by a click started to be applied. These authors introduced the technique of measuring vestibular evoked myogenic potentials by placing electrodes not on the back of the head but over the sternocleidomastoid muscle. By using high quality electromyographic measurement techniques, they documented the response that could be reproduced. This response was described as a "click evoked vestibulo-colic response" that was later renamed vestibular evoked myogenic potentials (muscle potentials originating from stimulation of the vestibular organ) and that term is used today [3].

Vestibular evoked myogenic potentials (VEMP) are exclusive to the evaluation of otoneurologic patients. VEMP are the inhibitory potentials of the sternocleidomastoid muscle in response to ipsilateral acoustic stimulation of the sacculus.

The aim of recording vestibular evoked muscle potentials is to determine whether there is a normal function of the saccule, lower vestibular nerve that innervates the saccule, and central vestibular pathways. The saccule, a lower part of otolithic organs, has a certain sensitivity to sound that can be measured by recording the muscle potential. The sensitivity to the sound of the saccule is believed to represent the rest of its functions as a hearing organ in the lower animals. A reflexive way responsible for causing the potentials originates from the saccule, which is stimulated by the sound intensity. The action potentials from the sacculus are transmitted through a lower vestibular nerve to the lateral vestibular nucleus. From here, impulses proceed through the medial vestibulospinal tract (MVST) towards the accessory nucleus and further on towards the ipsilateral sternocleidomastoid muscle. VEMP response consists of an initial positive wave (p13) followed by a negative wave (n23) **(figures 1 and 2)**. The following components with a lower stimulus threshold are not of vestibular origin [1–5]. Having in mind that peripheral and central pathways are activated in the vestibular evoked potentials, abnormal VEMP findings are recorded with lesions in any part of these structures. Sound that stimulates the saccule and causes VEMP should be transmitted to the saccule, which means that the middle ear should be intact. Vestibular evoked myogenic potentials mainly test the lower part of the brain stem while auditory evoked brain stem potentials provide data about the rostral part of the brain stem.

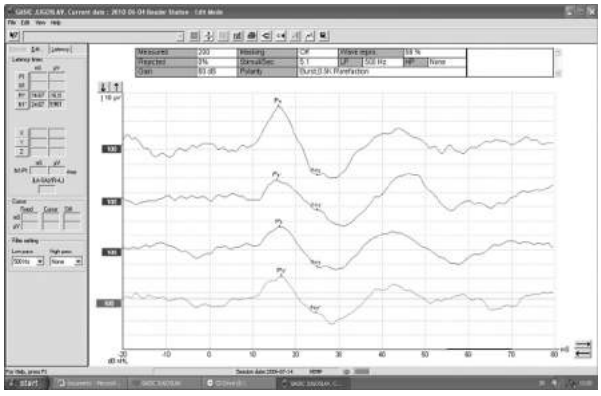


Figure 1. Normal finding of VEMP response on both sides
Slika 1. *Uredan nalaz vestibularno evociranog miogenog potencijala*

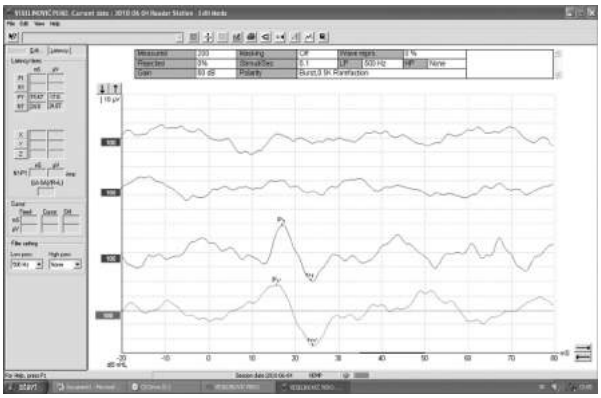


Figure 2. Normal response on the left side, no answer on the right side
Slika 2. *Normalan nalaz levo, bez odgovora na desnoj strani*

Material and Methods

The study was made at the Department for Audio and vestibulology, the Department of Ear, Nose and Throat Diseases of the Clinical Center of Vojvodina in Novi Sad, as a prospective study that included 30 healthy subjects of both sexes.

Upon obtaining the anamnesis, an otoscopic examination was made. The subjects with pathological findings during otoscopy and tympanometry were excluded from the study. Hearing threshold was determined by tonal liminar audiometry.

The saccular function was tested by vestibular evoked myogenic potentials (VEMP). VEMP measuring was performed by placing the electromyography (EMG) electrodes in the middle third of m. sternocleidomastoideus of a patient in the sitting position with the head turned to the side trying to touch the shoulder with the chin, thus allowing maximum contraction of m. sternoceleidomastoideus without any activity of the neck muscles without VEMP. The reference electrode

was placed on the sternum and the ground one to the forehead.

Stimulation was conducted via the headphones by click-stimuli or burst-tones monaurally. Clicks, usually of 95-100 dBnHL intensity, were presented to each ear every 200 ms, a total of 200. Optimal frequency for tone-burst was 500 Hz and 5 stimuli were presented per second. VEMP responses were amplified, filtered, and the mean value of at least 100 presentations was calculated and then displayed on the monitor (Madsen Capella). Furthermore, the latency, amplitude of waves p13-n23 were measured, and their threshold determined. Due to the high intensity of the stimulus, the headphones had to be calibrated. In order to ensure that VEMP responses were reproductive, two repeated tests were made. Generally, VEMP was easily obtained since the potentials were robust. Sound evoked VEMP were almost entirely unilateral.

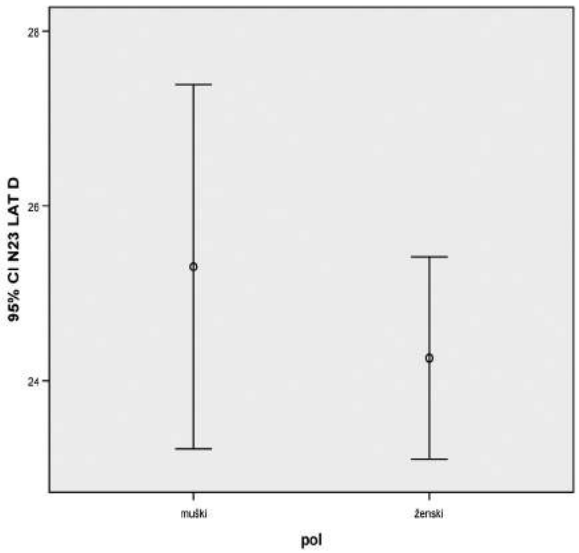
Results

The study included 30 healthy volunteers. The group consisted of 53.3% women and 46.7% men. The average age was 34.4 years (the youngest subject was 18 and the oldest was 57 years old). The average age of male subjects was 38.43 years, while women were slightly younger, their average age being 30.88 years.

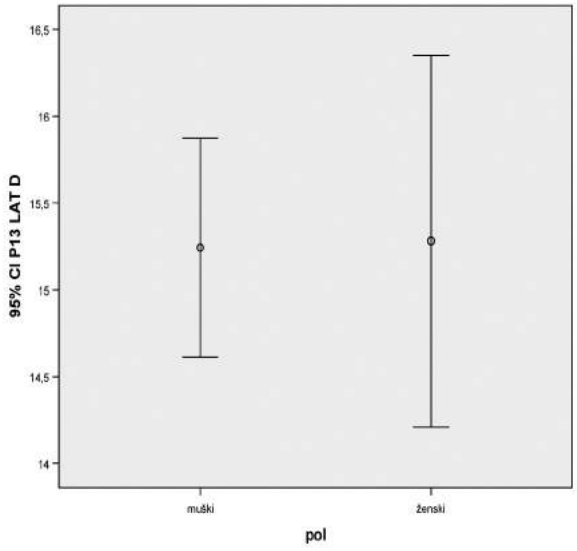
Normal otoscopic findings and tympanometry curve of type A were observed in all patients. All subjects had normal hearing threshold (up to 20 dBnHL).

Analysis of VEMP Responses

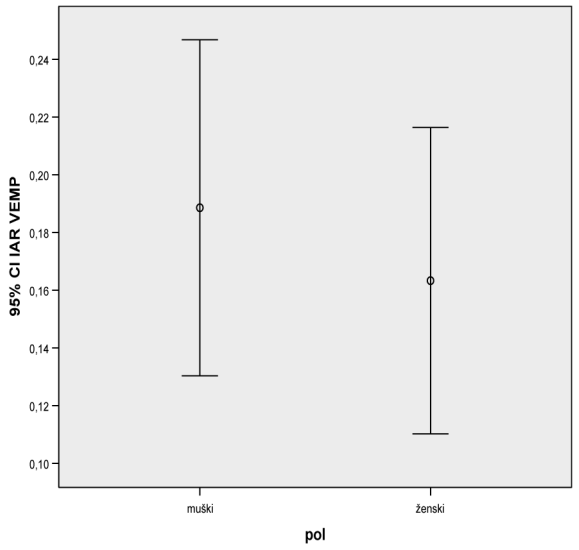
For clinical interpretation of vestibular evoked myogenic potentials, the most important parameter was the latency of waves p13 and n23. In addition, the response amplitude and interaural difference were observed. The average value of p13 wave latency in healthy subjects was 15.18 (±1.24) ms (males 15.25 (± 1.71) ms, females 15.12 (±1.14) ms)) (**Graph 1**), and the mean latency of n23 waves was 25.00 (± 2.23) ms (males 25.18 (± 3.1) ms, females 24.83 (±2.46) ms)) (**Graph 2**). The average amplitude value of p1-n23 wave was 80.28



Graph 2. Correlation of n23 wave latency between the sexes
Grafikon 2. *Korelacija latencije n23 talasa između polova*



Graph 1. Correlation of p13 wave latency between the sexes
Grafikon 1. *Korelacija latencije p13 talasa između polova*



Graph 3. Correlations between the amplitude p13 - n23 responses between men and women
Grafikon 3. *Korelacije između reakcija amplitude p13 – n23 između polova*

(±34.04) μV (males 77.21 (±42.18) μV, females 82.96 (±36.99) μV) (**Graph 3**).

The mean value of p13 wave latency of the right ear was 15.25 ms (±1.62). Similar values of p13 waves latency were observed in both sexes, 15.24 ms (±1.09) in males and 15.28 ms (±2.01) in females. There was no statistically significant difference in the measured values of the latency between men and women on the right ear ($r = 0.012$, $p > 0.05$).

When analyzing the mean value of p13 latency for the left ear expressed in ms it was found to be 15.10 (± 1.1) ms. Slightly higher values were observed in men 15.26 ms (± 0.7) compared with women 14.95 ms (±1.37), but with no significantly statistical difference ($r = -0.142$, $p > 0.05$).

The average n 23 wave latency of the right ear was 24.75 ms (± 2.93). The mean values for this parameter of 25.3 ms were in men (± 3.61) and 24.26 ms (± 3.61) in women. Statistical analysis showed no significant difference in the correlation between the sexes ($r = -0.181$, $p > 0.05$).

Approximately the same n23 waves latency was described for the left ear of 25.25 ms (±1.98), in males 25.07 (±2.59) and females 25.41 (±1.31).

There was no statistically significant difference between the sexes in the values of n 23 waves latency to the left ear ($r = 0.087$, $p > 0.05$).

The p13-n23 wave amplitude of the right ear was 83.85 μV (± 38.37). A slightly larger amplitude was recorded in women 87.36 μV (± 44.59) compared with men 79.85 μV (±44.59). There was no statistically significant difference between the sexes in the values of P13 amplitude waves in the right ear ($r = 0.099$, $p > 0.05$).

The p13-n23 wave amplitude of the left ear was 76.7 μV (± 34,112). In this case, there was a slightly higher amplitude in women, being 78.57 μV (± 29.49) compared with men, being 74.57 μV (±39.78). There was no statistically significant difference between the sexes in the values of p13 amplitude waves in the left ear ($r = 0.060$, $p > 0.05$).

The difference in the amplitude values between the two ears is considered pathological if its value is over 0:36. It is calculated by the formula: $AR\% = 100*(A_l - A_s)/(A_l + A_s)$ where A_l and A_s is the maximum and minimum amplitude of the observed ear.

The average difference in the amplitudes between the two sides was 0.17, 0.18 in men and 0.16 in women.

Discussion

Since VEMP test had been introduced as a new diagnostic method in audiology at the Department of Ear, Nose and Throat Diseases and used on patients with vestibular disorders, the aim of this study was to compile standardization of parameters of VEMP responses and to compare them with experience published in literature. The study subjects were healthy volunteers with normal hearing of both sexes. The group consisted of 14 (46.7%) men and 16 (53.3%) women, their average age being 34.4 years (ranging from 18 to 57 years). The subjects had no changes in hearing and denied the existence of other diseases. The standardization of values of VEMP responses was made. In order to interpret the findings accurately, the subjects had to have their hearing threshold in the normal/physiological range. Tympanometry curve was of type A in all subjects. Normal function of the middle ear was a prerequisite for further examination.

The mean value of hearing determined by tonal audiometry in 30 patients was within the normal values (up to 20 dBnHL) and by frequencies it was 500, 1000, 2000 and 4000 Hz respectively 6.26, 7.25, 8.25 and 9.48 dBnHL.

Vestibular evoked myogenic potentials are a neurophysiological method for examining the function of the sacculus and the integrity of the lower vestibular nerve. VEMP are ipsilateral inhibitory myogenic potentials caused by the impact of high intensive transient acoustic stimuli.

VEMP procedure is recommended to be done in sitting or lying position with the patient's head turned towards the opposite ear to allow maximum tension of the sternocleidomastoid muscle on the test side in order to place the electrode in the middle third of the muscle. The reference electrode was placed on the forehead and the grounding one on the sternum. Li recommends placing the reference electrode on the wrist [4]. A problem arises if there is no cooperation with the patient and he fails to achieve muscle tone tension, and in that case, it is impossible to conduct measurements. There are difficulties in performing the test with children, depending on their age. Aloud click or tone burst (recommended intensity of 95 and 100 dBnHL) in the interval of 200 ms (5/second) should be used for response stimulation.

Many authors agree that approximately the same answer is received no matter what kind of sound stimulation we used for [5, 6]. However, the advantage is given to the tone burst stimulation compared to a click (since it uses a lower intensity of absolute stimulation). Rauch et al. recommend tone bursts and the frequency of 500 Hz as the optimal stimulus [7]. The recommended stimulation parameters and frequencies were used in this study.

Stimulation can be unilateral or bilateral. Binaural measurement is faster but it is more accurate to perform unilateral measurement since there is a possibility of "transferring" response to the affected side when the test is done simultaneously stimulating both ears [8].

A high-intensity sound is needed as a stimulus in order to create VEMP response and it is necessary to check the position of headphones in the external auditory canal. The slightest mistake in terms of malposition or removing of headphones may result in the loss of VEMP response and poor

clinical interpretation due to sound intensity reduction.

In order to check the reproducibility of response or lack of it, it is necessary to make at least two measurements.

Measuring VEMP by bone conduction when using tone burst (through the forehead or lateral part of the skull, at frequency of 200 Hz) induces a significantly stronger VEMP test stimulus and does not lateralize as well as the tone click [10]. Galvanic stimulation can also cause VEMP response [9]. Stimulation by this technique is primarily used to differentiate lesions of the saccule, lower vestibular nerve and proximal nerve lesions. This technique requires special methodology due to a large number of electrical artifacts created by the stimulation. With galvanic stimulation of the vestibular nerve, it is expected that VEMP response is less sensitive with partial lesions of the vestibular nerve (vestibular nerve section) and that there is no response in a complete loss of function of the vestibular nerve. For this reason, galvanic stimulation cannot differentiate between the damage of the sacculus and lower vestibular nerve since the galvanic VEMP is expected to produce a response even when there is a damage of the lower vestibular nerve. Galvanic VEMP may be more reliable than the acoustic VEMP for methods of monitoring vestibulospinal connections through the spinal cord [11]. It is obvious that this method requires more research.

