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Betimi i Hipokratit

Në çastin kur po hy në radhët e anëtarëve të profesionit mjekësor premtoj solemnisht se jetën time do ta vë në shërbim të humanitetit. Ndaj mësuesve do ta ruaj mirënjohjen dhe respektin e duhur. Profesionin tim do ta ushtroj me ndërgjegje e me dinjitet. Shëndeti i pacientit tim do të jetë brenga ime më e madhe. Do t'i respektoj e do t'i ruaj fshehtësitë e atij që do të më rrëfehet. Do ta ruaj me të gjitha forcat e mia nderin e traditës fisnike të profesionit të mjekësisë.

Kolegët e mi do t'i konsideroj si vëllezër të mi.

Në ushtrimin e profesionit ndaj të sëmurit tek unë nuk do të ndikojë përkatësia e besimit, e nacionalitetit, e racës, e politikës, apo përkatësia klasore. Që nga fillimi do ta ruaj jetën e njeriut në mënyrë apsolute. As në kushtet e kërcënimit nuk do të lejoj të keqpërdoren njohuritë e mia mjekësore që do të ishin në kundërshtim me ligjet e humanitetit. Këtë premtim po e jap në mënyrë solemne e të lirë, duke u mbështetur në nderin tim personal.

The Oath of Hippocrates

Upon having conferred on me the high calling of physician and entering medical practice, I do solemnly pledge myself to consecrate my life to the service of humanity. I will give my teachers the respect and gratitude which is their due. I will practice my profession with conscience and dignity. The health of my patient will be my first consideration. I will respect the secrets which are confided in me, even after the patient has died. I will maintain by all the means in my power, the honor and the noble traditions of the medical profession.

My colleagues will be my brothers.

I will not permit considerations of religion, nationality, race, party politics or social standing to intervene between my duty and my patient. I will maintain the utmost respect for human life from its beginning even under threat and I will not use my medical knowledge contrary to the laws of humanity. I make these promises solemnly, freely and upon my honor

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Original scientific paper

IMMUNOGENETIC ASPECTS OF THE ORIGIN OF PREECLAMPSIA

Maja Pejkovska Ilieva[1*] Mirjana Kjaeva Pejkovska[2], Ana Pejkovska Ilievska[3]

[1, 3]University St. Cyril and Methodius, Faculty of Medicine, Skopje,
[2]PHO HCS Institute for mental health for children and adolescents – Youth, Skopje
Republic of North Macedonia

*Coresponding author: Maja Pejkovska Ilieva majapejkovska@yahoo.com

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ABSTRACT

The combinations of genes of the fetal HLA-C and the maternal KIR affects the pregnancy outcome.

Objective: to examine patients in second trimester of pregnancy by predicting that a change in the immune response may be demonstrated before the development of preeclampsia symptomatology.

Material and Methods: For the purpose of this study, 100 patients were examined in the second trimester, at the University Clinic of Gynecology and Obstetrics and at the Institute of Immunobiology and Human Genetics in Skopje, which analyzed serum levels of cytokines, proinflammatory compared to antiinflamatory antibodies.

Results: The results were obtained using ELISA methodology. Of the above 100 patients, 21% developed clinical preeclampsia syndrome. In them, there was a change in values in addition to an increase in TNF - α, IL-6, IL-2, IL-1α at the same time a tendency for a decrease in IL-10 was observed. IL-4 showed no variation in its value.

Conclusion: In our research paper, proinflammatory interleukin TNF-α increases, and by means of Pearson's correlation between variables it is verified that not only does it grow, but it grows concurrently with IL-6, which is a statistically significant result, or $p < 0.05$. IL-1α increases concurrently with TNF-α, which corresponds to the following studies in support of our study.

Key words: immunogenic aspects, prediction of preeclampsia, interleukins

INTRODUCTION

In healthy pregnancies, reduced Th1/Th2 ratio in favor of higher Th2 cell counts in the peripheral circulation of the mother maintains an immune tolerance to the fetus (1).

Immune balance is the most important and from its maintenance derive excreted circulatory cytokines, both proinflammatory and antiinflammatory (2).

The major histocompatibity complex MHC I class over expressed by extravillous trophoblast, interacts directly with numerous receptors for natural killer cells (uNK) and thereby transmit either inhibitory or activating signal to their cytotoxicity and production of cytokines (3).

The MHC I class express a unique combination of the classical HLA-C (human leukocyte antigen) and the nonclassical HLA-E, HLA-F and HLA-G class I ligands each with their respective roles in the immune acceptance of the fetus (4). HLA-C promotes cell degranulation and secretion of granulocyte macrophage colon-stimulating factor (GM-CSF) and tumor necrosis factor (TNF). HLA-E has a role in early implantation from the 5th to 7th weeks of gestation. HLA-G has a controlling or that is a restrictive role on the cytotoxic effect of uNK cells, i.e. it promotes immunotolerance by inhibiting the role of proinflammatory cytokines including IFN- γ, TNF, IL-1γ, IL-6 (5).

uNK cells are responsible for producing cytokines and several growth factors, but are also responsible for

producing multiple factors whose receptors are located precisely on the primary extravillous trophoblast. For example, uNK cells produce high levels of IL-8, INF-γ, TNF, TGFB1, CXCL10 as well as angiogenic factors such as VEGF-A, VEGF-C, and PGF (6). Maternal-fetal interphase produces receptors for these ligands by the extravillous trophoblast itself. The IL-8 receptor is CXCR1, the CXCR3 is CXCL 10 receptor (7), while TNFR1 as well as VEGFR-1 and VEGFR-3 later bind to VEGF-A and VEGF-C respectively (8). TNF and IFN- γ have the potential to inhibit trophoblast migration and invasion by inducing an increase in PAI expression and promoting MMP-induced proteolysis (9).

Macrophages, on the other hand, are divided into two groups: M1, representing the proinflammatory group, more specifically secreting IL-6, TNF and IL-8, as well as the M2, i.e. the anti-inflammatory phenotype with its typical M2 markers as CD209 and CD206 that directly secrete IL-10 and TGF-γ (10). Decidual macrophages have the ability to suppress T cell activity and induce T regulatory cells. The association of HLA-G homodimers with macrophage-associated leukocyte immunoglobulin like receptor B1 (LILRB1) has been shown to increase secretion of IL-6, IL-8, and TNF.

There is some evidence to suggest that in cases of preeclampsia, polarization to the M1 type of macrophages is likely to exacerbate proinflammatory cytokine production (11).

In contrast, M2, i.e., anti-inflammatory cytokines such as IL-10 and TGF-γ, restrict extravillous trophoblast to its migratory potential.

Disruption of the KIR (killer-cell immunoglobulin-like receptor) interaction with uNK cells with HLA-C on the interstitial trophoblast gives an abnormal decidual immune response resulting in inappropriate remodeling of the spiral arteries (12). It is presented on Figure 1. Vinketova et al. (2016). Human Decidual Stromal Cells as a Component of the Implantation Niche and a Modulator of Maternal Immunity (25)

In preeclampsia, there is a limited invasion of the spiral arteries only to the superficial layers of the decidua.

Failure of trophoblast invasion results in decreased uterine perfusion pressure and consequently placental ischemia.

In that function, blood samples as well as placenta samples at genetic level are analyzed in details.

Numerous homologous KIR genes are mapped to the 19q chromosome and the two basic genetic clusters are classified as haplotypes A and B. The first type encodes KIR, thus inhibiting natural killer cells, while the second type stimulates it.

Preeclampsia is more common in homozygous and inhibitory A haplotypes (AA) than in homozygous B (BB) (13).

The HLA-G gene polymorphism is a gene located at 6p21.3 and belongs to the HLA1 class and has an immunosuppressive effect. It is an important feature implicated in modulating the mother's immune system in terms of inhibiting pregnancy when the mother makes contact with the fetus. It is associated with recurrent miscarriage and preeclampsia (14).

Trophoblast expression of CD200 and CD200R promotes the production of inflammatory cytokines in the preeclamptic placenta (15).

In preeclampsia, trophoblast produces significantly more TNF-γ, sTNFR-1, IL-6, and IL-8, as well as significantly less IL-10, compared to trophoblast in normal placenta. That is, reduced regulation of CD200 expression results in an imbalance of elevated Th1 cytokines and decreased Th2 cytokines in the production of placental trophoblast in preeclampsia.

The risk of complications from preeclampsia during conservative (expectative) treatment is development of severe hypertension (10-15%), eclampsia (0.2-0.5%), HELLP (hemolysis, elevated liver enzymes, thrombocytopenia 1-2%), abruption of the placenta (0.5-2%), fetal growth restriction (10-12%), and fetal death (0.2-0.5%) (16).

In contrast, emergency delivery is associated with preterm neonates and thus the need for stay and treatment at the intensive care unit, neonatal respiratory complications and an increase in neonatal mortality.

With the hypothesis that a change in the immune response may be demonstrated before the development of preeclampsia symptomatology, patients in the second trimester were examined.

MATERIAL AND METHODS

For the purpose of this study, 100 patients were examined in the second trimester, at the University Clinic of Gynecology and Obstetrics and at the Institute of Immunobiology and Human Genetics in Skopje, which analyzed serum levels of cytokines, proinflammatory

compared to antiinflamatory antibodies. Patients signed informed consent to participate in the study. Important anamnestic data were obtained and an ultrasound examination was performed.

