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Содржина/Contents

III. Ревиијални/ Review

ETHICAL AND LEGAL ISSUES IN TELEMEDICINE APPLICATIONS: A COMPREHENSIVE REVIEW

ЕТИЧКИ И ПРАВНИ ПРАШАЊА ВО ТЕЛЕМЕДИЦИНСКИТЕ АПЛИКАЦИИ: СЕОПФАТЕН ПРЕГЛЕД

Nafiye Ebru Terzi 127

I. Оригинални трудови/ Original Articles

EVALUATION OF HEALTH-RELATED QUALITY OF LIFE USING ST GEORGE'S RESPIRATORY QUESTIONNAIRE BEFORE AND AFTER PULMONARY REHABILITATION IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE: A PROSPECTIVE STUDY

ЕВАЛУАЦИЈА НА КВАЛИТЕТОТ НА ЖИВОТ ПОВРЗАН СО ЗДРАВЈЕТО СО КОРИСТЕЊЕ НА РЕСПИРАТОРНИОТ ПРАШАЛНИК НА „СВ. ЃОРЃИ“, ПРЕД И ПО ПУЛМОНАЛНА РЕХАБИЛИТАЦИЈА КАЈ ПАЦИЕНТИ СО ХРОНИЧНА ОПСТРУКТИВНА БЕЛОДРОБНА БОЛЕСТ: ПРОСПЕКТИВНА СТУДИЈА

Suzana Arbutina 132

METABOLIC VARIATIONS AMONG WOMEN WITH POLYCYSTIC OVARY SYNDROME ACCORDING TO BODY MASS INDEX

МЕТАБОЛНИ ВАРИЈАЦИИ КАЈ ЖЕНИ СО ПОЛИЦИСТИЧНО ОВАРИЈАЛЕН СИНДРОМ СПОРЕД ИНДЕКСОТ НА ТЕЛЕСНА МАСА

Aleksandra Atanasova Boshku, Daniela Ivanova Panova, Gligor Tofoski, Rosa Naumova and Jadranka Georgieva 136

THE ROLE OF PLACENTAL ANGIOGENIC MARKERS IN DIFFERENTIATING FETUSES WITH INTRAUTERINE GROWTH RESTRICTION FROM THOSE SMALL-FOR-GESTATIONAL-AGE

УЛОГАТА НА ПЛАЦЕНТАРНИТЕ АНГИОГЕНИ МАРКЕРИ ВО ДИФЕРЕНЦИЈАЦИЈАТА ПОМЕЃУ ФЕТУСИ СО ИНТРАУТЕРИНИ ЗАСТОЈ ВО РАСТОТ И МАЛИ ЗА ГЕСТАЦИСКАТА ВОЗРАСТ

Maja Koteva Mirakovska, Ana Daneva Markova, Ivo Kjaev, Eli Gjorgievska Nikolovska, Arta Bina, Daniel Milkovski and Onur Dika 143

WORK-RELATED BURNOUT DIMENSIONS AS PREDICTORS OF THE RISK OF PERSISTENT HUMAN PAPILLOMAVIRUS INFECTION

ДИМЕНЗИИТЕ НА СИНДРОМОТ НА ПРЕГОРУВАЊЕ ПОВРЗАНИ СО РАБОТАТА КАКО ПРЕДИКТОРИ НА РИЗИКОТ ОД ПЕРЗИСТЕНТНА ИНФЕКЦИЈА СО ХУМАН ПАПИЛОМА ВИРУС

Megi Micevska, Dragan Mijakoski, Goran Dimitrov, Saso Stoleski, Valentina Tofiloska, Elena Dzikova, Verdi Stanojevik and Biljana Zafirova 151

QUALITY OF ANTICOAGULATION IN PATIENTS WITH ATRIAL FIBRILLATION ON ACENOCOUMAROL

КВАЛИТЕТ НА АНТИКОАГУЛАЦИЈА КАЈ ПАЦИЕНТИ СО ПРЕТКОМОРНА ФИБРИЛАЦИЈА НА АЦЕНОКУМАРОЛ

Biljanka Koleva, Hristina Leskaroska and Emilija Antov 159

THE IMPACT OF *GARDNERELLA VAGINALIS* INFECTION ON PRETERM BIRTHS IN OUR CLINICAL CASES

ВЛИЈАНИЕТО НА ИНФЕКЦИЈАТА СО *GARDNERELLA VAGINALIS* ВРЗ ПРЕДВРЕМЕНОТО ПОРОДУВАЊЕ НА НАШИОТ МАТЕРИЈАЛ

Fisnik Sinani and Jadranka Georgievska 164

III. Прикази на случај/ Case reports

RECONSTRUCTION OF COMPLEX SCALP DEFECT WITH LOCAL FLAP AND SKIN GRAFT

РЕКОНСТРУКЦИЈА НА КОМПЛЕТЕН ДЕФЕКТ НА СКАЛПОТ СО ЛОКАЛЕН ФЛАП И КОЖЕН ГРАФТ

Iliina Gadjevska Tomulevska, Konstantin Mitev, Mihail Taushanov and Sasho Mladenovski 169