The following is observed in VEMP responses: how they are formed by sides, p13 and n23 latency, amplitude response and interaural difference.

VEMP response consists of a biphasic wave with an initial positive or p13 polarity, whose latency is in the range of 10 to 18 ms, and a subsequent n23 negative wave, which usually appears between 17 and 26 ms. The amplitude reflex shows an increase with an increasing intensity of tone bursts lasting up to 7–10 milliseconds which is followed by a decrease in amplitude. It is believed that this decrease in the amplitude response results from the activation of the stapedius reflex. Later response components (n34, p44) have a lower threshold of stimulation and are not of the vestibular (probably cochlear) origin. This short response latency (about 8 ms) indicates the transmission through oligosynaptic, possibly even via disynaptic ways, comprising primary vestibular afferent projections towards the complex of vestibular nuclei and over the medial vestibular tract to the accessory nuclei [12–15].

The amplitude of p13–n23 varies considerably, from 25 μV to over 200 μV, so there are no reference values for this parameter. In this neurophysiological method, the amplitude is proportional to the contraction strength of the sternocleidomastoid muscle.

The reflex depends on the integrity of transmission of the middle ear, normal saccular anatomy, integrity of the lower vestibular nerve and central nervous system [16].

There are several ways to conduct VEMP measuring. There is the recommended intensity of an intensive click around 95–100 dB above the normal hearing threshold (the equivalent of 140 to 150 dB-SPL) well tolerated by patients. The existence of tinnitus is a relative contraindication for click and tone burst VEMP testing. In addition, the normal function of the conductive system is a prerequisite for performing VEMP. Specifically, it was found that the presence of even the smallest air-bone gap (7–8 dB) affects the attenuation of responses [17]. Recommendation for VEMP measuring is a sound stimulus of 500 Hz tone burst (duration 2 ms), intensity of 100 dBnHL, 4 stimuli per second, ipsilaterally which is very similar to the click measurements [5, 18, 19]. The 200 stimulations were repeated twice and the mean value was recorded.

In this study, all healthy subjects had a response. The analysis of absolute latency of p13 waves defined their mean value of 15.18 ms (±1.24) and the mean value for n23 wave was 25 ms (±2.23). The analysis was made for the p13 latency of each side in men and women. It was concluded that the latency values of p13 right (15.26 ms ± 1.6) and left (15.10 ms ± 1.10) do not show any significant difference. There was no statistically significant difference in the correlation of latency values of p13 wave in men and women (right $r = 0.012$, $p < 0.05$, left $r = -0.142$, $p > 0.05$).

By analyzing the latency of n23 wave, it can be concluded that there is no significant difference between the right (24.75 ms ± 2.93) and left side (25.25 ms ± 1.98), nor there is any difference between the sexes ($p > 0.05$).

When using unilateral stimulation of SCM and electromyographic monitoring, the obtained latency values in the works of other authors are similar to those in this study. Wang et al. found the latency mean value of p13 to be 14.49 ms (± 1.28) and for n 23 it was 21.83 ms (± 1.65) [20]. Basta at al. describe the following values p13 16.2 ms (± 2.5) and n 23 wave of 24 ms (±2.6) [21]. Similar mean latency values of p13 and n23 waves were found in the study of Isaradisaikul et al. standing at 14.44 ms (±1.92) and 21.16 ms (±2.11), respectively [22]. In their research conducted by bilateral activation of SCM, Cheng et al. included 30 subjects, aged from 17 to 43, and presented the mean latency value of p13 wave to be 12.49 ms (± 0.94) and 19.79 ms (± 1.40) for the n23 wave [23].

Young et al. examined the right and the left side in their research and did not find any significant difference in the p13 wave latency (right 13.37 ms, left 13.53 ms). In addition, they did not notice any significant differences in the latency of n23 waves which was right ear 20.20 ms and left ear 20.58 ms [24].

The amplitude of the response is in proportion to the tonic electromyographic activity of m. ster-

nocleidomastoideus and is less important for the clinical interpretation of responses [25].

In this study, the mean value of the amplitude was 88.85 μV (±38.37) right and 76.7 μV (±34.11) left, with no significant differences between the sexes.

The study of Carnauba et al., which included 40 subjects of both sexes, confirmed that there was no difference in latencies and amplitudes in either men or women. The latency of p13 for the right ear stood at 14.13 ms (±1.39) in women and 14.15 ms (±1.21) in men, and for the left ear, it was 14.14 ms (±1.42) in women and 14.35 ms (±1.41) in men. The n23 latencies were about 24 ms [26].

Clinical Application of VEMP

How important is VEMP test in the diagnosis of superior semicircular canal dehiscence (SCDS), impairment of the vestibular nerve, bilateral loss of vestibular function after ototoxic effects of aminoglycosides, central vestibular disorders, Meniere's disease and hearing impairment?

VEMP is a useful method in patients with Tullio phenomenon, which is defined as vertigo provoked by a strong sound. It occurs in cases of superior semicircular canal dehiscence, perilymphatic fistula, Meniere's disease, after surgery of fenestra and vestibulofibrosis. It is of particular importance in patients with fistula of the superior semicircular canal [27]. In this syndrome, VEMP responses register asymmetry in the amplitudes as well as the occurrence of very large amplitudes with the diagnosis of conductive hearing loss and the presence of air-bone gap. Having in mind that VEMP is sensitive to disturbed function of the sacculus and reflex ways, Osch et al. applied this method in the diagnosis of vestibular neuritis, which occurred with the damage of lower vestibular nerve in their study [28].

In cases when the saccule is innervated by the lower branch of the vestibular nerve, the absence of VEMP response should be observed. However, during the VEMP test it is not possible to distinguish between the damage of the sacccule and the vestibular nerve. If an inflammatory process covers the lower branch of the vestibular nerve, the lack of response is expected. When VEMP findings are changed in neuronitis of the vestibular nerve, the recovery and normalization of findings will happen faster than normalization of responses of lateral semicircular canal during caloric stimulation [29].

Therefore, VEMP can help to conclude how much of the vestibular nerve is affected, whether it is fully affected or the lower branch is spared. New clinical entity, neuritis of the lower branch of the vestibular nerve, can only be confirmed by VEMP. Sometimes, in rare cases, vestibular neuronitis can affect only the lower branch of the vestibular nerve, and spare the upper one. Then the patient has no horizontal nystagmus, head-impulse test is negative, while the caloric test produces normal response. The only diagnostic tool which can explain the clinical picture of neuritis in these patients is VEMP. The absence of vestibulo-cervical reflex points to the fact that the lower branch of the vestibular nerve is affected by a pathological process. Murofuschi et al. found an abnormal VEMP finding in 25% of patients with neuronitis. It is believed that in this case, the first VEMP wave may simply be missing but the waves that occur later and are related to cochlear function have been preserved [30].

The complete absence of VEMP response is found in people with vestibular schwannoma, mutual loss of vestibular function after the use of aminoglycosides and after section of the vestibular nerve, when the importance of examining the residual function of the vestibular nerve after section of the same. In addition, no VEMP responses are observed in patients with otosclerosis [31].

After testing a large number of patients with the loss of vestibular function caused by aminoglycosides and without hearing impairment, Hain et al. included this test in the test battery of vestibular tests as a very good one [32]. Furthermore, there is no VEMP response in patients after instillation of gentamicin with unilateral Meniere's disease [33].

Using VEMP with patients suffering from Meniere's disease is of no importance since it reads the low amplitude on the side of the ear affected by disease [34]. The increase in response amplitudes in the early stage of Meniere's disease, when there is a hearing fluctuation, is caused by dilation of the saccule while the absence of responses indicates its collapse. The assumption that the VEMP response amplitude increases after Glycerol test or injections of furosemide indicates the existence of Meniere's disease [35]. Controversial opinion of Hain et al. [32] states that the increase in the VEMP response amplitude is due to dilatation of the saccule and therefore, the opposite effect would be expected (decrease, not increase in response) after taking glycerol and furosemide.

The absence of vestibular evoked myogenic potential response and prolonged latency are encountered in patients with multiple sclerosis [36] and damage to the brain stem [37]. The most common pathological finding in these patients is prolonged P13 wave latency [38].

Function test of the lower part of the brainstem (medulla) is possible with vestibular evoked myogenic potentials while the early auditory evoked potentials of the brainstem are important for examination of function of the upper part of the same (pons and midbrain) [39, 40].

Conclusion

Vestibular evoked myogenic potentials is a relatively new diagnostic method that is applicable to patients with specific vestibular disorders and is a measurement of the inhibitory potentials during tonic contraction of the sternocleidomastoid muscle

in response to intense sound stimulation. It is believed that the vestibular evoked myogenic potential response is of the vestibular origin. Vestibular evoked myogenic potential measuring is a simple, non-invasive method for examining the otolith organ function and functional integrity of the lower vestibular nerve. Normal function of the middle ear is a prerequisite for vestibular evoked myogenic potential measurement while a minimum reduction of conductive hearing compromises it. Vestibular evoked myogenic potential response is induced in people with sensorineural hearing loss.

Since vestibular evoked myogenic potentials is a new diagnostic method, it was necessary to make the standardization of response parameters. The mean value of the p13 wave latency in healthy subjects in this study was 15.18 ms (±1.24) and the mean value of n23 wave latency was 25.00 ms (±2.23). The amplitude mean value of the p13–n23 wave was 80.28 (±34.04) microvolts. No differences were observed in the values of latency and amplitudes between the right and the left ear. In addition, there were no differences in the values of the basic parameters of vestibular evodd myogenic potentials responses between men and women.

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UNILATERAL TINNITUS AS A SINGLE SYMPTOM OF UNUSUALLY LARGE VESTIBULAR SCHWANNOMA

JEDNOSTRANI TINITUS – JEDINI SIMPTOM NEOBIČNO VELIKOG VESTIBULARNOG ŠVANOMA

Zoran KOMAZEC, Slobodanka LEMAJIĆ KOMAZEC, Rajko M. JOVIĆ, Ljiljana VLAŠKI and Dragan DANKUC

Summary

Introduction. Vestibular schwannomas are relatively rare tumors whose symptoms are based on its location and as the tumor grows, the symptoms usually advance. **Case Report.** An 18-year old patient was examined by an otolaryngologist due to buzzing in her right ear that had lasted for about 1 month. Her pure-tone audiometry findings showed slight asymmetry; a slight ascendant type sensorineural hearing loss was found in the right ear (25 dB HL at 125 Hz, 20 dB HL at 250 Hz, and 10 dB HL at other frequencies), while the threshold in the left ear was 15 dBHL at 125 Hz and 10 dB HL at other frequencies. Electronystagmography, otoacoustic emissions and auditory brain-stem responses suggested retrocochlear etiology of tinnitus. Magnetic resonance imaging examination revealed a large right cerebellopontine angle tumor, measuring 5 x 3 x 3 cm, which had shifted the brain stem laterally. **Conclusion.** Every case of unilateral tinnitus, asymmetric sensorineural hearing loss, or hypotonia of labyrinth not strictly accompanied by vertigo, needs to be further evaluated using a battery of audiologic tests whose findings may be normal. Audiologic tests should be repeated in cases of persistent symptoms and accompanied by cranial magnetic resonance imaging, which is today considered the gold standard for diagnosis of vestibular schwannoma.

Key words: Tinnitus; Neuroma, Acoustic; Hearing; Adolescent; Diagnosis; Magnetic Resonance Imaging; Audiology; Hearing Loss, Sensorineuronal

Sažetak

Uvod. Vestibalrni švanomi su relativno retki tumori čija se simptomatologija bazira na njihovoj lokalizaciji; sa rastom tumora obično napreduje i simptomatologija. **Prikaz slučaja.** Pacijentkinja starosti 19 godina pregledana je kod otorinolaringologa zbog zujanja i desnom uvu koje je trajalo mesec dana. Nalaz tonalne audiometrije pokazivao je laku asimetriju; na desnom uvu, ascedentna senzorineuralna nagluvost lakog stepena (25 dB HL na 125 Hz, 20 dB HL na 250 Hz, i 10 dB HL na ostalim frekvencijama), dok je prag sluha na levom uvu bio 15 dBHL na 125 Hz i 10 dB HL na ostalim frekvencijama. Nakon elektronistagmografskog ispitivanja, otoaksutičkih emisija i auditivnih potencijala moždanog stabla, posmunjano je na retrokohlearnu etiologiju tinitusa. Pregled magnetnom rezonancijom pokazao je veliki desnostrani tumor u pontocerebelarnom uglu, veličine 5 x 3 x 3 cm, koji je pomerao moždano stablo lateralno. **Zaključak.** Svaki slučaj jednostranog tinitusa, asimimetričnog nalaza sluha ili hipotonije lavirinta, koji ne mora obavezno da se javlja sa vrtoglavicom, zahteva dalju evaluaciju baterijom audioloških testova čiji nalazi mogu biti uredni. Audiološka dijagnostika mora biti ponavljana u slučajevima perzistentnih simptoma, a dijagnoza mora da se potvrdi magnetnom rezonancijom glave, koja se danas smatra zlatnim standardom u dijagnostici vestibularnog švanoma.

Ključne reči: Tinitus; Švanom; Sluh; Adolescent; Dijagnoza; Magnetna rezonanca; Audiologija; Senzorineuralni gubitak sluha

Introduction

Vestibular schwannomas are relatively rare tumors with the average incidence of 13 cases per million inhabitants [1].

Vestibular schwannoma is a slow-growing, benign tumor usually arising from the neurilemma sheath of the vestibular portion of the eighth cranial nerve within the internal auditory canal. Histologically benign, the tumor extends from the internal acoustic meatus towards the cerebellopontine angle. Clinical symptoms are based on its location and as the tumor grows, the symptoms usually advance accordingly. In the case reported here, however, there was a remarkable discrepancy between the symptoms and the size of the tumor.

Case Report

An 18-year-old nursing school student was seen by the practicing otolaryngologist due to buzzing in her right ear lasting for about 1 month. The tinnitus had been continuous, of low intensity, and was not seen subjectively as a serious problem. The patient never experienced discharge or pain, nor did she suffer from hearing loss or vertigo. On the clinical ear, nose and throat examination, all findings were within normal limits. Pure-tone audiometry findings showed slight asymmetry; in the right ear, a slight ascendent type sensorineural hearing loss was found [25 decibels hearing level (dBHL_ at 125 Hz, 20 dBHL at 250 Hz, and 10 dBHL at other frequencies], while the threshold in the left ear was 15 dBHL

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Abbreviations

ENT – ear, nose and throat
dBHL – decibels hearing level
ABR – auditory brain-stem response
MRI – magnetic resonance imaging
CSF – cerebrospinal fluid

at 125 Hz and 10 dBHL at other frequencies **(Figure 1).**

The otoneurologic evaluation resulted in the following findings: spontaneous nystagmus was absent, Romberg test was negative, Unterberger test showed lateralization to the right. Vestibular impairment of the right labyrinth was suspected, accompanied by discreet sensorineural hearing loss at one frequency and tinnitus in the right ear, suggestive of the right retrocochlear hearing loss. Therefore, otoacoustic emissions, electronystagmography, and auditory brain-stem response (ABR) tests were performed.

Evoked otoacoustic emissions were normal on the left ear and completely missing on the right one. Electronystagmographic findings showed the absence of spontaneous nystagmus, and the findings during the rotatory test were normal. The caloric stimulation suggested vestibular impairment of the right labyrinth, while the function of the left labyrinth was normal (CP=61%). Fixation suppression was bilaterally present. The findings suggested partial impairment of the right labyrinth function with the central vestibular compensation.

ABR examination yielded only the wave I in the right side, whereas the findings were normal during the stimulation of the left side.

The patient was then referred to magnetic resonance imaging (MRI) examination, which showed right cerebellopontine angle tumor, surprisingly measuring 5 x 3 x 3 cm, which had shifted the brainstem laterally in a grotesque way, displacing it altogether to the left of the midline **(Figure 2)**.