The results were obtained using ELISA methodology. Of the above 100 patients, 21% developed clinical preeclampsia syndrome. In them, there was a change in values in addition to an increase in TNF - γ, IL-6, IL2, IL-1γ at the same time a tendency for a decrease in IL-10 was observed. IL-4 showed no variation in its value. A statistically significant result was obtained, with $p < 0.05$ in relation to the values obtained from patients who were affected, compared to those who did not develop clinical signs of preeclampsia. It is presented in Table 1: Results from the examined interleukins, with correlation of proinflamatory and antiinflamatory and in the Table 2: Pearson correlation coefficient in women with developed clinical preeclampsia syndrome..

The sensitivity and specificity of the interleukins were calculated individually, sensitivity of TNF-γ -91% and specificity of 41%, IL-6 85% with 40% respectively, IL-4 46/49%, IL-10 95/25 %, IL-1γ 83/29%, IL-2 77/35%.

Among them, i.e., the mutual increase of proinflammatory cytokines is 78-91.2% sensitivity for a predictive parameter.

DISCUSSION

Considering feto-maternal microchimerism as clearly recognized in normal pregnancy, fetal cells are those that continuously induce maternal immune activation verified by detecting anti-fetal HLA antibodies in the mother's serum during pregnancy. The fetal cells themselves are clearly separated from the mother's immune system and are contacted by the fetal extravillous trophoblast which in turn has a low antigenic effect due to poor expression by classical MHC class I (except HLA-C) and MHC class II.

Fetal antigens are presented through the maternal antigen presenting cells (APCs) of the fetal maternal interphase, that is, the decidua. In fact, up to 50% of the decidual cells make up the maternal immune cells. Therefore, the decidua is an important site of events where the maternal immune system encounters fetal antigens and creates a mechanism of tolerance. It is therefore not surprising that recurrent miscarriages as well as preeclampsia occur due to impaired immune tolerance.

The most commonly studied variant of preeclampsia is the -308G> A transition region of the promoter region, which is associated with increased production of TNF-γ and increased risk of preeclampsia, but also diabetes mellitus type II, coronary artery disease and dyslipidemia.

On the other hand, variation in IL-10 values in the pathogenesis of preeclampsia have been investigated, providing an appropriate inflammatory response to trophoblast cells resulting in appropriate invasion and remodeling of the spiral arterioles.

Studies have suggested that preeclampsia may be a consequence of the development of cardiovascular disease, renal disease, several years after the end of pregnancy (17).

Increased values of microalbuminuria up to 5 years after pregnancy have been demonstrated in women with preeclampsia. This finding is compatible with the presence of underlying unrecognized renal disease or the damaging effect of preeclampsia on the kidney (18).

It has been diagnosed so far when symptoms of hypertension, proteinuria, deviations in laboratory parameters in addition to an increase in degradative products, and a decrease in protein derivates in the blood and the presence of proteinuria, subsequently rich symptomatology of sight disorder, have been developed. Edema, develops or worsening of the mother's condition or endangerment of the fetus.

Many authors and colleagues appreciate Professor Redman as one of the founders of the understanding of the etiology, pathology, diagnosis and management of preeclampsia. The importance of the immune system and the presence of immune factors Redman analyzes in detail (19). The inflammatory response according to him, is induced by placental particles, ranging from large deposited multinuclear fragments to subcellular fragments distributed along the placenta surface. Changes in the number and magnitude of syncytrophobic exosomes and microscopic dimensional damages of the blood vessel are very important in maternal preeclampsia syndrome. Yanfang Guo is al. through numerous studies elaborates the immunological base as a trigger in the maternal systemic circulation (20). Walker JJ elaborates on the same topic, arguing that it is a failure or deficiency in the normal defense mechanism to the fetus. Interleukins such as IL-6, IL-8, and TNF-γ co-grow with lipid peroxidase, proving their monocyte origin (20). Stimulated monocytes produce free radicals that cause oxidative damage. Maternal cells are protected from plasma and intracellular oxidants.

The very imbalance between oxidants and antioxidants and subsequent change in membrane oxidation leads to instability of membrane permeability which is the basis of clinical manifestations of preeclampsia. To modify both genetic modification and differentiation in the production of TNF-γ and nitric oxide enables modification in the development of the disease (21).

In our study, proinflammatory interleukin TNF-γ increases, and by means of Pearson's correlation between variables it is verified that not only does it grow, but it grows concurrently with IL-6, which is a statistically significant result ($p < 0.05$). IL-1γ increases concurrently with TNF-γ, which corresponds to the following studies in support of our study.

Siddiqui et al. have found the presence of agonist autoantibodies to the angiotensin type 1 receptor (AT1-AA). (22) Their amount correlates with the severity of the mother's clinical condition. Jensen et al. find that CD19 (+) CD5 (+) from the B lymphocyte population are a potential source of AT1-AA and are significantly higher in preeclampsia and in advanced pregnancy (23).

Krasnyi AM et al. in 2018 performed a detailed and complex analysis of the ratio of total and fetal DNA to cytokines, which resulted in a significant increase in IL-6 in preeclampsia and the same values are in significant correlation with fetal extracellular DNA in mothers with preeclampsia (24).

CONCLUSION

In preeclampsia, an increased amount of circulating proinflammatory cytokines activate the endometrium, provoking exacerbation of the systemic immune response.

The immunogenetic aspects of the origin of preeclampsia are very important and they need to be emphasized and to be in the final results of the investigation of this condition. In view of the above, there is a need for additional methods in the early diagnosis of pregnant women with preeclampsia before it is even manifested.

Predictive importance is perceived in order to prevent the pathological condition by appropriately prescribing therapy, counseling, a hygienic diet and careful monitoring of the health of both the mother and the fetus.

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Table and Legends

Table 1: Results from the examined interleukins, with

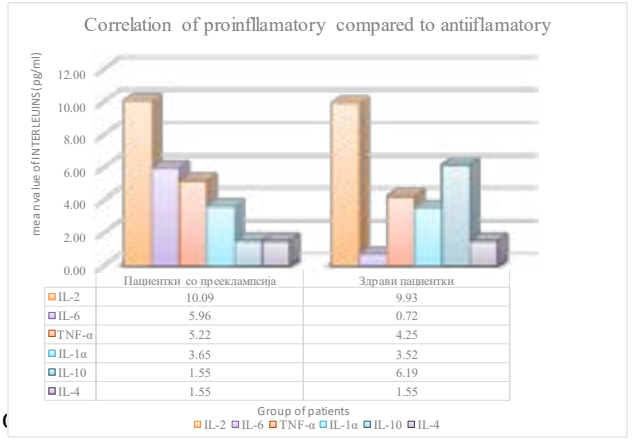

Figure 1. Vinketova et al. (2016). Human Decidual Stromal Cells as a Component of the Implantation Niche and a Modulator of Maternal Immunity (25)

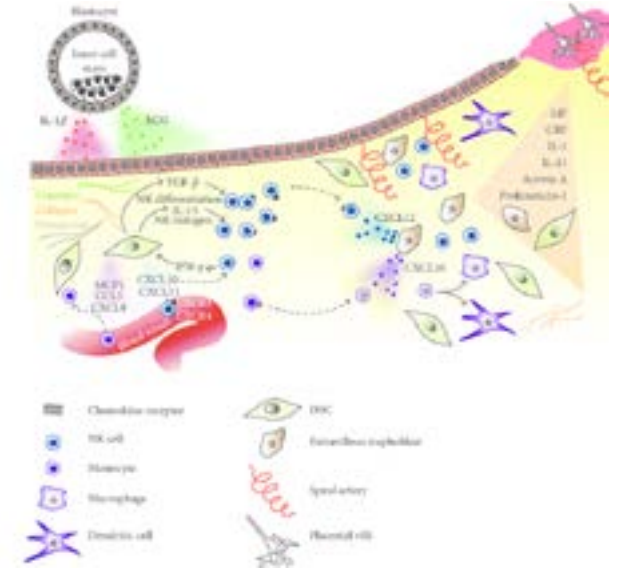

Table 2: Pearson correlation coefficient in women with developed clinical preeclampsia syndrome.

		TNF-γ	IL-6	IL-10	IL-1γ	IL-4	IL-2
TNF-γ	Pearson correlation coefficient	1	0.256	-0.053	0.505	.b	-0.138
	P significance		0.305	0.833	0.032	.	0.586
	Number	21	21	21	21	21	21
IL-6	Pearson correlation coefficient	0.256	1	-0.356	-0.193	.b	0.273
	P significance	0.305		0.146	0.442	.	0.274
	Number	21	21	21	21	21	21
IL-10	Pearson correlation coefficient	-0.053	-0.356	1	0.004	.b	0.016
	P significance	0.833	0.146		0.987	.	0.950
	Number	21	21	21	21	21	21
IL-1γ	Pearson correlation coefficient	0.505	-0.193	0.004	1	.b	0.392
	P significance	0.032*	0.442	0.987		.	0.107
	Number	21	21	21	21	21	21
IL-4	Pearson correlation coefficient	.b	.b	.b	.b	.b	.b
	P significance	.	.	.	.		.
	Number	21	21	21	21	21	21
IL-2	Pearson correlation coefficient	-0.138	0.273	0.016	0.392	.b	1
	P significance	0.586	0.274	0.950	0.107	.	
	Number	21	21	21	21	21	21

Original scientific paper

INDICATIONS FOR OPERATION AND RESULTS FROM SURGICAL TREATMENT OF VESICOURETERAL REFLUX

Gani Çeku[1], Mile Petrovski[2], Shaban Memeti[2], Nexhmi Hyseni[1], Sejdi Statovci[1], Blerim Berisha[1]

[1]Clinic of Pediatric Surgery, University Clinical Centre of Kosova Prishtina -Kosova

[2]University Clinic for Pediatric Surgery, Faculty of Medicine – Skopje, "Ss. Cyril and Methodius" University – Skopje, Republic of North Macedonia

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ABSTRACT

Purpose: The main objective of this paper is to evaluate the value of surgical approach in the treatment of children with the vesicoureteral reflux (VUR) through a retrospective study.