LEG PAIN OR LIMB THREAT ANKLE-BRACHIAL INDEX AS A GATEWAY TO PERIPHERAL ARTERIAL DISEASE DETECTION БОЛКА ВО НОГАТА ИЛИ ЗАКАНА ЗА ЕКСТРЕМИТЕТИТЕ, ГЛУЖЕНО-БРАХИЈАЛЕН ИНДЕКС КАКО ПРЕВОЗ ЗА ДЕТЕКЦИЈА НА ПЕРИФЕРНИ АТЕРИСКИ ЗАБОЛУВАЊА Hristina Leskaroska, Biljana Koleva, Katerina Kovachevikj, Biljana Petreska-Zovic, Lidija Poposka and Marijan Boshev	171
INCIDENTAL STUMP DURING CESAREAN SECTION IN IVFEGG DONATION PREGNANCY: A CASE EMPHASIZING THE IMPERATIVE OF ROUTINE HISTOPATHOLOGICAL EVALUATION OF MYOMAS ИНЦИДЕНТАЛЕН STUMP ЗА ВРЕМЕ НА ЦАРСКИ РЕЗ ВО БРЕМЕНОСТ СО ДОНАЦИЈА НА ЈАЈЦЕ-КЛЕТКА ПО ИВФ: СЛУЧАЈ ШТО ЈА ПОТЕНЦИРА ПОТРЕБАТА ОД РУТИНСКА ХИСТОПАТОЛОШКА ЕВАЛУАЦИЈА НА МИОМИТЕ Ivo Kjaev, Onur Dika, Jana Nivichka, Maja Pejkovska Ilieva, Irena Aleksioska Papestiev, Sasha Anastasova, and Daniel Milkovski	177
SINUSITIS TREATMENT IN PREGNANCY- PERSONALISED AND INTEGRATED MEDICINE ЛЕКУВАЊЕ НА СИНУЗИТИС ВО ПРЕМЕНОСТ – ПЕРСОНАЛИЗИРАНА И ИНТЕГРИРАНА МЕДИЦИНА Maja Pejkovska Ilieva, Goran Kochoski, Ana Pejkovska, Sofija Nikolovska and Budima Pejkovska Shahpaska.....	180

Case report

SINUSITIS TREATMENT IN PREGNANCY- PERSONALISED AND INTEGRATED MEDICINE

ТРЕТМАН НА СИНУЗИТИС ВО БРЕМЕНОСТ – ПЕРСОНАЛИЗИРАНА И ИНТЕГРИРАНА МЕДИЦИНА

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Abstract

Introduction. Sinusitis in pregnant patients is a disorder with incidence of around 3-4% worldwide, dependent from the impaired immune system. Long lasting symptoms are sometimes accompanied with nasal polyposis that is aggravated due to pregnancy hormones. The chronic condition has its relapses, with inflammatory or noninflammatory causes. Systematic analysis, diagnostic evaluations, treatment options must be personalized and dependent of the pregnancy trimester for a favorable pregnancy outcome with the help of integrated medicine.

Methods. We present a pregnant patient in the second trimester of her third pregnancy. The symptoms that occurred in the 17.5 week of gestational age included headache, high body temperature, fatigue, muscle cramps, loss of appetite, nasal congestion and discharge. After clinical examinations of microbiological samples, nasal endoscopy, mechanical vacuum suction, chronic sinusitis aggravated by nasal polyposis with propagation from maxillary sinus was diagnosed. The treatment according to antibiogram and FDA approval for the trimester included local topic treatment with diluted cephalosporins, corticosteroids (fluticasone propionate), inhalations, antibiotics, probiotics and vitamins per os.

Results and Discussion. Improvement of the subjective and objective symptomatology of the patient occurred after 5 weeks of treatment. Relapse occurred in the third trimester and two months postpartum. Immunopathohistologically, there is an antagonism of IgE, of interleukin IL-4, IL-5 and IL-13. The increase of IL-17 is proven for frequent exacerbations. Long lasting sym-

ptoms are sometimes accompanied with nasal polyposis that is aggravated due to pregnancy hormones.