The patient underwent surgery by a neurosurgeon, who performed retrosigmoid approach. The surgery was followed by transient facial nerve palsy. The follow-up audiologic and vestibular evaluation showed the loss of cochleovestibular function on the right side. The follow-up MRI examination showed a small (remaining part) of tumor which was thereafter observed by a neurosurgeon.

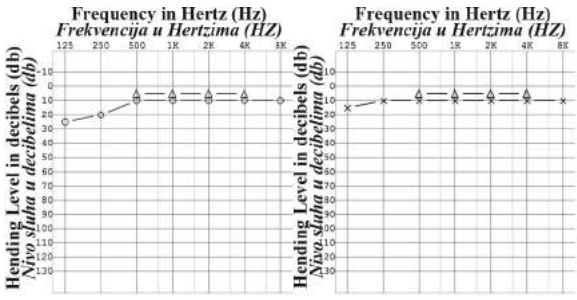

Figure 1. Pure-tone audiometry finding
Slika 1. *Nalaz audiometrije čistog tona*

Figure 2. MRI finding
Slika 2. *Nalaz magnetne rezonancije*

Three years later, the patient came back with a sudden hearing loss in her functional left ear. Pure-tone audiometry showed a linear type of sudden sensorineural hearing loss with a threshold at an average of 60 dBHL. Intravenous corticosteroid injections and vasoactive drugs were administered immediately. During the next follow-up, 4 days later, normal hearing was recorded in the left ear.

Discussion

Asymmetric sensorineural hearing loss and unilateral tinnitus inevitably raise suspicion of retrocochlear pathology [2–4]. It is therefore mandatory to discriminate cochlear from retrocochlear hearing loss [5]. As a rule, a battery of audiologic tests is necessary to establish the type of hearing loss in patients with asymmetric pure tone thresholds. However, some patients may have normal hearing, defined as s pure-tone average <20 dBHL, speech discrimination score >90%, and interaural differences ≤10 dB [6, 7]. Numerous studies suggest that vestibular schwannoma may also be present in patients with the normal threshold. This fact is frequently overlooked during routine practice. Furthermore, it is generally considered that patients with normal or almost normal hearing have small schwannoma [8]. In our case report, the tumor of a young patient was large and accompanied by very few symptoms. Similar cases were reported by Magdziarz DD et al. [7].

The purpose of this case report is to draw attention to the fact that every case of asymmetric sensorineural hearing loss, unilateral tinnitus, or unilateral vestibular loss not strictly accompanied

by vertigo needs to be further evaluated using a battery of audiologic tests whose findings may be normal [9, 10].

Audiologic tests should be repeated in case of persistent symptoms and accompanied by cranial MRI, which is today the gold standard for establishing diagnosis in all cases of cerebellopontine angle tumors.

Although the contralateral hearing loss after surgery of vestibular schwannoma was seen in 1.3% of patients because of brainstem shift, brainstem edema, labyrinthine fluid imbalance due to cerebrospinal fluid (CSF) release and contralateral sympathetic labyrinthitis due to injury of the ipsilateral labyrinth after translabyrinthine resection of tumors [11], the onset of contrateral hearing loss in our patient (3 years after surgery) suggested sudden hearing loss which was completely recovered on prescribed therapy.

Conclusion

Every case of unilateral tinnitus, asymmetric sensorineural hearing loss, or hypotonia of labyrinth not strictly accompanied by vertigo, needs to be further evaluated using a battery of audiologic tests whose findings may be normal. Audiologic tests should be repeated in cases of persistent symptoms and accompanied by cranial magnetic resonance imaging, which is today considered the gold standard for diagnosis of vestibular schwannoma.

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LOCAL ALLERGIC RHINITIS

LOKALNI ALERGIJSKI RINITIS

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Summary
Local allergic rhinitis is a localized allergic response of the nasal mucosa to aeroallergens in the absence of atopy with characteristic production of specific local immunoglobulin E antibodies in the nasal mucosa, T helper type 2 cellular infiltration response during the exposure to aeroallergens and positive results via the nasal allergic provocation test with the release of inflammatory mediators (triptase and eosinophil cationic proteins). Even though the prevalence of local allergic rhinitis has been and is still being investigated, a large number of patients with diagnosed non-allergic rhinitis or idiopathic rhinitis are currently classified as having local allergic rhinitis. The causes of local allergic rhinitis are most commonly house dust, dust mites, pollens and many others. Diagnosis of local allergic rhinitis is made using nasal allergen provocation tests when the prick test for standard inhalation allergens and the serum specific immunoglobulin analysis for aeroallergens are negative. The increasing amount of data on localized allergic response in non-atopic patients asks for many answers regarding local allergic rhinitis. These answers can be obtained by a study on the prevalence and incidence in children and adults, the impact of positive family atopy in the development of disease, the impact of associated diseases of the lower respiratory tract and conjunctiva, the effectiveness of drug treatment and the issue of administration of specific immunotherapy.
Key words: Rhinitis; Rhinitis, Allergic, Seasonal; Rhinitis, Allergic, Perennial; Nasal Mucosa; Allergens; Immunoglobulin E; Prevalence; Signs and Symptoms; Diagnosis; Therapeutics

Sažetak
Lokalni alergijski rinitis lokalizovani je alergijski odgovor nosne mukoze na aeoroalergen u odsustvu atopije, sa karakterističnom produkcijom lokalnih specifičnih imunoglobulin E antitela u nosnoj mukozi, *T helper type 2* odgovorom mukozne ćelijske infiltracije tokom ekspozicije aeroalergenima i pozitivnim nazalnim alergijskim provokacionim testom (odgovorom) sa oslobađanjem inflamatornih medijatora (triptaze i eozinofilnog katjonik proteina). Iako se prevalencija lokalnog alergijskog rinitisa ispituje, veliki broj pacijenata sa dijagnozom nealergijskog rinitisa ili idiopatskog rinitisa sada je klasifikovana kao lokalni alergijski rinitis. Uzročnici su najčešće kućna prašina, grinje, poleni i mnogi drugi. Dijagnoza se postavlja nazalnim alergenskim provokacionim testom, jer je prik test na standardne inhalatorne alergene negativan, negativan je i nalaz serumskih specifičnih imunoglobulin na aeroalergene. Povećani broj podataka o lokalizovanom alergijskom odgovoru kod "neatopičara", traži mnoge odgovore o lokalnom alergijskom rinitisu: studije o prevalenciji i incidenciji kod dece i odraslih, uticaj pozitivne porodične atopije u razvoju bolesti, uticaj udruženih oboljenja donjih disajnih puteva i konjuktivitisa, efikasnost farmakološke terapije i pitanje primene specifične imunoterapije.
Ključne reči: Rinitis; Sezonski alergijski rinitis; Perenijalni alergijski rinitis; Nosna sluznica; Alergeni; Imunoglobulin E; Prevalenca; Znaci i simptomi; Dijagnoza; Terapija

Introduction

Local allergic rhinitis (LAR) is a localized allergic response of the nasal mucosa to aeroallergens in the absence of atopy with characteristic production of specific local immunoglobulin (Ig)E antibodies in the nasal mucosa, T helper type 2 (TH2) cellular infiltration response during the exposure to aeroallergens and positive results via the nasal allergic provocation test with the release of inflammatory mediators (triptase and eosinophil cationic proteins). Even though the prevalence of LAR has been and is still being investigated, a large number of patients with diagnosed non-allergic rhinitis or idiopathic rhinitis are currently classified as having LAR. The causes of LAR are most commonly house dust, dust mites, pollens and many others. Diagnosis of LAR is made using nasal allergen provocation tests when the prick test for standard inhalation allergens (SIA) and the serum specific IgE analysis for aeroallergens are negative. In a certain number of cases of LAR, it is possible to detect local specific IgE with combined asthma and conjunctivitis. Numerous current studies are aimed at investigating whether patients with

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Abbreviations

LAR – local allergic rhinitis
Ig – immunoglobulin
TH2 – T helper type 2
SIA – standard inhalation allergens
ENT – ear, nose and throat
NAPT – nasal allergen provocation test
ECP – eosinophil cationic protein
AR – allergic rhinitis
NAR – non-allergic rhinitis
NARES – non-allergic rhinitis with eosinophilia
IR – idiopathic rhinitis
NAP – nasal allergen provocation
HDM – house dust mites
NAPT – nasal allergen provocation test
FLCs – free light chains
SPT – skin prick test
SCIT – subcutaneous immunotherapy
SLII – sublinqual immunotherapy

LAR will develop a systemic atopy in the future or not and what that depends on. Further studies are necessary in order to find out the incidence of LAR and develop new diagnostic methods, therapeutic approaches and effects of immunotherapy.

In 1975, Huggins and Brostoff were the first to report the production of local IgE antibodies in the nasal mucosa of patients with allergic and non-allergic rhinitis [1–9]. This discovery preceded the development of the idea of local allergic rhinitis (LAR), as well as the state of the local allergic response of the nasal mucosa in the absence of atopy [7]. Further research in the field of LAR was conducted by a group of Spanish ear, nose and throat (ENT) allergists led by Rondon et al. This condition is characterized by the local production of sIgE antibodies [1, 8, 9], TH2 inflammatory response [5, 7–10], the positive response to nasal allergen provocation test (NAPT) [6, 8, 9, 11] with overt symptoms and increased levels of sIgE, tryptase and *eosinophil cationic protein* (ECP) in nasal secretions [12, 13].

Etiologic Classification of Rhinitis

From the etiological point of view, non-infectious rhinitis has traditionally been classified as allergic and non-allergic and the diagnosis was based on the history of health problems, skin prick test and serum level of IgE antibodies to aeroallergens [14] (**Table 1**).

Table 1. Etiologic classification of rhinosinusitis (according to Rondon et al.)
Tabela 1. *Etiološka klasifikacija rinosinuzitisa (prema Rondon i sar.)*

1. Allergic rhinosinusitis/*Alergijski rinosinuzitis*
• Allergic rhinitis(rinosinusitis) (with systemic atopy)/*Alergijski rinitis(rinosinuzitis) (sa sistemskom atopijom)*
i. Classic classification/*i. Klasična klasifikacija*
1. According to exposure to aeroallergen: perennial, seasonal, and occupational *Vreme ekspozicije na aeroalergen ili aeroalergene: perenialni, sezonski, i okupacioni*
ii. ARIA classification (14)/*ii./ARIA klasifikacija (14)*
1. Duration of symptoms: persistent and intermittent/*Dužina simptoma: perzistentni i intermitentni*
2. Severity of symptoms: light, moderate, severe/*Težina simptoma: laki, umereni, i teški*
• Local allergic rhinitis (rhinosinusitis) (without systemic atopy) *Lokalni alergijski rinitis(rinosinuzitis) (bez sistemske atopije)*
i. Classic classification/*i. Klasična klasifikacija*
1. According to exposition to aeroallergen: perennial, seasonal, and occupational *Vreme ekspozicije na aeroalergen ili aeroalergene: perenialni, sezonski, i okupacioni*
ii. ARIA classification (14)/*ii./ARIA klasifikacija (14)*
1. Duration of symptoms: persistent and intermittent/*Dužina simptoma: perzistentni i intermitentni*
2. Severity of symptoms: light, moderate, severe/*Težina simptoma: laki, umereni, i teški*
2. Nonallergic rhinosinusitis/*Nealergijski rinosinuzitis*
• Infectious/*Infektivni*
• Occupational (irritating)/*Okupacioni (iritantni)*
• Medicamentous/*Medikamentozni*
• Hormonal/*Hormonalni*
• Food induced/*Hranom indukovan*
• Emotional/*Emocionalni*
• Atrophic/*Atrofični*
• GERD induced or laryngopharyngeal reflux induced rhinosinusitis (GERD - gastroesophageal *reflux* disease) *GERBom ili faringolaringealnim refluksom udružen rinosinuzitis (GERB - gastroezofagna refluks bolest)*
• NARES/*NARES*
• Idiopatic rhinosinusitis/*Idiopatski rinusitis*

Allergic rhinitis (AR) is the most common form of non-infectious rhinitis [14]. However, the prevalence of non-allergic rhinitis (NAR) is unknown and a minimal effort has been made in the identification of NAR phenotypes using standard methods [14]. NAR is a heterogeneous group of disorders of nasal inflammation. Some of these disorders are caused by a visible trigger or causative agent although the cause remains undiscovered in most cases. NAR with a known cause include medical, hormonal, emotional, food-induced, atrophic, occupational/professional (irritants from the environment), rhinitis associated with Gerbe or laryngopharyngeal reflux. However, as much as 60% of non-allergic rhinitis has no detectable cause and is diagnosed as idiopathic rhinitis. According to the pathophysiological mechanism, idiopathic rhinitis is divided into two phenotypes: the one conditioned by neurogenic mechanisms and the one with inflammatory mechanisms. Knowing the type of idiopathic rhinitis is very important for the therapeutic action, namely idiopathic rhinitis caused by an imbalance of the sympathetic and parasympathetic nervous system that will not respond to topical corticosteroids, whereas the inflammatory type of idiopathic rhinitis will react. Vasomotor rhinitis, which is essentially an idiopathic rhinitis caused by neurogenic mechanism, is often mentioned in the literature. The neurogenic mechanism involves the imbalance of parasympathicus / sympathicus, hyperreactivity of the *nonadrenergic*, non-cholinergic or peptidergic nervous system leading to neurogenic inflammation, hyperesthesia or dysesthesia of the central nervous system and the strong localization of nitrite oxide synthase in the smooth muscle of blood vessels of the cavernous sinus [15–19]. Non-allergic rhinitis with eosinophilia (NARES) was first described by Jacobs et al. in 1981 as a phenotypically distinct group of non-allergic rhinitis of unknown etiology with perennial nasal symptoms of profuse watery secretion, choppy sneezing attacks, itching of the nose with the recorded eosinophilia in nasal discharge with no obvious allergies (a negative skin prick test on SIA and absence of specific IgE in the serum) [20]. NARES is often associated with nasal polyposis, bronchial hyper-responsiveness, non-allergic asthma and sleep apnea syndrome [21]. In the presence of aspirin intolerance with nasal polyposis and non-allergic asthma, it is diagnosed as ASA SY [22, 23]. Most authors identify NARES with idiopathic rhinitis, while some authors define it as a separate entity [24–26].

Patients with NAR have negative skin prick test and a lack of serum sIgE. However, over the past decade, several studies showed that a greater number of patients with negative skin prick test, negative intradermal skin test and the absence of serum sIgE had nasal symptoms following nasal provocation tests with airborne allergens, including house dust mites, pollens and others [8, 9]. Further studies have shown that the local production of specific IgE occurs in these patients [8, 9, 12, 13]. As a result of the above mentioned, the term LAR is preferred, leading to a new etiological classification of rhinitis [14, 15]. After describing LAR in patients previously labeled with the diagnosis of NAR, further studies were aimed at defining the clinical and immunological differences between idiopathic rhinitis (IR), NARES and LAR.

Prevalence

According to the studies performed by European centers, the prevalence of LAR among patients with negative skin prick test and negative serum specific IgE is about 47% to 62.5% of patients with perennial and seasonal symptoms of the disease [6, 8, 9, 11]. LAR was previously diagnosed in many patients with IR or NARES, thus indicating that this is a common entity. Large-scale studies including adults and children, which use the procedure of the nasal provocation test, nasal secretion collection and laboratory analysis are aimed at identifying the epidemiological characteristics of LAR. Their objective is to define whether LAR has one or more unique clinical phenotypes, including co-morbidities, which will distinguish them from other forms of rhinitis.

Is this entity more common in some areas due to different levels of allergens? Do external factors such as air pollution, smog and air temperature affect the development of LAR in relation to the development of AR? The answer is still in the research phase and it is the subject of numerous studies conducted in different geographical areas with different airborne allergens, different levels of air pollution and climatic factors.

Previously published studies indicate that LAR is usually caused by dust mites, house dust, grass pollen and olives [1, 6, 8, 9, 11, 13]. However, it is unknown whether some less common allergens are involved. Other possible triggers include mold, animal hair and professional aeroallergens. In the study performed by Carney et al., which included 13 patients with LAR, only one patient responded to nasal provocation with cat/dog hair [6]. It is also necessary to determine the appropriate, optimal dose of the allergen for nasal allergen provocation (NAP) and to develop a more practical method.