Material and method: Retrospective study was prepared for the period, from January 2006 until December 2014 on children with symptomatic VUR who were surgically treated. Number of children who were treated was 72, of whom 56 were female and 16 were male, aged between two and 16 years. They were treated with IV and V grade reflux ureters. 32 of the unilateral refluxes were left-sided, 18 right-sided, and 22 both-sided. VUR was diagnosed with Voiding cystourethrography (VCUG). The operation was performed under general endotracheal anesthesia. Cohen technique was performed in 64 patients or 90%, Politano-Lead better technique in 4 patients or 5% and Lich-Gregoir technique in 4 patients or 5%.

Results: Out of 72 treated patients, 69 patients had post-operative negative finding of VUR on the performed VCUG, indicating a high 95% success rate. In three girls, persistent post-operative reflux was found in postoperative VCUG. In the first patient persistent VUR was unilateral, of the V-grade. The second patient a third-degree VUR was found and the third patient was diagnosed with II grade VUR. Post-operatively, non-febrile UTIs (urinary tract infections) were diagnosed in 23 patients (20 female children and 3 male children) out of a total of 72 patients. One female child was hospitalized with febrile UTI, and 8 patients or 10% developed febrile UTI within one year of operative treatment.

Conclusion: Open surgery, despite excellent results is used for more complicated cases, VUR grade IV – V or in previously failed cases and it does not appear to provide definitive correction of VUR in all patients and does not prevent certain low incidence of UTI postoperatively. Non-febrile UTIs can occur several years after a surgical correction. Endoscopic treatment is an alternative treatment for VUR.

Key words: children, vesicoureteral reflux, surgical treatment.

INTRODUCTION

Vesicoureteral reflux (VUR) represents the retrograde flow of urine from the bladder to the upper urinary tract. The true prevalence of VUR is unknown due to the fact that many children are asymptomatic. The prevalence of VUR in pediatric population has been estimated to be 0.4–1.8%(1). The prevalence of VUR is significant in the siblings of patients with VUR (46%), children with urinary tract infections (UTI) (30%), infants with prenatal diagnosed hydronephrosis (16%) and urogenital abnormalities: posterior urethra valve (PUV) (60%), cloaca (60%), and duplex kidney (46%)(2,3,4). Primary VUR may be due to either abnormal position or integrity of the ureterovesical junction (UVJ) (60%), and duplex kidney (46%) (2,3,4). The risk for primary VUR varies based on ethnicity, gender and age. Reflux is usually a congenital defect. In most cases, the reflux is lost with the child's development. VUR is defined as active if it occurs during a micturition, while VUR is passive if it is manifested during bladder filling. There are two forms of VUR:

primary and secondary.

Primary VUR as the most common form of reflux, is due to incompetent or inadequate closure of the ureterovesical junction (UVJ), which contains a segment of the ureter within the bladder wall (intravesical ureter). Normally, reflux is prevented during bladder contraction by fully compressing the intravesical ureter and sealing it off with the surrounding bladder muscles.

Secondary VUR is a result of abnormally high voiding pressure in the bladder that results in failure of the closure of the UVJ during bladder contraction. Secondary VUR is often associated with anatomic (eg, posterior urethral valves) or functional bladder obstruction (eg, bladder bowel dysfunction (BBD) and neurogenic bladder (5).

In the majority of cases, UTI is diagnosed when evaluating a urinary tract infection. Reflux in children is often hidden behind the symptoms of acute, chronic or recurrent urinary infection. In some cases, VUR is "accidentally" diagnosed when screening patients at risk (those with a parent, brother or sister with reflux, polycystic kidney or hydronephrosis). Visualization after first urinary tract infection is indicated in all children younger than 5 years with urinary tract infection, children of any age with febrile urinary tract infection, as well as children with pre-identified hydronephrosis.

A routine renal and bladder ultrasound is obtained in any child after an initial UTI to assess the size and shape of the kidneys, and to detect any renal anatomical abnormality.

Laboratory examination: urine culture, Blood counts, serum C-reactive protein, and other hematological tests are routinely determined(6).

VCUG is the gold standard for diagnosing VUR, giving accurate anatomical details and gradation of reflux. Radionuclide cystography (RNC) is also used to detect reflux. Its advantage is the reduction of radioactive exposure, and its weakness is the distortion of the reflux levels. Radioisotope methods: static (DMSA) and dynamic (DTPA) renal scan for visualization of scar changes, renal function assessment and urine transport dynamics(7,8). Dimercaptosuccinic acid (DMSA) renal scan is superior in detecting renal cortical abnormalities compared with other imaging modalities and should be obtained in patients who are at risk for scarring or appear to have loss of renal parenchyma on renal ultrasound.

The VUR grading system was proposed by the International Committee for Reflux Study, established in 1981(9,10). In 1981, The International Reflux Grading System proposed a 5-degree VUR system. The degree of reflux is assessed after VCUG. It defines the extent to which the reflux ranges, as well as the appearance of the ureter, renal pelvis, and calyx.

Grade I - reflux at the beginning of the urethra.

Grade II - reflux in ureter and pyelon with normal cups.

Grade III - moderate dilation of the urethra, the pylon and the cups.

Grade IV - Moderately pronounced dilatation of the urethra, the pylon with ureteral puncture, as well as marked dilatation of the cups but with papillary prints.

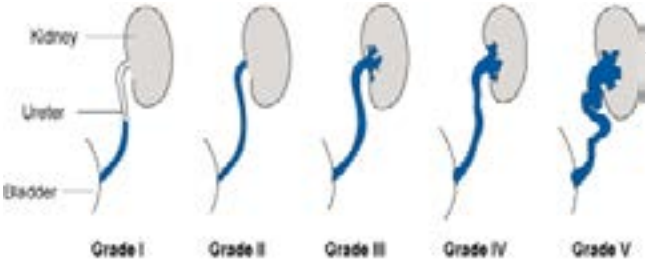


Fig. 1 Degree of VUR (International Committee for Reflux Study - 1981)

Hutch in 1952 initially described the technique of elongating the intravesical ureter to create an anti-reflux valve in paraplegic patients with VUR (11). Since then, multiple additional techniques have been described.

MATERIALS AND METHODS

This retrospective study was realized for the period January 2006 until December 2014 in children with symptomatic VUR who were surgically treated at the University Clinical Center, Department of Pediatric Surgery in Prishtina, Kosovo. Grading of the severity of reflux in all patients was made according to the International Reflux Study committees in 5 groups. The degree of reflux is estimated based on VCUG. Generally accepted indications for surgical treatment were the following: high-grade reflux, low probability of spontaneous resolution, after unsuccessful endoscopic treatment, renal scarring, recurrent pyelonephritis, breakthrough febrile UTI while on continuous antibiotic prophylaxis, parental preference(10).

Number of children who were treated was 72, of whom 56 were female and 16 were male, aged between two and

16 years. Refluxiv ureters of grade IV and V were treated. VUR was diagnosed with VCUG. The operation was performed under general endotracheal anesthesia.

Open repairs prevent reflux by increasing the length of the intravesical ureter, facilitating compression of the ureter against the detrusor muscle during bladder filling (Table 1). These procedures generally require inpatient hospitalization for management of post-operative pain as well as temporary urinary catheter drainage. In contrast, endoscopic repair is an outpatient procedure with minimal post-operative pain and no need for urinary catheter. The average time of the intervention was about 80 minutes in unilateral reflux and in bilateral reflux was about 110 minutes. During the operation, only 10 % of patients received 1 dose of unit of blood or blood derivate. After the open surgical operation, all patient received double antibiotic therapy (ceftriaxone and aminoglycoside). All patients usually received pain therapy for 3 days. Hematuria was noted in all children in duration from 3 to 4 days. The majority of children had no need for blood transfusion. Urinary catheter is extracted at the 7th postoperative day. Retrovesical drain wasn't necessary in all patient. Retrovesical catheter was present only in few of them and it was removed after 2 days. Ureteric stent was placed in only 2 cases. After removing stent and catheter, control ultrasonography was performed. Complete blood count, examination of urine sediment, urea, creatinine, was made every second day.

The postoperative evaluation protocol included renal echo and VCUG after 3 - 6 months. If VCUG and renal ultrasound are normal, prophylaxis with antibiotics is discontinued. Follow-up lasted an average of 4 years.

RESULTS

Out of 72 surgically treated patients due to VUR , 56 were female and 16 were male (Fig 2.) aged between two and 16 years. Refluxiv ureters of grade IV and V were treated. 32 of the unilateral refluxes were left-sided, 18 right-sided, and 22 two sided. A total of 94 ureters were treated. (Table1.) VUR was diagnosed with VCUG. 64 patients or 90% of cases used the Cohen technique, 4 patients or 5% used the Politano-Leadbetter technique and 4 patients or 5% the Lich-Gregoir technique (Fig 3).

The average age of operated children was median of x = 5 years. Indications for surgical intervention were pronounced grade of UTI (patients with grade IV and V).

The postoperative evaluation protocol included renal ultrasound and VCUG after 3 - 6 months. If VCUG and renal ultrasound are normal, prophylaxis with antibiotics is discontinued. Follow-up lasted an average of 4 years.