Conclusion. The immune system in pregnancy changes, with exaggerated inflammatory reaction inadequate to recover from sinusitis for a shorter period of time. Therefore, detailed examination and adequate therapy is obligatory as soon as the diagnosis is settled. All corticosteroids are not allowed in the second trimester due to proven unfavorable outcome for the fetus. Mechanical treatments and topic antibiotics were main therapeutic solution. Modern medicine aims to combine genetics and detection of the phenotype for chronic type of inflammation and the type of the immune response in order to stratify patients for appropriate treatment.

Keywords: sinusitis, pregnancy induced, treatment, outcome

Апстракт

Вовед. Синуситот кај бремените пациентки е заболување со инциденца од околу 3-4% на глобално ниво, поврзано со ослабениот имунолошки систем. Долготрајните симптоми понекогаш се придружени со носни полипозии, кои се влошуваат поради хормоналните промени во бременоста.

Хроничната состојба има рецидиви, предизвикани од воспалителни или невоспалителни причини. Систематската анализа, дијагностичките процедури и тераписките опции мора да бидат персонализирани и да зависат од триместарот на бременоста, со цел да се обезбеди поволен исход на бременоста преку интегрирана медицина.

Методи. Прикажана е бремена пациентка во вториот триместар од нејзината трета бременост. Симптомите кои се појавиле во 17.5-тата гестациска недела вклучуваа главоболка, повисока телесна

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температура, замор, мускулни грчеви, губење на апетит, носна опструкција и секреција. По клинички прегледи и микробиолошки испитувања, носна ендоскопија и механичко вакуумско чистење, дијагностициран е хроничен синусит, комплициран со носни полипозии кои се прошириле од максиларниот синус. Третманот, според антибиограмот и FDA препораките за овој триместар, вклучува локална терапија со разредени цефалоспорици, кортикостероиди (флутиказон пропионат), инхалации, антибиотици, пробиотици и витамини per os.

Резултати и дискусија. Подобрување на субјективната и објективната симптоматологија кај пациентката се случи по 5 недели терапија. Сепак, дојде до рецидив во третиот триместар и два месеци по породувањето. Имунопатолошките испитувања покажаа антагонизам на IgE, интерлеукините IL-4, IL-5 и IL-13, додека покачувањето на IL-17 е потврдено како фактор за чести егзацербации. Долготрајните симптоми понекогаш се придружени со носни полипозии, кои се влошуваат поради хормоните од бременоста.

Заклучок. Имунолошкиот систем кај бремените жени се менува, што доведува до претерана воспалителна реакција и отежнато закрепнување од синусит во пократко време. Затоа, детален преглед и адекватна терапија се неопходни веднаш по поставувањето на дијагнозата. Сите кортикостероиди се забранети во вториот триместар поради нивниот негативен ефект врз фетусот. Механичките третмани и локалните антибиотици беа главните терапевтски решенија. Современата медицина се стреми кон комбинација на генетски испитувања и фенотипска детекција за хроничниот тип на воспаление и одговорот на имунолошкиот систем, со цел подобро да се насочи терапијата.

Клучни зборови: синусит, бременост, третман, исход

Introduction

The qualitative pathohistological evaluation of chronically inflamed sinus mucosa performed in our study indicated the existence of two different divergent pathohistological types: polypoid mucosal eosinophilia and glandular hyperplasia. The pathogenetic mechanism in the first entity, polypoid mucosa with eosinophilia, is associated with severe edema that causes obstruction of the narrow areas of the ostiomeatal complex, i.e. mechanical blockage of the natural sinus openings. Due to the chronic mucosal inflammation, the paranasal mucosal outgrowths forming nasal polyps. On the other hand, the released toxic substances eosinophil cationic protein (ECP) and major basic protein (MBP) cause damage to the epithelium of the sinus mucosa

and thus suppression of ciliary activity. In the second type, glandular hyperplasia, the continuous increased secretion and production of mucus originating from hypertrophic and hyperplastically altered submucosal glands leads to obstruction of the paranasal openings.

Based on the inflammatory response, four main pathohistological types of chronic maxillary rhinosinusitis are distinguished: edematous or hyperplastic, infiltrative, fibrotic, and mixed type. The symptomatology can derive from intracranial problems, parafunctional habits, infections, sinusitis and many more. The secondary headaches need to be diagnosed meticulously since they derive from medical underlying conditions [1].