Pathophysiology

Certain genetic predisposition and pathophysiological reaction mechanisms to airborne allergens (endotype) and the expression of specific problems-clinical manifestations (phenotype) are required for the development of LAR.

An allergen in the nasal mucosa causes the production of a local sIgE response, which launches a Th2 inflammatory mechanism, increasing the levels of inflammatory mediators and the consequent reduction in nasal volume, but with negative skin prick test and the absence of IgE antibodies in the peripheral blood.

Local Production of Inflammatory Mediators and sIgE in Patients with AR and NAR

Several authors have studied the concept of local production of IgE in the nasal mucosa of patients with AR. Platt-Mills showed the increased levels of sIgE to grass pollen in the nasal secretions of patients with AR. Durham et al. found the expression of the ε embryonic gene and the m ribonucleic acid (RNA) transcript of the ε heavy chain of IgE in the nasal B cells. Further research has shown the existence of class switch recombination to IgE in the nasal mucosa of patients with AR [2–4]. Upon detection of nasal sIgE in patients with NAR [1], Rondon et al. [8, 9] demonstrated the presence of nasal sIgE in patients with seasonal and perennial LAR symptoms during the natural exposure to aeroallergens in earlier (22%) and later (35%) responses.

A possible reason for the inability to detect local sIgE to a large extent in patients with LAR and positive nasal allergen provocation test (NAPT) response may be the low sensitivity of diagnostic tests, dilution effect of nasal lavage, lack of inclusion of occult allergen, existence of other immune mechanisms as well as the possibility of non-specific protease activity of stimulation of house dust mites (HDM) on the innate immune cells of the respiratory system and others. The development of non-invasive in-vitro diagnostic techniques with high sensitivity detection of nasal sIgE would be a breakthrough in diagnosing and screening of LAR.

Recently published research data corroborate the concept of the synthesis of local sIgE in nasal mucosa [26]. Powe et al. have demonstrated the localization of free light chains (FLCs) in the tissue and nasal secretions of patients with AR and patients with NAR, assuming that they can mediate a hypersensitive immune response including the mast cells [26]. Further studies are needed to shed light on whether FLCs has a helpful or independent role in patients with IgE-mediated allergy and shed light on the presence of FLCs in patients with LAR.

TH2 Nasal Inflammatory Response (Mechanism)

Although the cause of IR is unknown, a number of pathophysiological mechanisms have been proposed including the inflammatory and neurogenic mechanism as well as a change in mucosal permeability [14]. The importance of the inflammatory mechanisms in patients with NAR was much disputed in the past. Though several histological and in situ hybrid studies found a Th2 inflammatory mechanism with an increase in the number of mast cells, eosinophils, IgE + B cells and T cells [5, 10], other studies found no significant difference between subjects with NAR and the controls [5, 10, 27, 28]. These apparently contradictory results can be explained by heterogeneity of NAR and recently diagnosed LAR in non-atopic patients. These early studies included patients with different pathogenesis that was predominantly inflammatory in patients with NARE and possibly patients with LAR [5, 10] and neurogenic mechanisms for patients with IR or vasomotor rhinitis [5, 8–10, 27, 28].

The existence of a TH2-mediated inflammatory IgE response has recently been confirmed in patients with LAR [8, 9]. Flow cytometric studies of a nasal lavage sample have shown that the patients with LAR and those with AR have a similar leukocytic-lymphocytic phenotype with an increase in the level of eosinophils, basophils and mast cells, CD3 + T cells, and CD4 + T cells during the exposure to aeroallergens [8, 9].

In addition, more than 70% of patients with NAR and LAR have characteristics of NARES (nasal eosinophilia> 20%). Previously, Powe et al. found an increase in CD8 + prior to CD4 + T-cells in patients with NAR and patients with AR compared to the numbers in the control studies and the reduction in number of antigen-presenting cells in patients with IR compared to those seen in patients with AR [10]. In this study, sIgE antibodies were not determined, neither was NAPT used. Therefore, the number of patients with LAR and their pathophysiological characteristics were not evaluated.

Positive Response to Nasal Allergen Provocation Test

Several studies have confirmed that more than 47% of patients with a previous diagnosis of IR have LAR with a positive NAPT response followed by a subjective (symptomatic) score and objective parameters (acoustic rhinometry, anterior rhinomanometry, nasal secretions with presence of sIgE and inflammatory mediators) [6, 8, 9, 11–13]. The first kinetic study of local production of IgE and inflammatory mediators after NAPT was administered to patients with LAR sensitized to grass pollen [12]. The results showed the activity of mast cells, eosinophils and IgE production caused by nasal stimulation with airborne allergens. Patients had a direct or dual response to NAPT, followed by release of triptase, ECP and sIgE in nasal secretions. A kinetic study involving triptase showed a strong correlation with nasal itching and secretions (runny nose) with the release of tryptase, which varied with the type of response. An immediate response was presented with a significant increase in the level of triptase 15 minutes to 1 h after the exposure compared with the baseline values where patients with delayed dual responses reacted to increased triptase from 15 minutes to 6 hours [12]. López et al. confirmed these results in patients with perennial LAR with positive response to the NAPT for Dermatophagoides pteronyssinus [13]. A significant finding in the two studies was a progressive increase in the level of the nasal sIgE from 1 to 24 hours after the NAPT [12, 13].

This sudden secretion of sIgE upon provocation with the basic detection of sIgE in some patients su-

pported the presence of the local production of sIgE in the nasal mucosa, which was increased upon allergic stimulation. All these findings prompt the scientists to consider the need to evaluate whether there is a local production of sIgE in patients with other non-allergic respiratory diseases, such as chronic rhinosinusitis with or without nasal polyps, asthma or conjunctivitis [29–33].

Local Production of IgE Associated with Nasal Polyps

Nasal polyposis is a chronic inflammatory process of the nasal and sinus mucosa of unknown etiology. In recent years, scientists have shown that Staphylococcus aureus can modify respiratory disease by inducing the synthesis of polyclonal IgE antibodies against *S aureus* super antigen and environmental allergens in tissues of nasal polyps [29, 30].

This mucosal polyclonal IgE production against several antigens (aeroallergens or not) represents a model of the local synthesis of IgE different from LAR. In this model, the specific antibodies to aeroallergens correlate with the clinical response and allergen-specific activation of B cells, mast cells and eosinophils, often associated with low total IgE levels. However, the clinical significance of this phenomenon needs to be explained.

Local Production of IgE Associated with Asthma

Evidence suggests some overlapping between atopic and non-atopic asthma. There is an increased number of B cells with an increase in IL4 and IL5 mRNA expression in lung tissue of asthmatic patients, who may be either atopic or non-atopic ones [31, 32]. These findings lead to important questions: Is there the sameness of LAR among patients with asthma, conjunctivitis or both? Do patients with asthma also produce local IgE antibodies and bronchial allergic response in the absence of systemic atopy? A recent study by Campo et al. described the presence of positive response to bronchial stimulation of D pteronyssinus with the number of eosinophils and basophils in the sputum of non-atopic asthma patients, justifying further studies [33].

Clinical Manifestations
Nasal Symptoms and Comorbidities

Patients with LAR have typical symptoms of AR (rhinorrhea, nasal blockage, runny and itching nose), which is usually associated with ocular symptoms and a good response to oral antihistamines and nasal corticosteroids [8, 9, 12]. Patients with LAR, as well as those with AR, have anterior rhinorrhea, nasal itching and secretion as the most common symptoms [8, 9]. Patients with LAR are classified according to the classical division of seasonal, perennial and occupational AR instead of the new division of intermittent and persistent AR [14] (**Table 1**). The earlier division was made according to the time of allergen exposure, while the new division is based on the presence of symptoms [14]. Most patients with LAR have persistent rhinitis with moderate to severe symptoms often associated with conjunctivitis (25% to 57%) and asthma (33% to 47%) [8, 9, 34]. So far, no data on the topic of LAR in the pediatric population have been published. Large epidemiologic studies including both the adult and pediatric population are required to define the prevalence, severity of symptoms, comorbidities, impact of airborne allergens and clinical effects of LAR.

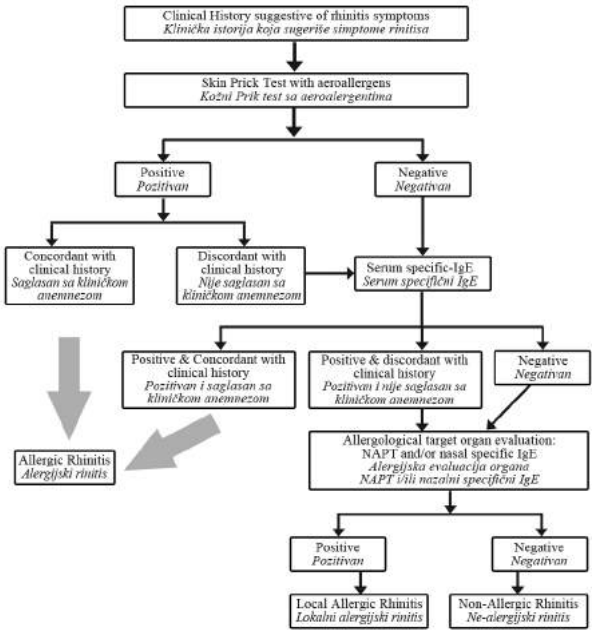
Pre-Investigation of Allergic March

Since LAR occurs relatively late in life with a high percentage of patients who do not report any symptoms referring to systemic allergy, the question remains whether these patients are truly atopic. Furthermore, a large group of patients with NAR having had negative skin prick test (SPT) and serum sIgE levels throughout life become positive in 24% of cases. This suggests that the vast majority remains negative [35]. In this context, the concept of atopy must certainly be expanded. If patients with LAR develop AR over time, this event would then support the atopic march. For this purpose, more details as well as more prospective studies including patient groups should be evaluated in the case of LAR associated with asthma and/or conjunctivitis. One study that helps clarify atopic march is the study of the evolution of LAR during immunotherapy. Developing studies indicate that patients with LAR undergoing immunotherapy for grass pollen with an initially negative skin prick test become positive and have serum sIgE antibodies, regardless of clinical improvement, which occurs during classical AR [34].

Diagnostic Protocol

Awareness of the existence of local allergic response of the nasal mucosa suggests that allergy processing is necessary. Rondón et al. proposed a new protocol with nasal allergen evaluation in all patients with clinical history indicative of AR but having negative SPT and sIgE antibodies or in those whose clinical history is not coherent [36] (**Graph 1**).

Diagnosis of LAR can be done by detecting nasal sIgE or according to the positive NAPT response or both, provided that systemic atopy is absent. Laboratory testing of nasal lavage (mucus) is a non-invasive method for examining cells, inflammatory mediators and other immunological markers. Determination of the level of sIgE with nasal lavage has been proved to be useful for detecting local hypersensitivity during natural exposure and after NAPT. This in vitro assay has a high specificity but a low sensitivity of 22% to 40% [8, 9]. Whether the effect of dilution of lava-



Graph 1. Diagnostic algorithm for LAR
Dijagram 1. *Dijagnostički algoritam za LAR*

ge samples, non-specific response to the HDM, other factors or both may contribute to this low sensitivity is still under consideration. The nasal provocation test with one aeroallergen (NAPT-S) is a highly useful diagnostic tool in patients with LAR, having high sensitivity of discovery of nasal sIgE, triptase or ECP levels [6, 8, 9, 11, 12]. However, it is a very time-consuming technique and its application in clinical practice can be problematic. Due to this fact, a new NAPT protocol was designed with multiple aeroallergens in a single session. It has since been proved to be useful, specific, sensitive, reproducible and less time-limited for screening patients with LAR. The sequential application of a number of airborne allergens in a single session did not cause any irritating response and showed 100% compatibility with the gold standard, that is NAPT-S. This application resulted in a 75% decrease in the total number of visits required for a definitive diagnosis in a patient group with NAR and a 55% decrease in patients with LAR compared with NAPT-S results [37].

Therapeutic Options

Distinguishing between LAR and NAR is the main basis for further successful treatment. AR therapy includes avoidance of allergens, pharmacological treatment, immunotherapy and education [14]. Patients with LAR respond well to topical nasal corticosteroids and oral antihistamines [8, 9]. This may be one of the phenotypic characteristics of the patients with LAR compared to those with the non-atopic rhinitis. A double-blind, placebo-controlled clinical study is of great importance when comparing the efficacy of pharmacological therapy in patients with LAR and AR. An important question is whether patients with LAR can benefit from immunotherapy. A pilot study by Rondón et al. included patients with LAR who were allergic to grass pollen [35]. Fifty percent of the patients were treated with subcutaneous immunotherapy (SCIT) for grass pollen for 6 months and, when necessary, they were medically treated in spring (the SCIT group), while the other half of patients received medication only (the control group). In this study, SCIT with grass pollen increased tolerance to aeroallergens and reduced symptoms as well as the amount of medication in patients with LAR, compared to those in the control group. These interesting results have increased the necessity for phase II double-blind placebo-controlled clinical trials for evaluating whether LAR can be regarded as a new indicator for the specific immunotherapy [34].

Future Research

The increasing amount of data on the localized allergic response in non-atopic individuals asks for many answers on the subject of LAR. These answers can be given by studies on the prevalence and incidence in children and adults, impact of positive family atopy in the development of the disease, impact of diseases of the lower respiratory tract and conjunctiva, effectiveness of drug treatment and the issue of administration of specific immunotherapy.

It is very important to know if patients remain stable over the years or their symptoms turn into a form of allergic rhinitis. The fact that many patients have history of LAR for numerous years without the progression of systemic AR supports the idea that this is an independent entity.

However, there is a possibility that local sensitization would be the primary event in each AR and could later develop into classic systemic AR over time. This claim requires further prospective studies [38].

In addition, further research should discover more characteristics of the inflammatory response in patients with LAR, This can be achieved by carrying out comparative studies among the patients with LAR and those with AR, by assessing the presence of a local allergic response in patients with professionally induced rhinitis with or without asthma, by considering feasibility of genetic studies in large groups of patients diagnosed with LAR and by comparing them with patient groups having systemic AR and NAR.