In this study are included 72 patients, out of which 69 patients had normal postoperative VCUG, representing a 95% success rate. No patient had significant postoperative hydronephrosis on postoperative renal ultrasound. Persistent postoperative reflux was found in three patients. One was a female child with unilateral VUR grade V, and the other girl had grade III reflux . In the third patient, also a female child, a grade II VUR was found, which we expect to spontaneously recede. Also included in this study are cases of postoperative urinary tract infections (UTIs). Non-febrile UTIs were found in 23 patients (20 female and 3 male children) out of a total of 72 patients. One patient, a female child, was hospitalized due to febrile UTI, and the other 8 patients or 10% had febrile UTI. These UTIs are diagnosed up to one year after surgery.

Average time of hospitalization for these patients was 7 days (from 5 to 9 days)

One sided surgery was used in 50 patients with VUR of the left or right ureter, and bilateral surgery due to VUR was performed in 22 patients.

Desired results represented the achievement of proportion for the length of the submucosal tunnel of the ureter to the ureter 4-5:1. With the open surgical technique, 72 ureters showed lowering of the rate of VUR by three or more grades.

Table1. Characteristics of the study group

	Male	Female	Male	Female
Number and percentage of patients	16	56	22%	78%
Total number of ureters	94		100%	
Left sided refluxes	32		34%	
Right sided refluxes	18		19%	
Two sided refluxes	22		47%	
Patients treated with Cohen method	64		90%	
Patients treated with Politano-Leadbetter method	4		5%	
Patients treated with Lich-Gregoir method	4		5%	

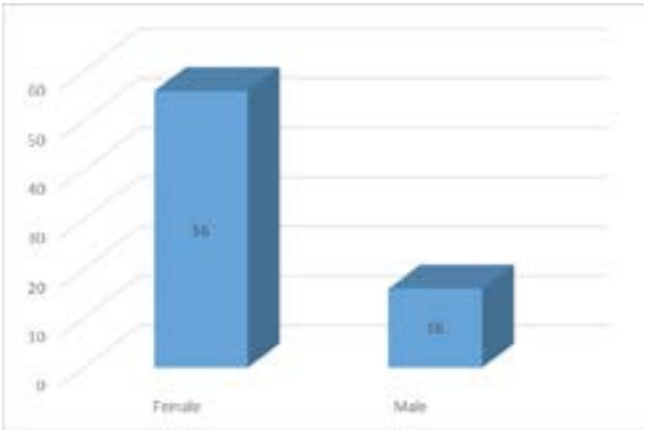


Fig 2. Percentage of the side of ureter affected

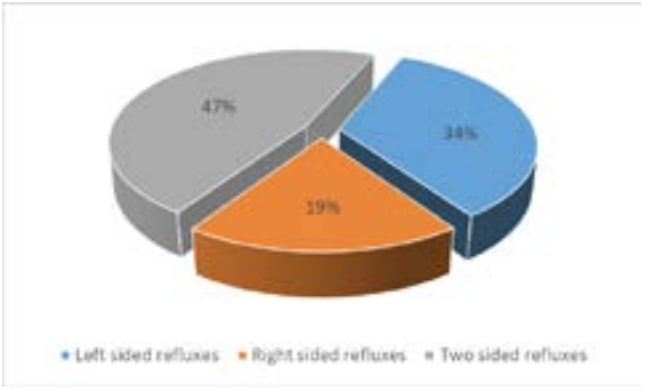
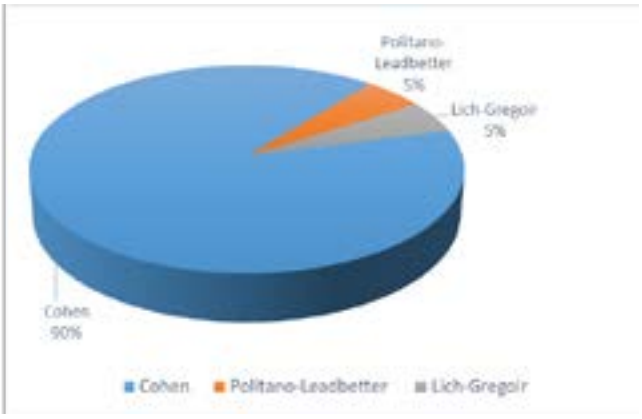


Fig.3. Percentage of surgical methods used for VUR treatment



DISCUSSION

VUR is the most common uropathy in children. Treatment of children with reflux tend to prevent kidney infection, kidney damage and complications caused by kidney damage. Treatment included: pharmacotherapy, surgical treatment and monitoring. Although spontaneous resolution in primary reflux is about 70%, it is common in children younger than 5 years and in lower grade of reflux (gr I, gr II). It is considered that Grade III reflux has spontaneous resolution of 50%, and the resolution is less likely in children over 5 years. It is unlikely that expressed reflux will spontaneously withdraw. Sterile reflux usually does not lead to reflux nephropathy. Long term antibiotic prophylaxis in children is considered safe, and surgery used to corrected the VUR is highly successful (12,13). Antibiotic prophylaxis is considered successful if child doesn`t get urinary infection; doesn't develop kidney damage, and scaring in parenchyma and the VUR spontaneously resolves (14).

Anticholinergic and bladder treeing can reduce symptoms of dysfunctional voiding and risk of infection.

Depending on sex, age of the patient, grade of reflux, the changes in the renal parenchyma, systemic changes that can note in the presence of VUR will decide which type of treatment would be appropriate choice for the particular patient. Each treatment is indicated in varying degrees of development of the disease (15).

Open surgery involves modification of dysfunctional ureter – vesical circuit, which creates a ratio of 4:1 to 5:1 in the length for intramural ureter to the diameter of ureter (16).

Surgical correction of VUR hade excellent results. The success rate was about 95%. Urinary tract infections have been reported in the postoperative period. The risk of anesthesia as well as the general surgical risks of open surgery should not be neglected (17).

Open surgery, despite its excellent results, does not seem to promise a definitive correction of VUR by eliminating the possibility of UTIs. Non-febrile UTIs can also occur several years after surgery.

The International Reflux Study, demonstrates the incidence of UTI and febrile UTI in a 10-year study in patients undergoing open surgery. Some of the operated children in this series with pyelonephritis had early surgical complications with ureteral obstruction(18). Recurrent reflux was rare, and other factors such as urinary diffusion were the main cause of these recurrences. Most patients were not febrile and were not accompanied by VUR.

Although statistics shows that open surgical technique is superior to endoscopic procedure, however endoscopy proved better in terms of time of verticalization of the patients, the need to receive additional drug therapy, blood loss during operation and the duration of the

operation (19). But we cannot favor any operational method because we believe that both methods have their indicational area in appropriate developmental stage of VUR (20).

CONCLUSIONS

Open surgical procedure is reserved for more complicated VUR cases (grade IV-V), and for patients with previously failed endoscopic procedure. This surgical method is superior in terms of satisfactory end results. This is relatively inexpensive method, but the time of verticalization of the patients, the need to receive additional drug therapy, long time of operation and anesthesia, increases the cost.

Summary points

Children with VUR are more likely to develop acute pyelonephritis and renal scarring compared to children without VUR.

Surgical correction of VUR reduces the occurrence of febrile UTIs.

The 2010 AUA guidelines recommend consideration of surgical (open or endoscopic) correction of VUR in patients receiving continuous antibiotic prophylaxis with a febrile breakthrough UTI.

Pre-operative reflux grade is the single most important factor affecting the success rate of endoscopic injection.

Patients with febrile UTI following treatment with endoscopic injection should be evaluated with VCUG to rule out recurrent VUR.

Conflict of interest

All authors agreed for this paper to be published, and report no conflict of interest.

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Original scientific paper

EVALUATION THE VALUE OF INFLAMMATORY BIOCHEMISTRY MARKERS AT THE NEWBORNS WITH SEPSIS IN THE INTENSIVE CARE UNIT

Aspazija Sofijanova, Silvana Naunova Timovska, Elizabeta Shuperliska, Sonja Bojadzieva, Olivera Jordanova

PHI University Clinic for Children Diseases – Skopje

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ABSTRACT

Objective: The aim of this study was to evaluate the predictive values of procalcitonin (PCT) as a early diagnostic and prognostic biochemical marker for sepsis in newborns in correlation withC reactive protein (CRP) and white blood cells count(WBC). Methods: In a prospective study, 110 newborns with two or three clinical signs of sepsis who admitted at the Intensive Care Unit (ICU) at the PHI University Clinic of Pediatric Diseases-Skopje were included . Diagnosis of sepsis in newborns diagnosed according to standard protocols for diagnosis of disease. Sample for blood culture, PCT CRP and WBC obtained by peripheral venous puncturewere taken the first at the admission, before initiation of antibiotic therapy in newborns suspected of sepsis, the second on 3-5 days and the third 6-14 days. Results: 110 newborns were recruited. At first 24 hours of the admission , PCT have a higher discriminative ability than the WBC in distinguishing a bacterial infection from another inflammatory process the early infection diagnosis, and also found to have been more reliable than that of the CRP. The highest average values of PCT (40.37±53.79) were measured during admission with a subsequent sharp jump. The highest average values of CRP were measured (42.17±61.84) after the second during with a subsequent sharp jump. In the three measurements they had an average value WBC (16.83±8.35, 16.71±9.64. 16.31±11.72).Conclusion: The values of procalcitonin (PCT) is a important clinical significance in diagnosis treatment and predicting the prognosis of newborns with sepsis.