Group of authors refer that enlarged number of goblet cells are present at chronically inflamed mucosa of the maxillary sinus. Tos and Mogensen claimed that there are six times enlargement of the number and the density of submucosal glandular structures at chronic maxillary rhinosinusitis in comparison with group of patients without inflammation, which is a consequence of hyperplasia and productions of new glandular structures and widening of the glandular acinus elements. Another alert factor medical and dental staff should be trained for is the diagnosis of acute sinusitis. Acute sinusitis occurs six times more frequently in pregnant women and if left untreated many consequences can develop [2,3].

Besides making the pregnant women feel the difficulty breathing this symptom must be taken seriously at this time for the possibilities during pregnancy are limited [4]. Untreated sinusitis in pregnancy disease can lead to rare intracranial complications such as a subdural empyema. This chronic condition has its relapses, with inflammatory or noninflammatory causes. The patients can experience altered neurological status that might last for a different period of time if the patient doesn't take actions like visiting her doctors [5].

The etiology of sinusitis can have besides infectious, allergic factors can have odontogenic origin if the teeth are left untreated. Since the veins do not have valves and since in pregnancy the organism is susceptible to any infectious agents can be easily spread in the cranium or in the mediastinum if the origin is dental [6]. Systematic analysis, diagnostic evaluations, treatment options must be conducted with the help of personalized and integrated medicine dependent of the pregnancy trimester for a favourable pregnancy outcome.

Purpose

The purpose of this paper is to represent a case study of a pregnant patient with sinusitis treatment with the usage of personalised and integrated medicine.

Case report

A 32-year-old female, at the 17.5 weeks gestation

(second trimester) was administered to the University Clinic for Gynaecology and Obstetrics with a severe headache.

For the etiological factors causing the origin of the headache a team of specialist had conducted several medical examinations, such as the patients' gynaecologist, otorhinolaryngologist, dentist and neurologist. The patients was examined at the PHI University Clinic "St. Panteleimon" where at the examination it was proved that she does not have odontogenic infections. The patients' major complaints adjacent to the headache were: loss of smell, nasal obstruction, thick yellow discharge, sinus pressure and difference in the brain functioning.

In the medical history of the patient there weren't found previous such complaints nor infections of her sinuses at that level. As from the severity of the pain the patient experiences a scale of pain in 4 points (none=0, mild=1, severe=2, intense=3) the patient has stated that her severity of pain felt in the frontal region of the head is very intense.

Diagnosis was pointed towards taking intravenous blood samples for detection of infectious agents. Leucotitosis, elevated neutrophiles and eosinophils and CRP (resulted 86), and nasal and pharyngeal microbiological samples confirmed presence of *Streptococcus pneumoniae*.

Next the patient was administered to the University Clinic of Otorhinolaryngology where with the usage of flexible transnasal camera examination was conducted. The endoscopic evaluation discovered grapelike polypoid changes with dimension of 4 cm in the anterior and medium level parts of the maxillary sinus with airway obstruction of the osteoneasal complex. Immunopathohistologically analysis of the of IgE, and the increase of IL-17 were conducted in the blood samples of the patients on her controls.

Since Computer Tomography cannot be performed at this stage of pregnancy an Ultrasonographic examination was performed showing shades that prove the transnasal endoscopic evaluation.

After laboratory, clinically and endoscopically examinations have been performed bacterial sinusitis was confirmed for the pregnant patient.

After clinical examinations of microbiological samples, nasal endoscopy, mechanical vacuum suction, chronic sinusitis aggravated by nasal polyposis with propagation from maxillary sinus was diagnosed. The treatment according to antibiogram and FDA approval for the trimester included local topic treatment with diluted cephalosporins, corticosteroids, inhalations, antibiotics, probiotics and vitamins per os.

A treatment followed by local therapy using Ceftriaxone 2 grams diluted in saline solution-nasal irrigation was performed twice a day for a period of two weeks. Topical corticosteroids were also used-Budesonide na-

sal spray (Category B) prescribed 1 spray per nostril twice a day for a period of 5 weeks.

Systemic antibiotic consisted of Cefuroxime of 500mg (FDA category B) twice a day for 21 days.

Improvement of the subjective and objective symptomatology of the patient occurred after 5 weeks of treatment. Relapse occurred in the third trimester and two months postpartum as acute exacerbation of the chronic findings.

Discussion

From the subjective symptomatology of the pregnant patient it was seen that her symptoms showed improvement after 7 days, however the complete resolution of the inflammation was diagnosed after 5 weeks of treatment.