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IMPACT OF NASOFRONTAL ANGLE SIZE ON CHANGES IN NASAL AIRWAY RESISTANCE BEFORE AND AFTER RHINOSEPTOPLASTY

UTICAJ VELIČINE NAZOFRONTALNOG UGLA NA PROMENU OTPORA PROTOKU VAZDUHA KROZ NOS PRE I POSLE RINOSEPTOPALSTIKE

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Summary
The nose is the most prominent feature of the human face and in terms of esthetics, it has a significant impact on the overall facial appearance, its expression and beauty. In addition, it has other functions, which are much more important, above all breathing, protection, the sense of smell and the sound of the voice. The nasofrontal angle is the angle between the forehead and the dorsum of the nose. It determines the prominence of the nasal pyramid. A more acute nasofrontal angle is associated with a more prominent nasal pyramid. The nasofrontal angle in the Greek nose is 180°. Although authors have different opinions, the nasofrontal angle in Caucasian population should be between 127° and 150°. This prospective, cross-sectional study included 80 patients of both sexes who had undergone rhinoseptoplasty at the Department of Ear, Nose and Throat Diseases of the Clinical Center of Vojvodina. Of 80 patients, 22 were males. As for their age, 61% of patients were between 18 and 25 years old. Analysis of the nasofrontal angle before and after surgery, with a correlation coefficient of 0.4866, indicates that preoperative parameters of the nasofrontal angle have a moderate impact on the postoperative outcome. The impact analysis of the nasofrontal angle on the airway resistance in the preoperative and postoperative period showed distinct differences. Both functions can be best described by linear regression equations. The rhinoseptoplasty procedure reduces the nasofrontal angle to standard dimensions, consequently leading to reduction of the nasal airway resistance.
Key words: Nasal Bone; Nasal Septum; Frontal Bone; Rhinoplasty; Airway Resistance; Nasal Obstruction; Reconstructive Surgical Procedures; Esthetics; Male; Female; Young Adult

Sažetak
Nos je najistaknutiji deo ljudskog lica i u estetskom smislu daje pečat čitavom licu, njegovu izražajnost i lepotu. Daleko značajnija uloga nosa je u ostvarenju disajne, zaštitne, mirisne i rezonantne funkcije. Nazofrontalni ugao je ugao koji formira dorzum nosa sa čelom. On određuje prominentnost nosne piramide. Što je nos manji, nosna piramida je prominentnija. Kod „grčkog" nosa iznosi 180°. Nazofrontalni ugao bi trebalo da iznosi, u zavisnosti od autora do autora, 127–150° za belu rasu. Istraživanje je bilo prospektivno, ukršteno i obuhvatalo je 80 pacijenata oba pola koji su podvrgnuti rinoseptoplastici na Klinici za bolesti uva, grla i nosa, Kliničkog centra Vojvodine. Muškog pola su bile 22 osobe. Analizom starosne distribucije vidi se da je 61% pacijenata bilo starosti između 18 i 25 godina. Analiza vrednosti nazofrontalnog ugla pre i posle operacije, uz vrednost koeficijenta korelacije od 0,4866, upućuje na postojanje umerenog uticaja preoperativnih karakteristika nazofrontalnog ugla na postoperativne karakteristike. Analizom uticaja nazofrontalnih uglova na otpor protoku vazduha u preoperativnom i postoperativnom periodu, uočene su izrazite razlike. Obe funkcije se mogu najbolje opisati jednačinama linearne regresije. Izvođenjem operativnog zahvata dolazi do svođenja nazofrontalnog ugla u standardne dimenzije. Približavanjem nazofrontalnog ugla standardnim vrednostima dolazi do smanjenja otpora protoku vazduha kroz nos.
Ključne reči: Nosna kost; Nosni septum; Čeona kost; Rinoplastika; Otpor disajnim putevima; Nosna opstrukcija; Rekonstruktivne hirurške procedure; Estetika; Muško; Žensko; Mladi ljudi

Introduction

The nose is the most prominent feature of the human face and in terms of esthetics, it has a significant impact on the overall facial appearance, its expression and beauty. In addition, it has some other functions, which are much more important, above all breathing, protection, the sense of smell and the sound of the voice [1]. In order to provide all this, there must be an interaction between the nasal pyramid and the face, presence of a normal nasal septum and a corresponding trophic of the nasal mucosa. One of the parameters affecting the size and harmony between the nasal pyramid and the face is the nasofrontal angle. It is the angle between the forehead and the dorsum of the nose. It determines the prominence of the nasal pyramid. A more acute nasofrontal angle is associated with a more prominent nasal pyramid. The nasofrontal angle in the Greek nose is 180°. Although opinions differ from author to author, the nasofrontal angle in Caucasian population should be between 127° and 150° [2–5].

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Table 1. Parameters of nasofrontal angle before surgery, after surgery and their differences
Tabela 1. *Parametri nazofrontalnog ugla pre operacije, posle operacije i njihova razlika*

	Number of patients *Broj ispitanika*	Mean value *Srednja vrednost*	Minimum *Minimum*	Maximum *Maksimum*	Standard deviation *Standardna devijacija*
PR_N_FRON	80	137.5823	100	166	9.80790
PO_N_FRON	80	147.9494	130	153	4.13831
R_N_FRON	80	10.36709	-16	30	8.59065

PR_N_FRON - preoperative parameters of the nasofrontal angle/*preoperativni parametri nazofrontalnog ugla;* PO_N_FRON - postoperative parameters of the nasofrontal angle/*postoperativni parametri nazofrontalnog ugla;* R_N_FRON - differences between parameters of nasofrontal angle/*razlika parametara nazofrontalnog ugla*

The term rhinoplasty refers to plastic surgery that involves making changes to the size and shape of the nasal pyramid for purely cosmetic reasons to improve the appearance, or to restore adequate nasal breathing. According to the place where incisions are made, rhinoplasty can be either open or closed. Some authors use the term rhinoseptoplasty and believe that every surgery of the nasal septum is rhinoseptoplasty to some extent [6, 7].

Material and Methods

This prospective, cross-sectional study included 80 patients of both sexes treated at the Department of Ear, Nose and Throat Diseases of the Clinical Center of Vojvodina. The study sample consisted of 22 male (27.5%) and 58 female patients (72.5%).

The age of patients ranged from 18 to 50 years, and the average age was 26.75 years. Of the total number of patients, 61.25% were aged between 18 and 25 years.

Esthetic rhinoseptoplasty was performed in 36 (45%) patients, and the functional one in 44 (55%) patients.

Rhinomanometry test was performed in all patients preoperatively to evaluate objectively the respiratory function during decongestion of nasal mucosa in order to avoid mucosal components in the measurement process. Anemisation was conducted in accordance with the 2005 Consensus, with 0.1% oxymetazoline nasal spray, 50 μg in each nostril; the process was repeated after 5 minutes with a single dose in both nostrils. The test was performed 15-30 minutes after the application [7]. Rhinomanometry and acoustic rhinometry were done using the Interacoustics SRE 2000 device.

Six months later, the nasal pyramid was considered to be fully formed and postoperative recovery completed, the nasofrontal angle was redefined and respiratory function tests were performed using rhinomanometry with a decongestant nasal mucosa. Rhinomanometry was used to measure unilateral and bilateral nasal resistance during respiration.

Results

Table 1. shows basic statistical parameters of the nasofrontal angle before surgery, after surgery and differences between parameters of nasofrontal angle in all patients included in the study.

The analysis of the impact of nasofrontal angle on the nasal airway resistance in the preoperative and postoperative periods shows distinct differences. Both functions have been best presented in a linear regression equation.

In the preoperative period, there was a moderate proportional functional relationship between the independent variables of nasofrontal angle and the sum of the total resistance. In the postoperative period, the linear correlation coefficient was closer to zero **(Figure 1)**.

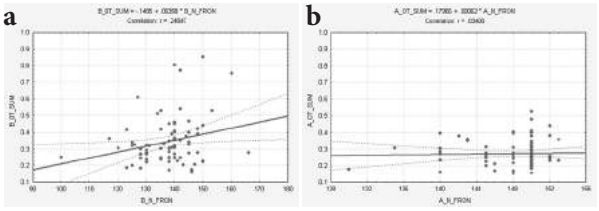

Figure 1. The impact of nasofrontal angle before surgery on preoperative total resistance (a) and the impact of postoperative nasofrontal angle on total airway resistance after surgery (b)
Grafikon 1. *Uticaj nazofrontalnog ugla posle operacije na ukupne otpore posle operacije (a) i uticaj nazofrontalnog ugla pre operacije na ukupne otpore pre operacije (b)*

Using a parametric t-test for normally distributed pre- and postoperative nasofrontal angles, a significant difference between mean values (t= -10.7262, p=0.00)

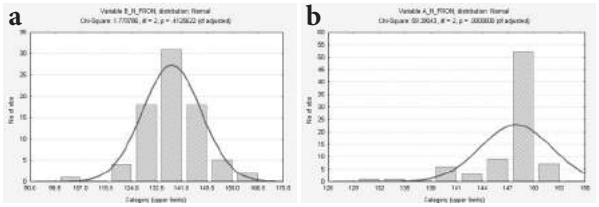

Figure 2. Nonparametric characteristics of the preoperative nasofrontal angle (a) and nonparametric characteristics of the postoperative nasofrontal angle (b)
Grafikon 2. *Neparametarske karakteristike nazofrontalnog ugla pre operacije (a) i neparametarske karakteristike nazofrontalnog ugla posle operacije (b)*

Table 2. Median values, asymmetry coefficient and excess kurtosis of the nasofrontal angle before and after surgery
Tabela 2. *Mediana, koeficijent asimetrije i ekscesa nazofrontalnog ugla pre i posle operacije*

	Mean values *Srednja vrednost*	Median *Mediana*	Asymmetry coefficients *Koeficijent asimetrije*	Excess kurtosis *Kurtosis Ekscesa*
PR_N_FRON	137.5823	139	-0.49039	2.358
PO_N_FRON	147.9494	150	-1.97756	4.542

PR_N_FRON - preoperative parameters of the nasofrontal angle/*preoperativni parametri nazofrontalnog ugla*
PO_N_FRON - postoperative parameters of the nasofrontal angle/*postoperativni parametri nazofrontalnog ugla*

was found. The preoperative nasofrontal angle was 137.58°, and the postoperative one was 147.94°.

The nasofrontal angle measures showed a significantly normal distribution. The postoperative measures of the nasofrontal angle showed no significant overall normal distribution. **Figures 1 a** and **1 b** show verified distributions, X^2, and significance threshold values of pre- and postoperative nasofrontal angles **(Figure 2)**.

Incomplete characteristics of mean values, asymmetry coefficient and excess kurtosis of the nasofrontal angle before and after surgery are given in **Table 2.**

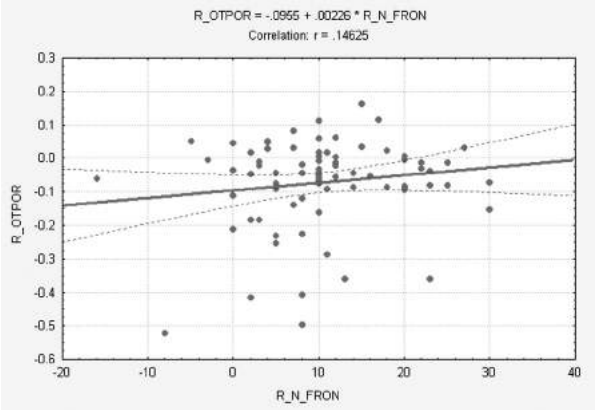

Figure 3. The impact of changes of the nasofrontal angle on changes of the total resistance
Grafikon 3. *Uticaj promene nazofrontalnog ugla na promenu vrednosti ukupnih otpora*

Median values were within the values of mathematical expectations, i. e. mean values. The asymmetry coefficients and excess kurtosis before surgery were close to the reference values (reference values equal 0). The impact of individual changes of the nasofrontal angle on the total resistance is presented in linear regression equations with a significant normal overall distribution. The mean values of changes and a significant nasofrontal angle increase by 10.36° using linear regression equation, correspond to the reduction in the total resistance by -0.07. The importance of these changes results from significant changes of the nasofrontal angle. The linear regression, correlation coefficient and verification of the normal distribution between differences of the nasofrontal angle are given in **Figures 3** and **4**.

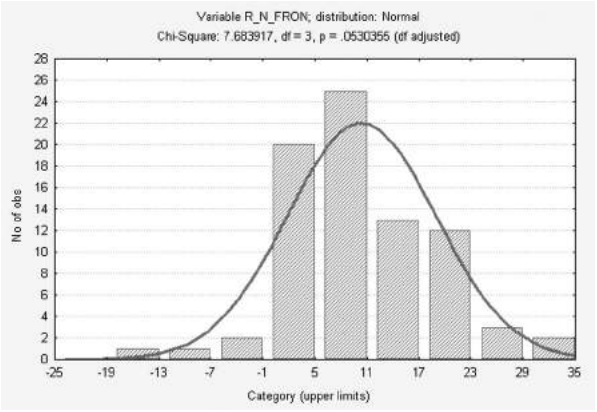

Figure 4. Verification of the normal distribution between differences of the nasofrontal angle
Grafikon 4. *Verifikacije normalne raspodele vrednosti razlika nazofrontalnog ugla*

Discussion

According to Huizinga, the ideal nasofrontal angle is 150° in both sexes [2]. The nasofrontal angle often depends on ethnicity, such as the Greek nose, which makes it more difficult to achieve ideal dimensions.

The analysis of the nasofrontal angle before and after surgery, with the correlation coefficient of 0.4866, suggests that the preoperative parameters of the nasofrontal angle have a moderate impact on the postoperative outcome.

The impact analysis of nasofrontal angles on the airflow resistance in the preoperative and postoperative period showed distinct differences. Both functions were presented in linear regression equations (**Figures 1 a** and **1 b**).

In the preoperative sample, there was a moderate proportional functional relationship between the independent variables of nasofrontal angle and the sum of the total resistance. In the postoperative sample, the linear correlation coefficient was closer to zero.

Using a parametric t-test for normally distributed pre- and postoperative nasofrontal angles, a significant difference between mean values ($t = -10.7262$, $p = 0.00$) was found. The preoperative nasofrontal angle was 137.58°, and the postoperative one was 147.94°. The nasofrontal angle measures showed a significantly normal distribution. The postoperative measures of the nasofrontal angle did not show a significant overall normal distribution.

The median values were within the values of mathematical expectations. The asymmetry coefficients and excess kurtosis before surgery were close to the reference values (reference values equal 0). The nasofrontal angle parameters of asymmetry and excess kurtosis changed significantly after the surgical procedure. As the mathematical expectations and median postoperative findings were within standard values, major changes in the asymmetry coefficients and excess kurtosis made it possible to reduce the nasofrontal angle to the standard level. At the same time, an increase in the asymmetry coefficient shows that the reduction to 150° was not possible in a small number of patients. This is due to the configuration of facial features or previous size of the nasofrontal angle.

Low linear regression coefficient values of the nasofrontal angle and postoperative airway resistance, as well as the absence of significant verification of normal nasofrontal angle distribution after surgery, resulted from the surgical procedure. In most cases, the postoperative nasofrontal angles were within the standard ranges: from 147° to 150°. The compliance with standard values of the nasofrontal angle is the reason for the absence of a significant normal distribution of nasofrontal angles in the postoperative period. In addition, low linear regression coefficient values of the nasofrontal angle and total resistance are due to the compliance with standards. This procedure has changed relations between the "natural", preoperative features of the nasofrontal angle variables. In the postoperative sample, the standard values have completely eliminated the impact of nasofrontal angle on the airflow resistance.

The impact of individual changes of the nasofrontal angle on the total resistance is presented in linear regression equations with a significant normal overall distribution. The mean value of changes, a significant nasofrontal angle increase by 10.36° using linear regression equation, corresponds to the reduction in the total resistance by -0.07. The importance of this change results from significant changes of the nasofrontal angle. This means that the compliance with the standard values of the nasofrontal angle during surgery consequently reduces the patient's total airway resistance. It is of special importance to note that in addition to increasing the nasofrontal angle to standard values and reducing the resistance, the compliance with standards significantly decreases the standard deviation from 9.80 before surgery to 4.13 after surgery. This also means that the postoperative nasofrontal angle is mostly within standard values (mean values) or close to mean values resulting from the almost 50% lower value of standard deviation.

The impact of nasofrontal angle on the respiratory function should be considerable. The nasofrontal and nasofacial angles are direct indicators of the dimensions of the nasal pyramid [8]. The nasofrontal angle is always greater in patients with rhinokyphosis, although patients without a pronounced nasion may have quite a small nasal pyramid with a large nasofrontal angle [9]. This is the case in patients with the Greek nose. In such cases, the nasofacial angle indicates the dimensions of the nasal pyramid. To the best of our knowledge, the impact of nasofrontal angle on the respiratory function has not been studied as an individual parameter, so there are no available data on this issue.

Conclusion

More than 60% of patients undergoing rhinoseptoplasty are under the age of 25 years

The rhinoseptoplasty procedure reduces the nasofrontal angle to standard dimensions

Reduction of the nasofrontal angle consequently reduces the nasal airway resistance.