Keywords: sepsis, Procalcitonin (PCT), C-reactive protein (CRP), white blood cells count (WBC)

INTRODUCTION

Neonatal sepsis is a common and life-threatening disorder in newborns at the intensive care unit.. Despite advances in perinatal medicine and the introduction of the latest life-saving procedures and antibiotics, sepsis remains the most important cause of morbidity and mortality. Sepsis is the systemic response to infection by microbial organisms and it is a leading cause of major cause of mortality and morbidity in newborns with the highest incidence occurring among infants of very low birthweight and gestation[1]. Early-onset sepsis develops in the first 2 to 3 days after birth.Early-onset sepsisis caused by the transmission of pathogens from the female genitourinary system to the newborns[2,3]. Newborns can become infected in utero or during delivery as they pass through the vaginal canal. Late-onset sepsis develops within 3 to 7 days after birth,usually be caused by a late manifestation of vertically transmitted infection,newborns that require intravascular catheter insertion, or other invasive procedure that disrupts the mucosa.Preterm newborns are at higher risk for sepsis than term newborns, as they tend to require more invasive procedures than term newborns[4,5,6].Early recognition and treatment significantly improve outcomes in newborns with sepsis infections. Initial treatment should lead to stabilization and correction of metabolic, circulatory and respiratory disorders[,7,8]. Diagnosis of infection caused by bacteria or other microbiological organisms is essential for effective treatment and prognostic assessment evaluation. Initial

administration of antibiotic therapy is often either unwarranted or delayed, due to the fact that the clinical signs of sepsis are very nonspecific and there are still no reliable and trustworthy laboratory indicators.[9,10,11].

One promising biochemical marker has been procalcitonin (PCT), whose concentration has been found to be elevated in sepsis[12].PCT is widely used together with other biomarkers, such as C reactive protein (CRP) and white blood cells (WBC) count.Procalcitonin (PCT) is more specific than other inflammatory markers in identifying newborns with sepsis and can be used to diagnose bacterial infections. Rapid elevation in the concentration of procalcitoninPCT is a promising indicator of sepsis in newly admitted critically ill newborns capable of complementing clinical signs and routine laboratory parameters, makes it an ideal biochemistry markerfor bacterial infection[13].

MATERIAL AND METHODS

In a prospective study, 110 newborns with two or three clinical signs of sepsiswho admitted at the Intensive Care Unit (ICU) at thePHI University Clinic of Pediatric Diseases-Skopje were included . Diagnosis of sepsis in newborns diagnosed according to standard protocols for diagnosis of disease.The clinical criteria taken as indicative of sepsis in newborns were:respiratory distress, lethargy, apnea, tachypnea, bradycardia, seizures, poor perfusion,lethargy,feeding intolerance, temperature instability,low birth weight,gestational age, gender, preterm newborns. All the laboratory examination were analyzedin the Clinical Laboratory at the PHI University Clinic of Pediatric Diseases-Skopje.Samplefor blood culture, PCT CRP and WBCobtained by peripheral venous puncturewere taken the first at the admission,before initiation of antibiotic therapy in newborns suspected of sepsis, the second on 3-5 days and the third 6-14 days. Procalcitonin was determined by immunoassay: patented ELFA (Enzyme-linked fluorescent assay) technology, automated Vidas Biomerieux immunoassay (ng/ml) CRP levels were determined by using immunoturbidimetric method Architect c4000 Abbott(mg/L). White blood cells (WBCs) were determined by using Flow citometry method on Sysmex xs 800i/1000i.

Blood culture media were incubated at 37 °C for 5days in BactAlert 3D 360. Positive blood culture were proven with the new multiplex polymerase chain reaction–based rapid diagnostic test (BioFire FilmAray Blood Culture Identification). Statistical analysis . SPSS program was used for statistical analysis,to compare means of the variables, one-way ANOVA test. Categorical variables between groups were analyzed using Chi-square test. Results were presented as percent (%), mean, standard deviation (SD), median, and minimum-maximum (min-max). A P-value< 0.05 was considered as significant.

RESULTS

In the study was designed as a prospective, we included 110 (M:F=68:42) newborns with two or three clinical signs of sepsis hospitalized in the Intensive Care Unit at the PHI University Clinic for Children Diseases – Skopje in period of January 2019 till 31 October 2019 y .The mean gestational age of newborns was 37.41 ± 3.2 weeks The mean birth weight of newborns was 2886.5 ± 768.3 grams. The newborns have been divided into investigation and control group. Investigation group included 55 proven sepsis newborns with positive blood culture and clinical sepsis and II group – 55 suspected sepsis newborns with negative blood cultures.

In the investigation group of newborns with proven sepsis in 25 (46%) the cause was ±RDS , in 20 the cause was Asphyxio, in 10 was Other comorbidities (figure 1).

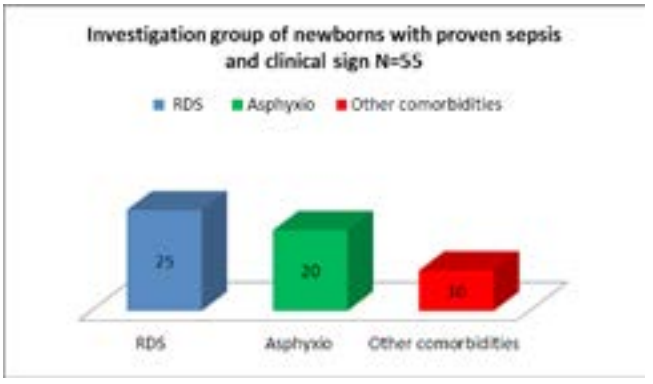

Figure 1. Distribution of sepsis according to the causes

Blood cultures were positive for all newborns with proven sepsis .Twenty nine had two or three bacteria at the same time. The identified bacteria included Staphylococcus aureus (n= 24) mecA, Streptococcus (n= 4), Acinetobacter baumannii (n= 4), Serratia marcescens (n= 1) and Entrobacteriaceae (n= 12), Candida albicans (n= 1) Candida parapsilosis (n= 2)

In the investigation group of newborns with proven sepsis, 32 (57,30%) were male and 23(42,70%)were female. The comparable values in the control group were 36 (64,70%)male and 19 (35,30%) were female. There is no

significant difference in this parameter between the two groups (p<0.01)

The average gestational age of the newborn with sepsis was 36,26± 3,2 weeks and the control group was 37,26± 3,5 weeks. There is no statistically significant difference in average gestational age between the two groups

Preterm newborns in both groups dominated (56,4% and 54,5%)The tested difference in relation to this parameter is statistically insignificant (p<0.01). The average birth weight of newborns was 2590,5 ±792,1 grams, and the control group was 2790,2±798,6 grams. There is no statistically significant difference in average birth weight between the two groups.

Statistical analysis confirmed significantly different values of PCT in the analyzed time period in neonates with sepsis p<0.001. The highest average values (40.37±53.79) were measured during admission with a subsequent sharp jump. After the second measurement, the average values of PCT slowly decreased(37.05±46.19), so that after the third measurement they slowly began to normalize(9.78±15.58) (figure 2).

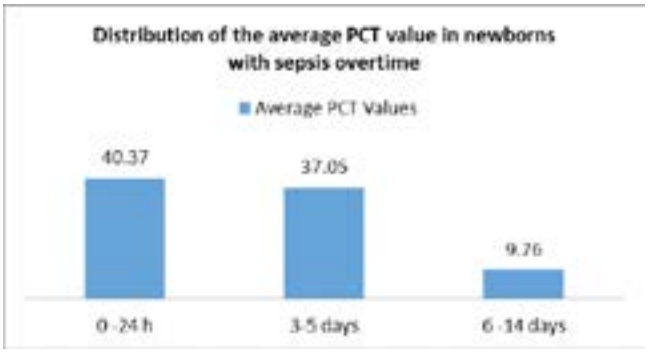

Figure2. Distribution of the average PCT value in newborns with sepsis over time sepsis

There was a significant difference between the mean of PCT level in control group and septic newborns (P< 0.05)

Statistical analysis confirmed significantly different values of CRP in the analyzed time period in newborns with sepsis p<0.001. At the first measurement, the average values of CRP slowly increased (25.4±44.37).The highest average values were measured (42.17±61.84) after the second during with a subsequent sharp jump. At the third measurement, the average values of CRP slowly decreased (21.53±29.59) (figure 3).

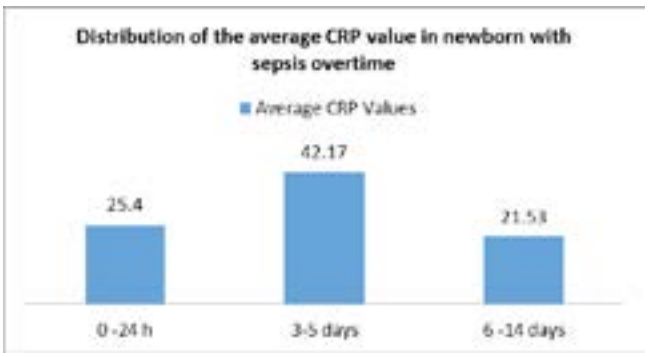

Figure3. Distribution of the average CRP value in newborns with sepsis over time sepsis

There was a significant difference between the mean of CRP level in control group and septic newborns (P< 0.05).Statistical analysis confirmed insignificantly values of WBC in the analyzed time period in newborns with sepsis. In the three measurements they had an average value WBC (16.83±8.35, 16.71±9.64. 16.31±11.72) (figure 4).