It is of great importance when treating infections in pregnancy to exclude adverse effects on the mother or fetus, which has been proven in the studies of Goldstein G *et al.* [7]. Corticosteroids (e.g., budesonide) are recommended for nasal use in pregnancy due to low systemic bio-availability. Norjavaara E *et al.* state that budesonide is category B in pregnancy and thus it remains an agent for which the preponderance of safety data exists [8].

Studies have shown that oral decongestants may increase the risk of fetal gastroschisis, and also contribute to hypertension in the first trimester [9].

Usage of topical corticosteroids is shown by studies that in the second and third trimester can lead to possible fetal adrenal suppression, but clinically significant effects are rare [10].

Some studies show that miscarriage is common and can occur in any pregnancy for many different reasons, but the use of topical corticosteroids is not expected to increase the chance for miscarriage [11].

Briggs G *et al.* have shown that usage for oral antibiotics that do not harm the fetus may be used for acute rhinosinusitis (ARS) or acute exacerbations of chronic rhinosinusitis (CRS). Long-term macrolide or doxycycline use for CRS is not recommended during pregnancy. Penicillin and cephalosporin are the safest classes, and can be given when endoscopic evidence of purulence is present, which is in correspondence with the patient in this case study. Antibiotics that put the fetus at risk such as tetracyclines, aminoglycosides, trimethoprim-sulfamethaxazole and fluoroquinolones should not be used during pregnancy [12].

For nasal polipoids surgery may be considered prior to the pregnancy if they are discovered before the patients get pregnant. Lal D. state that in general, surgery that is not for a life threatening process should be avoided during pregnancy. The authors say that emergency surgery for complicated and acute/chronic sinusitis may be done with close anesthesia supervision. Also office procedures under local anesthesia may represent helpful alternatives in severely symptomatic CRS

pregnant patients, such as polypectomy, indicated balloon sinuplasty, and turbinate surgery under local anesthesia [13].

The patient in this study has her acute sinusitis turn into chronic type. Sinusitis in pregnant patients is a disorder with incidence of around 3-4%, dependent from the impaired immune system.

Immunopathohistologically, there is an antagonism of IgE, of interleukin IL-4, IL-5 and IL-13. The increase of IL-17 is proven for frequent exacerbations. Long lasting symptoms are sometimes accompanied with nasal polyposis that is aggravated due to pregnancy hormones, like the patient in this study [14,15].

Gevaert P. have reported that most patients with chronic rhinosinusitis with nasal polyps have a type 2 inflammatory pattern characterized by eosinophilia and elevated levels of interleukin-4, interleukin-5, and interleukin-13 which is also case in pregnancy proven in our patient laboratorically [16].

Chiarella E *et al.* have reported that the formation of the nasal polyp involves histologically well-identified mechanisms that rupture the mucosal epithelium, the proliferation of fibrous tissue through the damaged epithelium, the accumulation of extracellular matrix (ECM) with oedema and the proliferation of a granular tissue formed by thin-walled vessels and infiltration of inflammatory cells [17].

(For a proper recovery a systematic review of the literature guidelines and medicine evidence based recommendations are necessary). According to FDA approvals, general recommendations as to which drugs should be avoided during pregnancy and then later on if the patient has sinusitis while breastfeeding.. For this controls to continue many follow ups should be done before, during pregnancy and after giving birth. Pregnant women and women breastfeeding must pay attention as to which drugs they can take topically, introrally and intravenously [18].

Another chapter of diagnose is when genetics and phenotyping are taken in consideration for distinguishing the ethiology of chronic sinusitis [19,20].

The patient in this study was treated successfully and there weren't found any harmful effects on her baby. The polipose grape like structure in the patients' maxillary sinus two months after giving birth was not present. Thus the personalized and integrated medicine treats each patient individually according to their etiological, genetical, phenotypical factors providing the best possible care for both the mother and the baby.

Conclusion

The immune system in pregnancy changes, with exaggerated inflammatory reaction inadequate to recover from sinusitis for a shorter period of time. Therefore, detailed examination and adequate therapy is obligetory as soon as the diagnosis has been obtained. All cor-

ticosteroids are not allowed in the second trimester due to proven unfavorable outcome for the fetus. Mechanical treatments and topic antibiotics were main therapeutic solution. Modern medicine is personalized and integrated and aims to combine genetics and detection of the phenotype for chronic type of inflammation and the type of the immune response in order to stratify patients for appropriate treatment.

Conflict of interests: None declared.

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