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THE INFLUENCE OF NASAL SEPTUM DEFORMITY DEGREE ON SUBJECTIVE NASAL BREATHING ASSESSMENT

UTICAJ STEPENA DEFORMITETA NOSNE PREGRADE NA SUBJEKTIVNU OCENU DISANJA NA NOS

Slobodan SAVOVIĆ[1,2], Vladimir KLJAJIĆ[1,2], Maja BULJČIK ČUPIĆ[1,2] and Ljiljana JOVANČEVIĆ[1,2]

Summary

Introduction. The aim of this paper is to determine the influence of nasal septum deformity degree on the subjective nasal breathing assessment as well as the existence of correlation between one side of the nose with nasal septum deformity and the subjective feeling of difficulty in breathing on that side in the subjects with different degrees of nasal septum deviation. **Material and Methods.** The research included 90 randomly chosen patients, who claimed to have nasal breathing difficulties. Every patient assessed subjectively which side of the nose made breathing difficult and scored the breathing on that side from 0 to 10 cm on the visual analogue scale. **Results.** The patients from the third group described their breathing as the most difficult, while the subjects from the first group claimed that their nasal breathing problems were the least difficult. The subjective feeling of heavy nasal breathing on the deformed nasal septum side was significantly different in all groups (H= 38.466, p= 0.000). In the second and the third group of patients there was a significant correlation between the deformed side of the nose and the subjective heavy breathing on that side (p< 0.05), whereas this correlation was not found in the first group (p> 0.05). **Conclusion.** The subjective feeling of difficulty in breathing on the deformed side of the nose is intensified with the degree of the nasal septum deformity, thus this feeling was reported only by the subjects with a higher degree of the nasal septum deformity.

Key words: Nasal Septum + abnormalities; Respiration; Self-Assessment; Nasal Obstruction; Diagnosis; Tomography, X-Ray Computed

Sažetak.

Uvod. Cilj ovog rada bio je da se utvrdi da li postoji uticaj stepena deformiteta nosne pregrade na subjektivnu procenu disanja na nos, kao i da li postoji podudarnost između strane nosa sa deformitetom nosne pregrade i subjektivnog osećaja težeg disanja na tu stranu nosa. **Materijal i metode.** Istraživanjem je obuhvaćeno ukupno 90 bolesnika, koji su se žalili na otežano disanje na nos. Svaki bolesnik je subjektivno odredio stranu nosa na koju teže diše i svoje disanje na nos je procenio na vizuelnoj analognoj skali od 0 do 10 cm. **Rezultati.** Bolesnici treće grupe svoje disanje na nos subjektivno procenjuju kao najteže, dok ispitanici prve grupe subjektivno imaju najmanje tegobe kada je disanje na nos u pitanju. Subjektivna ocena disanja na nos na stranu gde postoji deformitet nosne pregrade značajno se razlikuje između svih grupa (H = 38,466, p = 0,000). U drugoj i trećoj grupi ispitanika postoji značajna podudarnost između strane nosa na kojoj se nalazi deformitet nosne pregrade i subjektivno težeg disanja na tu stranu nosa (p < 0,05), dok u prvoj grupi ova podudarnost nije nađena (p > 0,05). **Zaključak.** Sa porastom stepena deformiteta nosne pregrade raste i subjektivni osećaj težeg disanja na tu stranu nosa. Poklapanje strane nosa na kojoj se nalazi deformitet nosne pregrade i subjektivnog osećaja težeg disanja na tu stranu nosa postoji samo kod ispitanika sa izraženijim stepenom deformiteta nosne pregrade.

Ključne reči: Nosna pregrada + deformiteti; Disanje; Samoprocena; Nosna opstrukcija; Dijagnoza; CT

Introduction

Heavy nasal breathing is one of the most common reasons why patients go to otorhinolaryngologists [1]. Nasal breathing difficulties result either from mechanical changes inside the nose (the most common being nasal septum deformity, anatomic structure variations in the medium nasal meatus as well as tumorous changes in the nose) or from nasal mucous membrane swelling (most commonly inflammatory changes of diverse etiology). Nasal septum deformities (NSD) can be associated with nasal pyramid deformities, or they can occur individually [2, 3].

Blaugrund [4] has found clinically significant nasal septum deformities in 20% of the general population, while Yang-Gi et al. [5] have given an accurate description of 22.38% of the general population in Korea, most commonly in men and the elderly. There is a great diversity regarding nasal septum deformity classification. Kamami et al. [6] classify them according to the size of the obstruction of the particular half of the nose, while Kaya-

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Abbreviations

VAS – visual analogue scale
CT – computed tomography
ENT – ear, nose, throat
NSD – nasal septum deformity

lioglu et al. [7] are of the opinion that the nasal septum is always deformed when its deviation from the middle facial line exceeds 3 mm at any point. Collet et al. [8] assess the significance of nasal septum deformity on the basis of any contact of nasal septum mucous membrane with the lateral wall mucous membrane before or after anemisation of the mucous membrane of the nose. Harar et al. [9] and Elahi and Frenkiel [10] classify nasal septum deformities based on computed tomography (CT) findings, determining the angle that is covered by the line from crista galli to spina nasalis anterior interior and the line drawn from crista galli to the point where the biggest nasal septum deformity is. Ingo and Helmut Baumann [11] have given a classification of nasal septum deformity on the basis of its leading and accompanying anatomic change. Within this division, they have described the accompanying changes on lower and medium nasal conchae.

In some patients, clinical findings of anterior rhinoscopy correlate greatly with the subjective nasal breathing assessment, while in other patients it is not the case [1]. According to the clinical practice, there are patients who have manifest nasal septum deviation but have no breathing difficulties whatsoever, while there are patients with no deviations who suffer from nasal breathing difficulties.

The aim of this paper is to determine the influence of nasal septum deformity degree on the subjective nasal breathing assessment as well as the existence of correlation between one side of the nose with nasal septum deformity and the subjective feeling of difficulty in breathing on that side in the subjects with different degrees of nasal septum deviation.

Material and Methods

The research included 90 randomly chosen patients, 26 women and 64 men who claimed to have nasal breathing difficulties. The patients who had any other nasal ailment besides nasal septum deformity were excluded from the study because its presence could have a direct influence on their subjective feeling of breathing difficulties. The average age of the examined patients was 31.12 years. On the basis of nasal septum deformity, the subjects were divided into three groups (30 patients in each group). The first group (I) included the patients with the deformity that was less than 10º. In the second group of patients (II), the degree of nasal septum deformity was from 10º to 15º. The third group (III) consisted of the patients with nasal septum deformity that was greater than 15º. The degree of deformity was determined by CT of the nose as an angle consisting of the line drawn from crista galli to spina nasalis interior inferior and the line drawn from crista galli to the point of the greatest degree of the deformity. The value of nasal septum deformity was expressed in whole numbers. Every patient subjectively assessed the side of the nose which made breathing difficult and it was compared with clinical and CT findings. Afterwards, the patients subjectively assessed their breathing on that side from 0 to 10 on the visual analogue scale (VAS), where 0 is no nasal breathing difficulties at all and 10 marks not being able to breathe on the side where deformity is. Mann-Whitney and Kruskal-Wallis test was used for statistical analysis.

Results

Subjective nasal breathing on the deformed nasal septum side was significantly different in all groups ($H= 38.466$, $p= 0.000$). The patients from group III described their breathing as the most difficult, while the subjects from group I claimed that their nasal breathing problems were the least difficult. Between the first and the second group of patients the values were $Z= 3.648$, $p= 0.000$; between the first and the third group of patients the values were $Z= 5.042$, $p= 0.000$; while the results of comparing the second and the third group were the following: $Z= 4.297$, $p= 0.000$ (**Table 1**).

In the second and the third group of patients there was a significant correlation between the deformed side of the nose and a subjective heavy breathing on that side ($p< 0.05$), while this correlation was not found in the first group ($p> 0.05$) (**Table 2**).

Discussion

The average age of our subjects was 38.6 years, with male patients being in majority (70.83%), which is in accordance with the results of other authors [6, 12, 13].

Nasal obstruction is the leading symptom in 15% of British outpatients who visit their ear, nose

Table 1. Subjective nasal breathing assessment on the side with a nasal septum deformity
Tabela 1. *Subjektivna procena disanja na nos na strani deformiteta nosne pregrade*

Group/*Grupa*	Side with nasal septum deformity/*Strana sa deformitetom nosne pregrade*		
	Average value/*Prosečna vrednost*	SD	Median/*Mediana*
I	1.84	1.30	2.00
II	3.57	1.22	3.00
III	6.83	1.54	7.00

Table 2. Correlation between the deformed side of the nose and the side with subjective heavy nasal breathing
Tabela 2. *Poklapanje između strane sa deformitetom nosne pregrade i strane subjektivno težeg osećaja disanja na nos*

Group, Side of deformity *Grupa, Strana deformitet*a	Right/*Desno*			Left/*Levo*			P
	Average value *Prosečna vrednost*	Median *Mediana*	SD	Average value *Prosečna vrednost*	Median *Mediana*	SD	
I, Right/*I, Desno*	1.62	2.00	1.04	2.15	2.00	1.34	0.319
I, Left/*I, Levo*	1.59	2.00	1.33	1.94	2.00	1.20	0.483
II, Right/*II, Desno*	3.63	4.00	1.15	1.06	0.00	1.48	0.001
II, Left/*II, Levo*	2.07	2.00	2.09	3.71	3.50	0.99	0.007
III, Right/*III, Desno*	6.75	7.00	0.91	2.05	1.00	2.40	0.000
III, Left/*III, Levo*	1.50	0.50	2.01	6.70	7.00	1.16	0.005

and throat (ENT) doctors [14], while Viano-Mattila [15] states that 200 patients, who visited their otorhinolaryntologists for other reasons primarily, complained of temporary or permanent nasal breathing difficulties as well. Since numerous reasons can lead to heavy breathing, it is very difficult to determine the real reason of this disorder on the basis of sheer clinical examination. Only in the patients in whom mucous component as well as tumorous changes and anatomic variations of the medium cochlae (which are exclusively described as anatomic variation causes of heavy breathing) are excluded as a culprit [16, 17], it can be said that if there is a nasal septum deformity, it really is the major cause of heavy nasal breathing. The definition of septum deviation is not standardized. It is subjective and restrictive because it is limited in the space and ignores the possibility of bilateral deviation [8]. Despite the fact that nowadays we have numerous objective methods to assess nasal breathing function, the subjective nasal breathing assessment is still the most relevant, and it is implemented as a method in indications for surgical procedures to cure nasal septum deformities as well as the evaluation of post surgical results [18–20].

Our results show that there is, among the examined groups with the rise of deformity degree, statistically significant heavy breathing more difficult breathing on the side of the nose where the deformity is; in every group $p < 0.001$. As for the correlation between the deformed side of the nose and subjective nose breathing assessment by the examined patients, it was found to be $p < 0.05$ in group II and III with a bigger nasal septum deformity, whereas it was not found in group I with the lowest degree of deformity, $p > 0.05$. Sipila et al. reported the same results, but they had implemented different methodology [21]. Namely, they found that there was a correlation between the side of subjective nasal breathing and the side with the actual nasal septum deformity only in patients with greater degrees of nasal septum deformity i.e. when the difference in the airflow resistance between the sides of the nose was at least 60–70%. While examining nasal breathing function, Badrkić [22] concluded that subjective nasal breathing assessment did not correlate with objective findings as well as that patients were aware of their nasal breathing improvement after rhinoplasty; however they were not able to give a precise assessment.

Conclusion

The subjective feeling of difficulty in breathing on the deformed side of the nose is intensified with the degree of the nasal septum deformity; thus, this feeling was reported only by the subjects with a higher degree of nasal septum deformity.

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"SILENT SINUS SYNDROME" – ONE MORE INDICATION FOR FUNCTIONAL ENDOSCOPIC SINUS SURGERY

SINDROM TIHOG SINUSA – JOŠ JEDNA OD INDIKACIJA ZA FUNKCIONALNU ENDOSKOPSKU HIRURGIJU SINUSA

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Summary

Introduction. Silent sinus syndrome is a rare condition, characterized by spontaneous and progressive enophthalmos and hypoglobus associated with atelectasis of the maxillary sinus and downward displacement of the orbital floor. Patients with this syndrome present with ophthalmological complaints, without any nasal or sinus symptoms. Silent sinus syndrome has a painless course and slow development. It seems to be a consequence of maxillary sinus hypoventilation due to obstruction of the ostiomeatal unit. The CT scan findings are typical and definitely confirm the diagnosis of silent sinus syndrome. **Case report.** We present the case of a 35-year-old woman, with no history of orbital trauma or surgery. She had slight righthemifacial pressure with no sinonasal symptoms. The patient had no double vision nor other ophthalmological symptoms. The diagnosis of silent sinus syndrome was based on the gradual onset of enophthalmos and hypoglobus, in the absence of orbital trauma (including surgery) or prior symptoms of sinus disease. On paranasal CT scans there was a complete opacification and atelectasis of the right maxillary sinus with downward bowing of the orbital floor. The patient was treated with functional endoscopic sinus surgery, with no orbital repair. **Conclusion**. Silent sinus syndrome presents with orbithopaties but is in fact a rhinologic disease, so all ophthalmologists, rhinologists and radiologists should know about it. The treatment of choice for silent sinus syndrome is functional endoscopic sinus surgery, which should be performed with extra care, by an experienced rhinosurgeon.

Key words: Enophthalmos; Maxillary Sinus; Diagnosis; Signs and Symptoms; Tomography, X Ray Computed; Adult; Female; Otorhinolaryngologic Surgical Procedures; Natural Orifice Endoscopic Surgery

Sažetak

Uvod. Sindrom tihog sinusa (eng. s*ilent sinus syndrome*) jeste retko stanje za koje su karakteristični spontani i progresivni enoftalmus i hipoglobus, udruženi sa atelektazom maksilarnog sinusa i spuštanjem poda istostrane orbite. Sindrom tihog sinusa ima bezbolan tok i sporo se razvija. Pacijenti sa ovim sindromom se javljaju lekaru sa oftalmološkim tegobama, dok su simptomi oboljenja nosa i sinusa po pravilu odsutni. Nalaz kompjuterizovane tomografije nosa i sinusa je tipičan i definitivno potvrđuje dijagnozu. **Prikaz slučaja.** U radu prikazujemo slučaj pacijentkinje starosti 35 godina, koja se žalila na lagani osećaj pritiska u desnoj polovini lica, dok sinonazalnih i oftalmoloških simptoma nije bilo. Dijagnoza sindroma tihog sinusa postavljena je na osnovu podataka o postepenom nastanku enoftalmusa i hipoglobusa u odsustvu orbitalne traume (uključujući hirurgiju) i prethodnih simptoma oboljenja sinusa. Na snimku kompjuterizovanom tomografijom paranazalnih sinusa dijagnoza je potvrđena nalazom kompletne zasenčenosti i atelektaze desnog maksilarnog sinusa sa spuštenim podom orbite nadole. Pacijentkinja je lečena operativno – funkcionalnom endoskopskom hirurgijom sinusa. **Zaključak.** Sindrom tihog sinusa je entitet koji se prezentuje u kliničkoj praksi poremećajem položaja očne duplje, ali je prema svojoj suštini rinološko oboljenja, te svi rinolozi i oftalmolozi, a naravno i radiolozi treba da ga poznaju. Tretman izbora za sindrom tihog sinusa je funkcionalna endoskopska hirurgija sinusa koju izuzetno pažljivo treba da izvede iskusni rinohirurg.

Ključne reči: Enoftalmus; Maksilarni sinus; Dijagnoza; Znaci i simptomi; CT; Odrasli; Žensko; Otorinolaringološke hirurške procedure; Endoskopska hirurgija prirodnih otvora

Introduction

Silent sinus syndrome (SSS) is a rare condition involving the maxillary sinus, characterized by unilateral collapse of the maxillary sinus and orbital floor, associated with negative antral pressure in the absence of sinus symptoms [1–3].

The main clinical features of SSS are spontaneous and progressive enophthalmos (eye recession into globe) and hypoglobus (globe displaced downward) [1–4]. SSS patients present with ophthalmological complains, without any nasal or sinus symptoms ("silent sinus"), with painless course and slow development [1, 5].