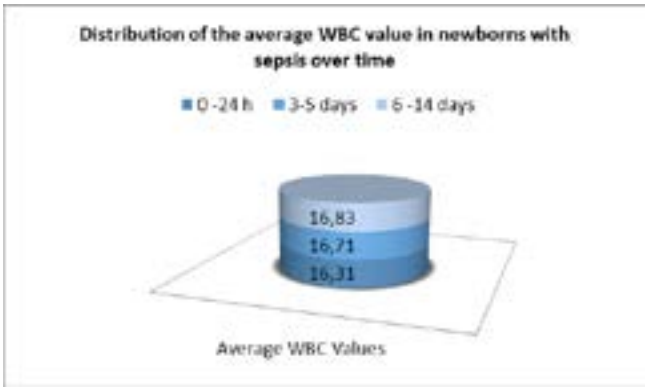

Figure 4. Distribution of the average WBC value in newborns with sepsis over time sepsis

The statistical analysis confirmed the difference in the examined parameter between the two groups as insignificant. Capillary blood test findings show lower mean pH in newborns with sepsis compared with control group (7,19±0,14 versus 7,22±0,12).Average serum albumin values in newborns with sepsis showed lower values compared with the control group(26,23±3,6g/L versus 32.87±5,2g/L).Average total serum protein values in newborns with sepsis showed lower values compared with the control group(47,03±6,6g/L versus 50.47±7,2g/L)

DISCUSSION

Neonatal sepsis is a life-threatening condition and still represents an important cause of mortality and morbidity in newborns at the Intensive Care Unit (ICU). It is a serious medical condition defined as a systemic inflammatory

response, occurring in the first four weeks of life, caused by the body's response to an infection. A newborns who develops sepsis can have inflammation throughout the body, leading to organ failure. The aetiology of sepsis is not always clear and an organism that initiates disease in one newborns may not in another. Bacterial infections are the most common cause of sepsis in newborns. The infection can be located in any of a number of places throughout the body. For pediatrician early identification of infections is still a challenge [14]. The research of new biochemical markers enabling a precocious identification of neonates at risk of neonatal diseases, allowing a close monitoring of the disease and providing information about prognosis,represents a strategic objective of several current researches. Biochemical markers are molecules released by or specific to aparticular organ, can give a glimpse into the physiologicor pathologic status of that specific organ [15].The last decades use of noninvasive laboratory biochemical markershas become a key element in clinical practice[16]. The research of new biochemical markersenabling a precocious identification of neonates at risk of neonatal diseases, allowing a close monitoring of thedisease and providing information about prognosis,represents a strategic objective of several current researches [17].One promising biochemical marker has been procalcitonin (PCT), whose concentration has been found to be elevated in sepsis. Many authors found that procalcitonin is a promising marker for the diagnosis of sepsis in newborns. An ideal biomarker for sepsis should have high sensitivity and specificity with early phase elevation, low cost and quick result [18,19]. The diagnostic performance of PCT in numerous studies from literature has suggested PCT to be useful marker in diagnosis of sepsis [20,21] During infection it is produced by extrathyroid tissue. Mononuclear leukocytes and liver are the most likely sources of PCT in sepsis. Endotoxin and septic-bound proinflammatory cytokines have a stimulating effect on PCT by expressing mRNA in human mononuclear leukocytes. The dynamic concentration of PCT varies from 0.5 to 500 ng / ml. Unlike CRP, which does not rise to very high limits, PCT rises and thus reflects the severity of the disease. Therefore, the diagnosis of severe septic condition, as well as organic dysfunction, is strongly related to the concentration of PCT. Therefore, it is considered particularly useful in monitoring the effect of anti-infective therapy in sepsis.We examined three parameters PCT. CRP, WBC in newborns with two or three clinical signs of sepsis in our study. Procalcitonin rises more rapidly than C-reactive protein in case of infection and decline more quickly in terms of recovery. PCT secretion begins within 4 h after stimulation and peaks at 8 h .CRP secretion starts within 4–6 h after stimulation, peaking only after 36 h[22]. Statistical analysis confirmed significantly different values of PCT in the analyzed time period in neonates with sepsis $p<0.001$. The highest average values of PCT (40.37*53.79) were measured during admission with a subsequent sharp jump. Statistical analysis confirmed significantly different values of CRP in the analyzed time period in newborns with sepsis $p<0.001$. At the first measurement, the average values of CRP slowly increased (25.4±44.37).The highest average values of CRP were measured (42.17±61.84) after the second during with a subsequent sharp jump. At the third measurement, the average values of CRP slowly decreased (21.53±29.59) Statistical analysis confirmed insignificantly values of WBC in the analyzed time period in newborns with sepsis. In the three measurements they had an average value WBC (16.83±8.35, 16.71±9.64. 16.31±11.72). PCT have a higher discriminative ability than theWBC in distinguishing a bacterial infection from another inflammatory process the early infection diagnosis, and also found to have been more reliable than that of the CRP[23].

CONCLUSION

Rapid identification of infection has a major impact on the clinical course, management, and outcome of critically ill intensive care unit (ICU) patients. However, procalcitonin is superior to C-reactive protein and WBC as marker of clinical severity. Procalcitonin should be included in diagnostic guidelines for sepsis in newborns in clinical practice at intensive care units in our country.

PCT is a useful biomarker for early diagnosis, treatment and for monitoring response to therapy of sepsis in newborns.

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Original scientific paper

CLINICAL AND MICROBIOLOGIC PATTERNS OF ACUTE GASTROENTERITIS IN INFANTS OF DIFFERENT AGE

Marija Dimitrovska-Ivanova[1]; Elizabeta Zisovska[2]

[1]Department of Pediatrics, Clinical Hospital, Shtip, North Macedonia
[2]University Clinic for Gynecology and Obstetrics, Skopje, North Macedonia

Corresponding author: Marija Dimitrovska-Ivanova, Department of Pediatrics, Clinical Hospital – Shtip, Ljuben Ivanov St. 25, 2000 Shtip, Republic of North Macedonia. Mobile:+38978393153. E-mail: dimitrovskamarija82@yahoo.com ORCID iD: https://orcid.org/0000-0001-8641-6979

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ABSTRACT

Objective: Acute gastroenteritis is one of the most common infections in childhood with increased frequency within the first 12 months of life, having higher risk of moderate and severe dehydration. The aim of this study was to to evaluate the clinical pattern of acute gastroenteritis in infants according to the age (0-6 months and 7-12 months), to correlate the severity of the disease related to the type of nutrition and to determine the possible microbiological causes of the acute gastroenteritis in infants in two age groups

Material and Methods: A total of 58 infants with acute gastroenteritis divided into 4 groups based on the feeding patterns (type of milk) were included in the study. Investigated indicators were severity of symptoms, dehydration degree and the need for parenteral rehydration.

Results: It was identified a statistically significant association between group affiliation and severity of symptoms depending on the feeding type between first and second group and between third and fourth group The most common cause of acute gastroenteritis in infants was Rotavirus. Our study has shown that exclusive breastfeeding reduces the risk of Rotavirus infection especially in the first 6 months of life OR=0.0758, 95% CI (0.0071-0.8074).

Conclusion: Breast milk has an effect on the severity of the clinical picture of acute gastroenteritis by reducing the vomiting frequency, the number and severity of diarrheal episodes, the risk of moderate and severe dehydration and fever frequency.

Key words: acute gastroenteritis, Rotavirus, breastfeeding, infants, diarrhea

INTRODUCTION

Acute gastroenteritis is a leading cause of morbidity and mortality in developing and undeveloped countries where malnutrition and poor local health care are responsible for the increased severity of the clinical signs of acute gastroenteritis[1]. Acute gastroenteritis can be particularly dangerous in the first 12 months of life with a higher risk of increased water and electrolyte loss with consequent moderate to severe dehydration. Acute gastroenteritis is defined as a decrease in stool consistency and/or an increase in the frequency of discharges (≥ 3 in 24 hours) with or without fever and vomiting[2]. Acute diarrhea lasts between 7 and 14 days. The incidence of acute gastroenteritis ranges from 0.5 to 2 episodes per child per year in children younger than three years. At this age, acute gastroenteritis is

the most common cause of hospitalization[2]. Rotavirus is the most common cause of acute gastroenteritis, rarer causes are Adenovirus, Norovirus, and Astrovirus. Bacterial pathogens include Salmonella, Shigella, and less commonly Escherichia coli, Campylobacter jejuni, and Yersinia enterocolitica. Enterocyte infection leads to cell death, lumen extrusion, and atrophy of the intestinal villi, resulting in reduced intestinal surface area, with impaired digestive and absorption functions and acute transient malabsorptive diarrhea.

Breast milk is an optimal nutrition for infants and key factor in maintaining health and building the solid ground for growth and cognitive development. Breast milk is not only a source of energy, but also a very complex dynamic biological fluid that has a protective and immunomodulatory role[3]. Human milk is a link between the mother's immune system and the infant's one. Although infants have antibodies vertically transmitted, they remain unprotected when they come in contact with new microorganisms. Breast milk can reduce this risk through the antibodies present in it and thus modify the infant's immune, metabolic and micro flora systems[3]. Human milk has its own immune system and a variety of soluble and cellular components that ensure the development and maturation of the immune system in infants[4]. Breast milk has antimicrobial activity against viruses, bacteria and protozoa, may reduce the incidence of gastrointestinal and non-intestinal infections in infants[5]. A number of studies have confirmed that breastfeeding has a protective role and reduces the risk of diarrhea, especially in infants up to 12 months of age[6-8].

The aims of the study were:

-to evaluate the clinical pattern of acute gastroenteritis in infants according to the age (0-6 months and 7-12 months).

-to correlate the severity of the disease related to the type of nutrition.

-to determine the possible microbiological causes of the acute gastroenteritis in infants in two age groups.

MATERAL AND METHODS

Study design

This was a prospective cohort study started in the period November 15, 2018 until December 31, 2019. The study included newborns and infants from birth to 12 months of age who were diagnosed with acute gastroenteritis. All infants were hospitalized at the Children's Department in Clinical Hospital - Shtip. Parents' written consent was obtained for each infant included in the study after extensive communication with them. An appropriate survey questionnaire was designed and responses were obtained from the infants' mothers. The questionnaire covered the following segments: infant age, nutrition (breast milk, milk formula or cow's milk) and weaning practice. Information on the onset of symptoms of acute gastroenteritis in the last 24 hours before admission, as well as information on the diet and health status of the nursing mother were included. Infants were divided into 4 groups according to age in months and according to milk nutrition and introduction of complementary food.

Group I included newborns and infants from birth to 6 months who were exclusively breastfed. Group II included newborns and infants from birth to 6 months of age who weren't exclusively breastfed and were on mixed milk nutrition. Group III included infants from 7 to 12 months of age in whom, were receiving complementary food and continued breastfeeding. Group IV included infants from 7 to 12 months of age in whom a complementary food was introduced and no breast milk at all but, milk formula or cow's/goat's milk. Exclusively breastfed were infants who were fed only with breast milk and didn't receive additional food or fluids (excluding oral rehydration solution, vitamins, minerals, and medications). The clinical picture and degree of dehydration were determined by physical examination and the degree of dehydration was graded as mild, moderate and severe through the use of a clinical scoring system. (World Health Organization: Integrated management of childhood illness-Module 4, Diarrhea). For each infant included in the study, a record sheet was filled and according to the severity of the clinical signs the need for parenteral rehydration was assessed during the hospital stay. The study didn't include infants whose diarrhea was due to a surgical or extra-intestinal cause, as well as infants who had received immunosuppressive therapy.

Laboratory methods

From each infant included in the study, one sample of diaper stool was taken with a plastic spatula. This stool sample was collected in a sterile plastic cup with the general data of the patient and the code written on it and within 30 minutes was brought to the Microbiological Laboratory in the Center for Public Health (CPH) - Shtip. In this stool sample the presence of Rotavirus and

Adenovirus with Immunochromatographic test (DUO ROTA-ADENOVIRUS - Check-1 VEDA.LAB, Alencon-France) was analyzed. From the same stool sample, a coproculture was performed which was supposed to identify the presence of enteropathogenic bacteria by sowing the stool sample on a suitable substrate.

Statistical analysis

The collected data were processed using the statistical program SPSS 20 and the following statistical methods:

-Descriptive method: attributive statistical series were analyzed by determining percentages and numerical series with central tendency measures and with data dispersion measures.

-Statistical significance of the probability between the distributions of the frequencies of two attributive variables was estimated by the Difference test, and between the numerical series exploring the Student t-test.

-The Odds ratio-OR cross-correlation is used to determine the relationship between the dependent-criterion variable and the independent. For CI (confidence interval 95% CI) statistical significance was defined at the level of standard error less than 0.05 (p). The results are shown in tables and figures.

RESULTS

The analysis included 58 hospitalized infants from birth to 12 months of age with a diagnosis of acute gastroenteritis, divided in four groups.

The first group included 7(12.1%) infants, the second group included 16(27.6%), the third group included 19(32.7%) and the fourth group included 16(27.6%) infants divided by age expressed in months and type of nutrition.

Table 1 and Table 2 present the infants with acute gastroenteritis by gender and sex

The average infant age in the first group was 2.1±0.9 months, in the second group was 3.4±1.5 months, in the third group was 9.3±1.2 months and in the fourth group it was 9.5±1.4 months.

Table 1. Distribution of the infants according to the gender and age (I and II group)

Group	I		II	
Gender	Number	%	Number	%
Male	4	57.1	9	56.25
Female	3	42.9	7	43.75
Age in months	Number	Mean ! SD	Number	Mean ! SD
	7	2.1 ! 0.899735	16	3.4 ! 1.454877

SD: Standard deviation

Table 2. Distribution of the infants according to the gender and age (III and IV group)

Group	III		IV	
Gender	Number	%	Number	%
Male	11	57.9	6	37.5
Female	8	42.1	10	62.5
Age in months	Number	Mean ! SD	Number	Mean ! SD
	19	9.3 ! 1.249561	16	9.5 ! 1.366260

SD: Standard deviation

The distribution of the clinical signs in the first two groups is presented in Table 3, which included the average number of vomiting, average number of liquid stools, fever, degree of dehydration, number of days of parenteral rehydration and length of hospital stay. The average number of vomiting 24 hours before admission in infants in the first group was 0.3±0.5, in the second group was 4.6±3.3, the difference was statistically significant (p=0.002669). The average number of liquid stools in infants 24 hours before admission in the first group was 3.7±0.8, in the second group 10.4±4.9, and the difference was statistically significant (p=0.002152). Fever was reported in 14.3% of infants in the first group and in 81.25% in the second group, with statistically significant percentage difference (p=0.0025). All infants from the first group had mild degree of dehydration, in the second group a mild degree of dehydration was registered in 25.0%, moderate in 43.75% and a severe degree of dehydration in 31.25% of infants. The average number of liquid stools during treatment in the first group was 9.0±2.2, and in the second group was 21.2±8.5, the difference between the average number of liquid stools was statistically significant (p=0.001419). The average number of vomiting during treatment in the first group was 0.3±0.8, and in the second group was 3.0±2.4, the difference between the average number of vomiting was statistically significant (p=0.008516). The average number of parenteral rehydration days in the first group was 0.7±0.8, and in the second group it was 2.0±1.0, the difference between the average number of parenteral

rehydration days was statistically significant (p=0.005246). The average number of hospital days (lenght of stay) in the first group was 4.1±1.6 and in the second group it was 4.9±1.8, the difference between the average number of hospital days was statistically insignificant for p>0.05 (p=0.318302).

Table 3. Clinical condition 24 hours before admission and during the hospitalization (I and II group)

Group	Average I	Average II	t-test	p	N I	N II	SD I	SD II
Number of vomiting 24 hours before admission	0.285714	4.56250	-3.40460	0.002669	7	16	0.487950	3.265348
Number of stools 24 hours before admission	3.7	10.4	-3.49610	0.002152	7	16	0.755929	4.951431
Number of stools during the hospitalization	9.0	21.2	-3.67211	0.001419	7	16	2.236068	8.549610
Number of vomiting during the hospitalization	0.3	3.0	-2.90250	0.008516	7	16	0.755929	2.394438
Number of parenteral rehydration days	0.7	2.0	-3.11436	0.005246	7	16	0.755929	0.966092
Number of hospitalization days	4.1	4.9	-1.02224	0.318302	7	16	1.573592	1.768945

SD: Standard deviation; N: Number

The distribution of the clinical signs in the second two groups is presented in Table 4. The average number of vomiting 24 hours before admission in infants in the third group was 2.7±3.3 in the fourth group was 4.6±3.3 the difference was statistically insignificant (p=0.113598). The average number of liquid stools in infants 24 hours before admission in the third group was 5.9±2.4, in the fourth group 9.0±4.2 and the difference was statistically significant (p=0.011505). Fever was reported in 26.3% of infants in the third group and in 68.75% in the fourth group with statistically significant percentage difference (p=0.0120). In the third group 78.9% of infants had mild degree of dehydration and 21.1% of infants had moderate degree of dehydration. In the fourth group mild degree of dehydration was registered in 18.75% of infants, moderate in 62.5% and severe degree of dehydration in 18.75% with statistically significant percentage difference between the two groups for mild (p=0.0004) and for moderate degree of dehydration (p=0.0128). The average number of vomiting during treatment in the third group was1.4±1.9, in the fourth group was 3.4±3.0 the difference between the average number of vomiting was statistically significant (p=0.025661). The average number of liquid stools during treatment in the third group was 14.1±7.9, and in the second group was 18.6±10.3 the difference between the average number of liquid stools was statistically insignificant (p=0.152484). The average number of parenteral rehydration days in the third group was 1.7±1.2 and in the fourth group it was 2.1±1.1 the difference between the average number of parenteral rehydration days was statistically insignificant (p= p=0.336684). The average number of hospital days (length of stay) in the third group was 3.9±1.6 and in the fourth group was 4.9±1.4 the difference between the average number of hospital days was statistically insignificant (p=0.054966)

Table 4. Clinical condition 24 hours before admission and during the hospitalization (III and IV group)

Group	Average III	Average IV	t-test	p	N III	N IV	SD III	SD VI
Number of vomiting 24 hours before admission	2.736842	4.562500	-1.62537	0.113598	19	16	3.280280	3.346018
Number of stools 24 hours before admission	5.9	9.0	-2.67615	0.011505	19	16	2.391505	4.242641
Number of stools during the hospitalization	14.1	18.6	-1.46463	0.152484	19	16	1.865350	3.03040
Number of vomiting during the hospitalization	1.4	3.4	-2.33692	0.025661	19	16	1.865350	3.03040
Number of parenteral rehydration days	1.7	2.1	-0.97494	0.336684	19	16	1.240166	1.08781
Number of hospitalization days	3.9	4.9	-1.98968	0.054966	19	16	1.629408	1.43614

SD: Standard deviation; N: Number

Rotavirus was positive in 26 stool samples with a prevalence rate of 44.8%. Rotavirus was positive in one (14.3%) infant in the first group, in 11(68.75%) in the second group, in 6(31.6%) in the third group, and in 8(50%) infants in the fourth group. In one infant from the second group was isolated Shigella flexneri and in one infant from the same group was isolated Adenovirus. In the fourth group Salmonella enteritidis was isolated in two infants, Proteus mirabilis in one infant and Adenovirus in one infant also (Figure 1).