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Abbreviations

SSS – silent sinus syndrome
ENT – ear, nose and throat
CT – computerized tomography
FESS – functional endoscopic sinus surgery
MS – maxillary sinus
MSH – maxillary sinus hypoplasia
CMA – chronic maxillary sinus atelectasis

Silent sinus syndrome is also known as primary or spontaneous imploding antrum syndrome, and is an idiopathic condition [1, 2, 4–6]. It typically presents unilaterally, in the third or fourth decade of life. This condition affects both genders equally [6]. Its development is gradual and progressive, so it may become symptomatic in a few months up to a few years, [1]. Besides esthetic problem of ocular (facial) asymmetry, caused by enophthalmos and hypoglobus, the patients might have diplopia, abnormal eyelid signs (retraction, ptosis, absent crease), lid lag, and dry eyes from lagophthalmos [3, 7, 8].

The diagnosis of SSS is made on the basis of typical clinical features (gradual onset of enophthalmos and/or hypoglobus, in the absence of orbital trauma, including surgery, or sinus disease), nasal endoscopy and imaging of the nose and paranasal sinuses [6].

Nasal endoscopy can reveal enlarged middle meatus with atelectatic uncinate process or not visible middle meatus because of the lateral displacement of the middle turbinate [3, 6].

The imaging of choice for SSS is computed tomography (CT). CT scans are typical and make the diagnosis definitive [3, 4, 8–10]. Coronal scans usually show laterally retracted uncinate process and medial sinus wall, enlarged medial meatus, inferiorly displaced orbital floor, increased orbital volume, and axial scans show inward retracted medial and superior walls of the maxillary sinus (MS), decreased MS volume (atelectasis of the maxillary sinus). In addition, partial to complete opacification of the involved sinus, with infundibulum always occluded is typical [1, 2, 4, 8, 11]. The maxillary sinus roof (orbital floor) is always retracted into sinus lumen and commonly thinned [1, 4, 11].

Figure 1. Coronal CT scan: lateralized right uncinate process and medial maxillary sinus wall, medial meatus enlarged; completely opacified right maxillary sinus, orbital volume increased.
Slika 1. *Koronalni CT sken: desni uncinatni procesus i medijalni zid maksilarnog sinusa su lateralizovani, proširen je srednji nosni hodnik; kompletno je homogeno zasenčen desni maksilarni sinus a povećan volumen orbite.*

Case Report

We present the case of a 35-year-old woman, with no history of orbital trauma or surgery. She had slight, right hemifacial pressure with no sinonasal symptoms. The patient had neither double vision nor other ophthalmological symptoms. The patient was referred for further management to our Rhinology Ward of the Department of Ear, Nose and Throat Diseases, the Clinical Centre of Vojvodina.

The diagnosis of SSS was based on the gradual onset of enophthalmos and hypoglobus, in the absence of orbital trauma (including surgery) or prior symptoms of sinus disease. Nasal endoscopy revealed the enlarged right middle nasal meatus with atelectatic uncinate process. The paranasal CT scans (coronal CT scan - **Figure 1** and axial CT scan – **Figure 2**) showed complete opacification and atelectasis of the right maxillary sinus with downward bowing of the orbital floor. The right maxillary sinus was imploded, middle meatus was enlarged and orbital volume was increased.

On ophthalmologic examination, the patient had normal visual acuity in both eyes with a 2 mm enophtalmos and 2 mm hypoglobus for the right eye.

The patient was treated with endoscopic sinus surgery by the first author. Uncinectomy was performed as the usual first step in functional endoscopic sinus surgery (FESS), but with special care,

Figure 2. Axial CT scan: inward retracted walls of the right maxillary sinus (MS), MS volume decreased (atelectasis of the maxillary sinus).
Slika 2. *Aksijalni CT sken: zidovi desnog maksilarnog sinusa su povučeni ka unutra a volumen smanjen (atelektaza maksilarnog sinusa).*

since the orbital floor was inferiorly displaced. Afterwards, anterior ethmoidectomy was done, followed by middle meatal antrostomy as wide as possible. The content of mucous, non-inflammatory, thick glue like secretion was removed from the maxillary sinus. An orbital wall reconstruction was done neither at the time of the surgery nor later.

After the FESS treatment, she was completely free of any symptoms, on follow up after 6 months and 1 year.

Discussion

If a clinician has a patient presenting with enophthalmos and hypoglobus, a wide range of diseases must be considered. The differential diagnosis for SSS must include trauma to the orbit (especially blow out fracture), prior orbital decompression for Graves orbithopathy, chronic rhinosinusitis, osteomyelitis, Wegener granulomatosis, orbital metastasis, human immunodeficiency virus (HIV) lipodystrophy, and prior orbital radiation therapy [6, 12, 13]. In addition, there are some extremely rare conditions to consider like orbital fat atrophy, Recklinghausen disease (absence of the sphenoid wing), linear scleroderma, Parry-Romberg syndrome (progressive hemifacial atrophy) and pseudoenophthalmos [11–13]. Our patient had neither trauma nor surgery, nor any other symptoms or diseases, so there was no doubt it was an idiopathic condition – Silent sinus syndrome.

When confirming the diagnosis of suspected SSS by CT scans, it should be taken into consideration that there are two similar conditions: maxillary sinus hypoplasia (MSH) and chronic maxillary sinus atelectasis (CMA) [7, 11, 14].

The presented patient had enophthalmos and hypoglobus of 2 mm, which is in accordance with the published data, since the average in these patients for enophthalmos is 2.96 mm (± 0.16 mm), and for hypoglobus it is 2.78 (± 0.25 mm) [6, 7].

SSS should be treated surgically. It is the functional endoscopic sinus surgery that must be performed because it restores sinus ventilation and drainage with no or minimal collateral damage [1, 6, 7, 15]. This is the first step of the treatment [4, 15, 16], and it was done in our case. The treatment has two objectives: to restore aeration of the sinus along with orbital reconstruction and to restore the orbital architecture [17]. These objectives can be achieved in a single or two-stage surgery. Whether an orbital wall repair should be performed at the time of the first surgery depends on the severity of the diplopia, the degree of the cosmetic alterations, and the postsurgical evaluation of the sinus [18]. Since there was neither diplopia nor cosmetic alterations, we did not do an orbital floor repair in the presented case.

The FESS procedure must be done with extreme caution since unintentional entry into the orbit is seen much more often. This complication happens because not only the antral walls are imploded, but the orbital floor is depressed, and for both reasons it is much easier to damage the orbital content [15, 16]. Middle meatal antrostomy must be made afterwards, which provides aeration to the maxillary sinus.

A rhinologist, an endoscopic surgeon, must perform a complete uncinectomy, anterior ethmoidectomy (adds exposure of the hiatus semilunaris and medial orbital wall), trimming of the inferior third of the middle nasal turbinate with gentle medial displacement (if it is lateralized) to prevent re-occlusion of the natural maxillary ostium. Besides, wide middle meatal antrostomy must be done, and sometimes even inferior meatal antrostomy for the purpose of MS ventilation and drainage [1, 6, 15, 16]. The finding of mucus secretion (like thick glue) in maxillary sinus is typical, and it was found in our patient as well.

The maxillary sinus, just like in our case, most often remodels spontaneously during some time after FESS (usually over 6 months), so it is rarely necessary to do a secondary repair of the orbital floor for aesthetic reasons. The recommendation today is to do a single [18] or two-stage approach to orbital repair and do a second operation after at least 6 months [1, 4, 6, 14].

Conclusion

Silent sinus syndrome is a rare entity of spontaneous progressive antral collapse. It presents with orbithopaties but is in fact a rhinologic disease, so all ophthalmologists, rhinologists and radiologists should know about it.

The treatment of choice is functional endoscopic sinus surgery, which should be performed with extra care by an experienced rhinosurgeon.

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TRACHEOBRONCHIAL FOREIGN BODY ASPIRATION – A 13-YEAR RETROSPECTIVE ANALYSIS

ASPIRACIJA STRANIH TELA U TRAHEOBRONHALNO STABLO − TRINAESTOGODIŠNJA RETROSPEKTIVNA ANALIZA

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Summary

Introduction. Foreign body aspiration into the respiratory tract remains a diagnostic and therapeutic challenge in clinical practice, especially in young children, who are the most frequently affected age group. The aim of this study was to present the results of treating the patients with foreign body aspiration in all age groups. **Material and Methods.** The medical and radiological records of 64 patients with confirmed foreign body out of 146 patients with suspected foreign body aspiration were retrospectively analyzed during the period of 13 years (from 2001 to 2013). **Results.** A foreign body was found in 64 (44%) of the 146 patients of all age groups with suspected foreign body aspiration. The patients' age ranged between 11 months and 80 years. There were 84% children and 16% adults, and 63% of patients were male. Time between the moment of aspiration and admission to the Department ranged between 0.5 hours and 14 days, with majority of patients (70%) being admitted during the first 24 hour. History of respiratory drama was present in 92% of patients. Physical and radiological findings were positive in 66% and 47% of patients, rescpectively. Organic vegetable foreign bodies accounted for 75% of all cases, and they were most frequently found in the right main bronchus (63%). All foreign bodies were successfully extracted by rigid bronchoscopy, without serious complications and fatal outcomes. **Conclusion.** Bronchoscopy should be performed in any case of suspected foreign body aspiration, even if clinical and radiological findings are normal, in order to avoid serious and possible life-threatening complications. More should be done to raise awareness of this potentially preventable condition.

Key words: Foreign Bodies; Respiratory Aspiration; Respiratory Tract; Treatment Outcome; Bronchoscopy; Infant; Child; Adolescent; Adult; Middle Aged; Aged; Aged, 80 and Over; Male; Female

Sažetak

Uvod. Aspiracija stranih tela u traheobronhalno stablo ostaje dijagnostički i terapijski izazov u kliničkoj praksi, posebno kod mlađe dece kao najčešće pogođene uzrasne grupe. Cilj rada bio je da se prikažu rezultati lečenja pacijenta sa aspiriranim stranim telom u svim starosnim grupama. **Materijal i metode.** Istorije bolesti i dostupni radiološki snimci od 64 pacijenta sa potvrđenim stranim telom od analiziranih 146 pacijenta primljenih zbog sumnje na strano telo u traheobronhalnom stablu retrospektivno su analizirani u trinaestogodišnjem periodu (između 2001. i 2013. godine). **Rezultati.** Strano telo pronađeno je kod 64 (44%) od 146 pacijenta svih starosnih grupa sa sumnjom na aspiraciju stranog tela. Starost pacijenata kretala se u rasponu od 11 meseci do 80 godina. Bilo je 84% dece i 16% odraslih. Muškog pola bilo je 63% pacijenata. Vreme od aspiracije do javljanja na Kliniku kretalo se od pola sata do 14 dana, a većina pacijenata (70%) javila se unutar 24 sata. Pozitivnu anamnezu o respiratornoj drami imalo je 92% pacijenata. Fizički pregled bio je pozitivan kod 66%, radiološki nalaz kod 47% pacijenata. Organska vegetabilna strana tela sačinjavala su 75% svih slučajeva, najčešće lokalizovana u desnom glavnom bronhu (63%). Sva strana tela uspešno su izvađena u rigidnoj bronhoskopiji, bez ozbiljnih komplikacija i smrtnih ishoda. **Zaključak.** Bronhoskopija je indikovana u svim slučajevima kada postoji sumnja na aspiraciju stranog tela, unatoč urednom kliničkom nalazu i radiografskim snimcima, da bi se izbegle potencijalno ozbiljne i životno ugrožavajuće komplikacije. Potrebno je više uraditi na podizanju svesti o ovom potencijalno preventabilnom stanju.

Ključne reči. Strana tela; Respiratorna aspiracija; Respiratorni trakt; Ishod lečenja; Bronhoskopija; Odojče; Dete; Adolescent; Odrasli; Odrasli, srednjih godina; Stari; Stari, preko 80 godina; Muško; Žensko

Introduction

Aspiration of foreign body (FB) presents a very serious, possibly a life-threatening condition. It usually occurs in young children 1–3 years of age since they explore the world with their hands and mouths, especially when their parents' close supervision is absent, and because of their incomplete dentition, limited oromotor control and immature judgment [1]. Medical history is the key for diagnosis of foreign body aspiration (FBA). If FBA is unwitnessed in children, the diagnosis can be easily overlooked since

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Abbreviations
FB – foreign body
FBA – foreign body aspiration
CXR – chest radiograph
CT – computed tomography

the signs and symptoms can be absent at the moment when medical help is being asked for. Tracheobronchial foreign bodies can be various, with organic ones being most frequently found. Once the aspiration is suspected, a chest radiograph (CXR) is usually requested, but a normal CXR does not rule out a tracheobronchial foreign body [2]. In the case of suspected foreign body aspiration, bronchoscopy is needed for evaluation and foreign body removal, if present. The importance of timely and appropriate therapy for this condition is best shown by Jackson who, in 1936, reported a decrease in mortality from foreign body aspiration (FBA) from 24% to 2% due to the application of endoscopic techniques for foreign body removal [3]. Rigid bronchoscopy is a preferred method for foreign body removal in the hands of a skilled endoscopist.

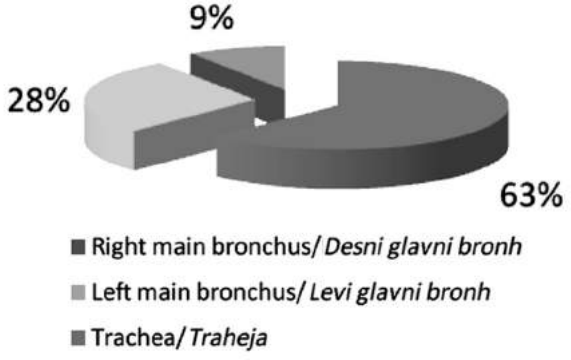
The study was aimed at evaluating the results of treating the patients hospitalized under a suspicion of FBA over the period of 13 years.

Material and Methods

In this study, the medical and radiological records of patients, of both sexes and from different age groups, admitted to the Department of Ear, Nose and Throat diseases, Clinical Center of Vojvodina in Novi Sad, Serbia, under a suspicion of foreign body aspiration during the period of 13 years, between 1st January, 2001 and 31st December, 2013 were retrospectively analyzed. During this period, 146 patients underwent rigid bronchoscopy under general anesthesia using a Storz ventilation bronchoscope with distal cold light illumination, when 64 tracheobronchial tree foreign bodies were found and extracted. The available data of medical history, signs and symptoms upon admission, physical and CXR findings, types of foreign bodies extracted, their localization and complications during bronchoscopy were statistically analyzed and presented.

Results

Out of 146 patients, 64 (44%) were diagnosed to have a tracheobronchial foreign body, which was successfully extracted during rigid bronchoscopy under general anesthesia. The age of the patients with the confirmed tracheobronchial tree foreign body ranged from 11 months and 80 years. Of 54 (84%) children under 18 years of age, 48 (that being 75% of all patients and 89% of all children) were under three years of age and 10 patients (16%) were adults. The majority of patients were male (40/63%), while 24 (37%) were female. Time passed from the moment of foreign body aspiration until admission to the Department ranged from 0.5 hour and 14 days - 70% of patients were admitted during the first 24 hours following aspiration, 14% were admitted between 1–3 days after the aspiration, 8% between 3–7 days and 8% after more than 7 days following foreign body aspiration. **Table 1** gives the distribution of patients according to the time passed from the moment of FBA until admission to the Department. History of previous respiratory drama with chocking crisis was present in 92% of patients. At the moment when medical help was being asked for, 8% had no complaints, while others had dyspnea or coughing. Physical findings were positive in 42 (66%) patients and normal in 22 (34%) cases. Chest radiographs were pathological in 30 (47%), normal in 23(36%) and no data were available for 11 (17%) patients. Vegetable foreign bodies accounted for 75% of all cases with peanut being the most frequently extracted foreign body – in 24 cases. Types of extracted FBs are shown in **Table 2**. Foreign bodies were localized in the right main bronchus, left main bronchus and in trachea in 40 (63%), 18 (28%), and 6 (9%) cases, respective-



Graph 1. Foreign body localization
Grafikon 1. *Lokalizacija stranog tela*

Table 1. Time passed from the moment of foreign body aspiration until admission to the Department
Tabela 1. *Vreme od aspiracije stranog tela do javljanja na Kliniku*

Time passed/*Proteklo vreme*	Number of patients/*Broj pacijenata*	%
0-24 hours /*0−24 sata*	44	70
1-3 days/*1−3 dana*	9	14
3-7 days/*3−7 dana*	5	8
>7 days/> *7 dana*	5	8
Total/*Ukupno*	64	100

Table 2. Types of extracted foreign bodies
Tabela 2. *Vrsta izvađenih stranih tela*

Type of FB/*Vrsta stranog tela*	Number of patients/*Broj pacijenata*
Peanut/*Kikiriki*	24
Walnut/*Orah*	8
Hazelnut/*Lešnik*	4
Pumpkin seed/*Seme bundeve*	3
Piece of apple/*Komad jabuke*	3
Corn grain/*Zrno kukuruza*	2
Cartilage/*Hrskavica*	2
Beans/*Zrno pasulja*	2
Sunflower seed/*Seme suncokreta*	1
Pork bone/*Svinjska kost*	1
Piece of dental prosthesis/*Deo zubne proteze*	1
Piece of carrot/*Parče šargarepe*	1
Pastry/*Komad bureka*	1
Endodontic needle/*Endodontska igla*	1
Metal screw/*Metalni šraf*	1
Feather/*Pero*	1
Chalk/*Kreda*	1
Biscuit/*Keks*	1
Sausage/*Kobasica*	1
Voice prosthesis/*Vokalna proteza*	1
Cherry stone/*Koštica višnje*	1
Popcorn/*Kokice*	1
Insulin needle/*Insulinska igla*	1
Garlic/*Beli luk*	1
Total/*Ukupno*	64

ly as shown in **Graph 1.** There were no serious complications and fatal outcomes, and one child had transitory bronchospasm during rigid bronchscopy. In 47 (73%) of cases, signs of edema and inflammation were found around the foreign body, requiring additional conservative treatment and further follow up by the pulmonologist.

Discussion

Foreign body aspiration presents a continuing, both diagnostic and therapeutic challenge [4] with serious and potentially lethal consequences, especially in early childhood. Majority of patients are children, as proven by this study, but it can sporadically occur in adults. The third year of life carries the highest risk for FBA [5]. Mu et al. find 90% of children with FBA under 3 years of age [6], Mehta et al. in 77% [7], Avdogan et al. in 74% [8].

The male female ratio in this study was 1.67:1. Mu et al. [6] found this ratio in children to be 1.2:1, and Mehta et al. reported a slightly higher ratio 2.1:1 [7].

Adults usually aspirate when their judgment and mental status is altered by alcohol, sedatives or head trauma. Those with cervicofacial trauma or with neurogenic diseases or physical conditions, such as dentures that impair sensation or control of the food bolus, are also at risk of aspiration [1]. Adults, especially psychiatric patients and prisoners, tend to aspirate metal objects during the attempt to swallow them. Foreign body aspiration through the tracheostoma in tracheotomized patients is also seen. In this study, one totally laryngectomized patient aspirated a voice prosthesis and it was successfully extracted through the tracheostoma using rigid bronschoscope. Similar FBs have been reported by other authors as well [9].

In order to avoid complications, early diagnosis is mandatory; however, this condition often remains unrecognized [10]. In the series published by Mallick [4], late presentation of this condition was due to the physician misdiagnosis and parental negligence in 41.6% and in 20.8%, respectively. This study has shown that the majority of patients (70%) were admitted within the first 24 hours after aspiration, but 8% of them had history of aspiration for more than 7 days before admission, so they were at a higher risk for development of serious complications which, luckily, did not occur in this series. Girardi et al. [11] reported early extraction within the first 24 hours in only

17.3%, Mu et al. in 28% [6], Mehta et al. in 31.4% [7], Avdogan et al. in 43.6% [8]. A higher percentage of patients admitted within the first 24 hours in this study is due to the study design since it included adults as well.

It is generally accepted that bronchoscopy should be performed if there is a slightest suspicion of foreign body aspiration in order to minimize the possibility of missed diagnosis and late complications. In this study, out of all 146 patients with suspected foreign body aspiration who had undergone bronchoscopy, foreign body was found in 64 (44%). Skoulakis et al. found a foreign body in 62% [12], Ciftci et al. in 85% [5], Mehta et al. in 95% [7], Avdogan et al. in 79.1% [8], Oncel in 74.3% [13] of all performed bronchoscopies.

Medical history, which is of the utmost importance for suspecting FBA [14], was positive in 92% in this study, suggesting the presence of FB. Ciftci et al. [5] found positive history in a similar percentage (91%), Girardi et al. in 75.8% [1], Black et al. [15] in 95%, Mu et al. in 98% [6], Mehta et al. in 90% [7], and Avdogan et al. in 96.3% [8]. The presence of positive history of respiratory drama is a contributing factor to a high percentage of patients seeking medical care within the first 24 hours in this study.

The type of inhaled FB varies. The organic vegetable FBs are the most frequently found ones in children. Mehta et al. [7] also found organic vegetable FB in 87% in children. Vegetable FB like seeds, peanuts and beans cause a diffuse violent reaction leading to congestion and edema of the tracheobronchial mucosa, called vegetable bronchitis, which tends to increase the risk of possible unfavorable course of disease. Their removal is more difficult due to their inherent soft nature. The organic vegetable FBs were recorded in 75%, peanut being the most frequently found as it is the most frequently found one in Western countries, while watermelon seeds are usually found in Africa [4]. Mu et al. found a FB in a higher percentage (95%) of patients [6] and Avdogan et al. diagnosed it in 89.9% [8], as was to be expected since his study included only children, who tend to aspirate organic FB more often than adults. Inert objects are usually found in older children and they are frequently visible on CXR. Since it causes little or no inflammatory reaction, it can remain undetected for some time. When aspirated, caustic substances such as disc batteries, which are commonly found in the nose and digestive tract, require emergent removal to avoid an alkaline injury with its associated tissue liquefaction necrosis. Being resistant to organic decay, with tendency to migrate distally during respiration, grass, when inhaled, may remain in the airway for a long period of time, causing unusual infections, abscess formation and osteomyelitis. A case of brain abscess was reported three months after grass inhalation [16].

Foreign bodies are usually situated in the right main bronchus due to the anatomical division of the tracheobronchial tree with the right main bronchus almost continuing the course of trachea and being the wider one. However, the tracheobronchial tree division develops to the shape of an adult one only after 15 years of age, and therefore, it is likely to have a foreign body in the same percentage in the left or right bronchial tree in children under this age [17].

In this study, foreign bodies were usually identified in the right and left main bronchus in 60% nad 33% of cases, respectively, in both main Bronchi in 5,4% and in subglotic region in 1,5% of patients. Skoulakis et al. [12] found FB in the right main bronchus in 60%, 33.1% in the left one, in 5.4% in both main bronchi and in 1.5% in subglottic region. In the series including 548 children, Black et al. [15] found a FB in the right bronchus in 49%, in the left one in 44% and in trachea and hypopharynx in 4%. Mu et al. [6] detected the majority of FB in the right main bronchus in 46%, Mehta et al. [7] found it in a percentage even higher than 70%.

When FBA is suspected, CXR is usually requested. CXR will reveal radio-opaque foreign bodies, but the majority of foreign bodies are radiolucent, and therefore not visible on CXR. In these cases, special attention should be paid to visible secondary changes in the associated lung or pulmonary lobe such as obstructive emphysema or overinflation and atelectasis of the lung or lobe distal to the airway obstruction. It is recommended to perform inspiratory and expiratory CXR, if possible, depending on the age-related ability of the patient to cooperate. Girardi et al. [11] suggest two radiological findings as useful in improving the diagnosis of FBA, especially in the absence of choking crisis history; these are hyperinflation or obstructive emphysema with atelectasis in the same hemithorax, and aeration within an area of atelectasis.

Radiological findings in this study were positive in 47%, normal in 36% and not available in 17%. Other series published by Ciftci et al. [5], Girardi et al. [11], Black et al. [15], Mu et al. [6], Mehta et al. [7], and Oncel et al. [13], reported radiological findings to be normal in 13%, 11.3%, 17%, more than 75%, 30% and 49%, respectively, thus proving that a normal radiological finding does not rule out the presence of FB. In this study, CXRs were not done separately during inspiration and expiration, as recommended, which can explain a relatively high percentage of normal CXR findings. Due to the retrospective design of this study, not all the data about the performed CXRs were available, thus making it impossible to establish the true specificity and sensitivity of this method to detect FBA.

Dynamic fluoroscopy, low-dose spiral computed tomography (CT) [18] and CT virtual bronchoscopy can be indicated in selected cases [19], usually in unrecognized FBA.

Since physical and radiological findings can be normal in patients with aspirated foreign body, only bronchoscopy gives certainty about the diagnosis [4]. Rigid bronchoscope remains the first choice

when FBA diagnosis is made. However, flexible bronchoscope, in the hands of a skilled endoscopist, can be used complementary with the rigid one, its advantage being in the possibility to reach more distal parts of bronchial branching than the rigid one, as well as to insert the scope orally or through the nasal passageway and even through the rigid bronchoscope. This is a method of choice for patients with limited neck mobility and mouth opening.

Complications that can occur in patients with aspirated FB can be very serious, potentially hazardous. They can arise from the presence of FB and developing cardiopulmonary arrest, but they can also appear during bronchoscopy, even when FB is absent. The most frequent serious complications are worsening of respiratory tract infection if accompanying FB, cardiac arrest, laryngeal edema, pneumothorax, pneumomediastinum, tracheal laceration, bronchospasm and death. Ciftci et al. [5] found life-threatening complications in 4% children with FBA, but also in 14% without FBA due to the worsening of respiratory tract infection. The same author reported 0.8% deaths and pointed out that long duration of procedure, presence of dense granulation tissue and type of foreign body are important predictors of complications. Possible sequelae of FBA are mediastinitis, bronchopleural or tracheoesophageal fistula formation, pneumonia or abscess, bronchiectasis and even scar carcinoma. In their study including 400 children, Mu et al. reported a mortality rate of 0.25% [6]; Avdogan reported 0.21% mortality rate in a larger series including 1887 bronchoscopies [8].

In order to prevent possible complications, Oncel et al. [13] recommended directing the object into the right main bronchus and then fragmenting and removing it. There were no serious complications during this study. The presence of edema and inflammation around the FB was recorded in a high percentage as it had been expected since the majority of FBs were the organic ones.

Secondary bronchoscopy should be done in patients with persistent signs and symptoms to rule out the overlooked organic foreign body particles or multiple FBs (reported in other series from 9–28.1%) [7, 20] or to remove persistent granulation tissue to avoid long-term complications necessitating lobectomy [5].

When a foreign body is too large to pass through the subglottic region or so sharp that it can cause an injury to the airway, tracheostomy can be indicated [21]. In rare cases, FB must be removed by thoratocomy and bronchotomy, which has not been reported by this study.

Conclusion

Bronchoscopy should be performed in any case of suspected foreign body aspiration even though the clinical symptoms or radiographic findings are normal.

Rigid bronchoscopy is a preferred method for foreign body removal and should be performed by a skilled endoscopist, in a well-equipped and well-prepared operative setting for foreign body extraction and for possible tracheotomy, in cooperation with experienced anesthesiologist, in order to avoid serious, potentially lethal complications.

More should be done to raise awareness of this potentially preventable condition.

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

∗ *Volumen sa suplementom*

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

∗ *Sveska sa suplementom*

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

∗ *Sažetak u Časopisu*

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

Knjige i druge monografije:

∗ *Jedan ili više autora*

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

∗ *Urednik(ci) kao autor*

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

∗ *Poglavlje u knjizi*

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

∗ *Rad u zborniku radova*

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

∗ *Disertacije i teze*

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

Elektronski materijal

∗ *Članak u Časopisu u elektronskoj formi*

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

∗ *Monografije u elektronskoj formi*

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

∗ *Kompjuterski dokument (file)*

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

6. Prilozi (tabele, grafikoni, sheme i fotografije).

Dozvoljeno je najviše šest priloga!

– Tabele, grafikoni, sheme i fotografije dostavljaju se na kraju teksta rukopisa, kao posebni dokumenti na posebnim stranicama.

– Tabele i grafikone pripremiti u formatu koji je kompatibilan sa programom *Microsoft Word for Windows.*

– Slike pripremiti u JPG, GIF TIFF, EPS i sl. formatu

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– Naslov, tekst u tabelama, grafikonima, shemama i legendama navesti na srpskom i na engleskom jeziku.

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– Ukoliko se koriste tabele, grafikoni, sheme ili fotografije koji su ranije već objavljeni, u naslovu navesti izvor i poslati potpisanu izjavu autora o saglasnosti za objavljivanje.

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Prijem rukopisa vrši se u elektronskoj formi na stranici: **aseestant.ceon.rs/index.php/medpreg/**. Da biste prijavili rad morate se prethodno registrovati. Ako ste već registrovani korisnik, možete odmah da se prijavite i započnete proces prijave priloga u pet koraka.

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21000 Novi Sad
Tel. 021/521 096; 063/81 33 875
E-mail: dlv@neobee.net

INFORMATION FOR AUTHORS

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2. Original studies – up to 12 pages – present the authors' own investigations and their interpretations. They should contain data which could be the basis to check the obtained results and reproduce the investigative procedure.

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4. Preliminary reports – up to 4 pages – contain scientific results of significant importance requiring urgent publishing; however, it need not provide detailed description for repeating the obtained results. It presents new scientific data without a detailed explanation of methods and results. It contains all parts of an original study in an abridged form.

5. Professional articles – up to 10 pages – examine or reproduce previous investigation and represent a valuable source of knowledge and adaption of original investigations for the needs of current science and practise.

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7. History of medicine – up to 10 pages – deals with history in the aim of providing continuity of medical and health care culture. They have the character of professional articles.

8. Other types of publications – The journal also publishes feuilletons, book reviews, extracts from foreign literature, reports from congresses and professional meetings, communications on activities of certain medical institutions, branches and sections, announcements of the Editorial Board, letters to the Editorial Board, novelties in medicine, questions and answers, professional and vocational news and In memoriam.

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The covering letter:

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Use Microsoft Word for Windows to type the text. The text must be typed in font Times New Roman, page format A4, space 1.5 (for tables as well), borders of 2.5 cm and font size 12pt. The manuscript should contain the following elements:

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

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

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

– review papers should have the introduction, subtitles corresponding to those in the paper and conclusion. It is to be followed by up to 10 Key Words from the list of Medical Subject Headings, MeSH of the American National Medical Library.

3. The summary in Serbian language. The summary in Serbian should be the translation of the summary in English, it should be structured in the same way as the English summary, containing up to 250 words, without any abbreviations.

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

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

– The text should be written in the spirit of Serbian language, without unnecessary abbreviations, whose first mentioning must be explained by the full term they stand for. Abbreviations should not be used in the title, summary and conclusion. Only commonly accepted abbreviations (such as DNA, MRI, NMR, HIV…) should be used. The list of abbreviations used in the text, together with the explanation of their meaning, is to be submitted at the last page of the manuscript.

– All measurements should be reported in the metric system of the International System of Units – SI. Temperature should be expressed in Celsius degrees (°C). and pressure in mmHg.

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

Material and methods should contain data on design of the study (prospective/retrospective, eligibili-

ty and exclusion criteria, duration, demographic data, follow-up period). Statistical methods applied should be clear and described in details.

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

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

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

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

Articles in journals

∗ *A standard article*

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

∗ *An organisation as the author*

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

∗ *No author given*

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

∗ *A volume with supplement*

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

∗ *An issue with supplement*

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

∗ *A summary in a journal*

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

Books and other monographs

∗ *One or more authors*

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

∗ *Editor(s) as author(s)*

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

∗ *A chapter in a book*

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

∗ *A conference paper*

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

∗ *A dissertation and theses*

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

Electronic material

∗ *A journal article in electronic format*

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

∗ *Monographs in electronic format*

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

∗ *Acomputer file*

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

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