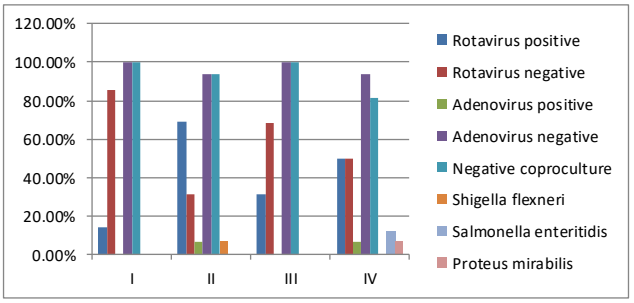

Figure 1: Microbiological findings in stool

DISCUSSION

Several studies have confirmed that breastfeeding has a protective role and reduces the risk of diarrhea, especially in infants up to 12 months of age. Frank et al. 2019[6] have shown that breastfeeding can play a protective role against respiratory and gastrointestinal acute illness in infants for at least the first 6 months of life by continuing to play the same role if breastfeeding continues after the sixth month of life. It has been observed that infants who are exclusively breastfed for up to 6 months and in which breastfeeding is continued for up to 12 months, have a lower rate of hospitalizations due to diarrhea, while in infants who have been fed with milk formula have had a higher incidence and rate of hospitalizations due to diarrhea[7]. Dialo et al. 2019[8] noticed that breastfeeding discontinuation before the third month was found to be significantly associated with a high incidence of diarrhea at 6 months of age and between 6 and 12 months. Breastfeeding discontinuation (weaning) before the sixth month was also associated with a higher incidence of diarrhea at 6 months of age. Infants who were on milk formula for ≥ 3 months had a higher incidence of diarrhea between 6 and 12 months.

In the studies by Duffy et al., 1986[9] and Misra et al. 2007[10] was found that there was no difference in the incidence of Rotavirus diarrhea among exclusively breastfed and non-exclusively breastfed infants. Contrary to these claims, a study by Maranhão et al. 2008[11] found that diarrhea was more common in infants less than 6 months of age who were not breastfed or were on non-exclusive breastfeeding. Krawczyk et al. 2016[12] and Plenge-Bönig et al. 2010[13] have found that exclusive breastfeeding is effective in preventing Rotavirus infection by reducing the risk of Rotavirus infection in children, especially in the first 6 months of life. Some studies have shown that Rotavirus is a more common cause of acute gastroenteritis in infants than Adenovirus[14,15]. These results support our findings that the most common cause of acute gastroenteritis in infants was Rotavirus. In this study, clinical signs and symptoms 24 hours before hospital admission were evaluated and clinical condition during treatment was assessed, as well as the need for parenteral rehydration, and the length of hospitalization. A statistically significant difference ($p<0.05$.) for the average number of vomiting before admission was registered between the first and second group with less frequent vomiting in exclusively breastfed infants in the first group, while between the third and fourth group that difference was insignificant ($p>0.05$). Regarding the number of liquid stool 24 hours before admission, high statistically significant difference was registered between the first and second group and less statistically significant difference between the third and fourth group. It has been proved that there is a statistically significant percentage difference for fever between the first two and between the second two groups. Sherif et al., 2015[16] did not prove statistical significance for the degree of dehydration between groups, but in our study all infants from the first group who were exclusively breastfeed had a mild degree of dehydration while in the second group only 25% of infants had a mild degree of dehydration, the rest had a moderate and severe degree of dehydration. Regarding the degree of dehydration in infants between the third and fourth group, it was noted that the mild degree of dehydration is more present in the third group while moderate degree of dehydration is more common in the fourth group. Similar results were obtained in a study by Fuchs et al. 1996[17]. In the present study vomiting during treatment was less common in infants in the first group versus the second group and in the third versus the fourth group with a statistically significant difference between the average number of vomiting by $p<0.05$. In the study of Weinberg et al. 1984[18] was shown that the vomiting frequency was significantly lower in breastfed infants. A study by Eaton-Evans and Dugdale, 1987[19]

found that infants up to 6 months of age had a lower number of liquid stools and a lower vomiting frequency in those who were breastfed compared to other types of milk, indicating that breast milk has a protective effect on the intestines of infants younger than 6 months. In infants older than 6 months, the protective role of breast milk was not confirmed. Regarding the average number of liquid stool during the treatment, there was a statistical significance for $p<0.05$ between the first and second group, but not for the third and fourth group $p>0.05$. In the study of Weinberg et al. 1984[18] it was noticed that there was no significant difference between the groups for diarrhea duration, the number of liquid stools in 24 hours period of time, or the fever frequency. In this study, it was observed statistical significance for the number of days of parenteral rehydration between the first and second group but not betwean third and the fourth group. For the number of hospital days, no statistical significance was proved either between the first and the second group and betwean the third and the fourth group In contrast to our results in a study by Boccolini et al. 2012[20] was shown that the increase in the prevalence of exclusive breastfeeding in infants younger than 4 months with acute diarrhea has a negative correlation with the duration of hospitalization (Rho=-0.483, p=0.014). This study has shown that exclusive breastfeeding is effective in preventing Rotavirus infection by reducing the risk of Rotavirus infection in children especially in the first 6 months of life OR=0.0758, 95% CI(0.0071-0.8074).

CONCLUSION

This study gives support to the findings that breast milk has strong effect on the severity of the clinical signs of acute gastroenteritis by reducing the vomiting frequency, the number and severity of diarrheal episodes, the risk for moderate and severe dehydration and fever frequency. The study will be continued exploring additional effects of the breast milk on the gastrointestinal function.

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Original scientific paper

EARLY DIAGNOSTIC OF SEPSIS IN NEWBORNS WITH RESPIRATORY DISTRESS SYNDROME

Elizabeta Shuperliska, Aspazija Sofijanova, Silvana Naunova Timovska, Sonja Bojadzieva, Avdi Murtezani

PHI University Clinic for Children Diseases - Skopje.

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ABSTRACT

Objective: Early diagnosis of sepsis in newborns with RDS is essential for life-threatening condition, for reducing severe sepsis and septic shock in the Intensive care Unit at the University Children's Hospital in Skopje.Methods: In this prospective study, we included 100 (M:F=59:41) newborns with Respiratory distress syndrome (RDS) suspected for sepsis admitted in the Intensive Care Unit in period of December 2019 till 31 May 2020 y. Procalcitonin levels were measured by using a immunoassay system Vidas based on the ELFA principles. Results: The newborns with RDS suspected for sepsis have been divided into two groups The first group included 50 newborns with RDS and positive blood culture and the second group included 50 newborns with RDS and negative blood culture. The average gestational age of the newborn with RDS and positive blood culture was 36,01± 3,1 weeks and the newborn with RDS and negative blood culture 36,26± 3,2 weeks. Preterm newborns in both groups dominated (64,2% and 58,2%). The average birth weight of the newborn with RDS and positive blood culture was 2490,5 ±791,6 grams, and the newborn with RDS and negative blood culture was 2690,2±788,5grams. There is statistically significant difference in average PCT between the two groups overtime ($p<0.05$). There is statistically significant difference in average PCT between the two groups overtime procedure (MV , BCPAP, OXYGEN MASK) ($p<0.05$).Conclusions: PCT is promising sepsis markers in newborns with RDS, capable of complementing clinical signs and routine lab parameters suggestive of severe infection at the time of ICU admission.

Keywords: Procalcitonin (PCT), newborns, Respiratory distress syndrome (RDS)

INTRODUCTION

Respiratory distress syndrome is also referred to as hyaline membrane disease or disorder due to a lack of surfactant in the lungs in newborns. It is most common in newborns under 37 weeks of gestation, as surfactant is produced in the largest amount at 34 to 37 weeks of gestation[1,2]. The risk of developing respiratory distress syndrome is inversely proportional to gestational week. Thus, this condition is most common in premature infants as a result of surfactant deficiency and underdeveloped lung anatomy [3,4]. Risk factors that contribute to respiratory distress syndrome include male sex, white race, caesarean section, prematurity, multiple short pregnancies and newborns from mothers with diabetes [5,6].Symptoms and signs of RDS include: labored, rapid, grunting respirations that occur immediately or a few hours after birth with flaring of the nasal alae and substermal and suprasternal retraction, tachypnea. Radiological studies show diffuse atelectasis which is described as ground-glass appearance with visible air bronchograms and low lung expansion[7,8,9].Differential Diagnosis for an infant with respiratory distress and / or cyanosis are: transient tachypnoea of newborn, pneumothorax, aspiration of blood / mucus, meconium aspiration, congenital pneumonia [Nb Group B Streptococcus (Gbs)], pulmonary hypoplasia, persistent pulmonary hypertension, hydrops fetalis, congenital malformation EG diaphragmatic Hernia, cystadenomatoid, malformation, congenital heart disease etc. [10].Complications of this disease are: bronchopulmonary dysplasia, pneumothorax, hypoxia, persistent ductus arteriosus, retinopathy, intraventricular haemorrhage, cardiovascular arrest[11,12]. The therapy

consists of supportive measures (electrolyte balance, intravenous fluid administration, glycemic control) and initial placement of the newborn on Nasal CPAP with a PEEP of 3–8 cm H2O. If respiratory failure persists, endotracheal intubation and mechanical ventilation are performed and a surfactant is administered endotracheally within two hours of delivery [13,14]. Sepsis is a leading cause of death in newborns with RDS, defined as a systemic inflammatory response syndrome (SIRS) caused by blood stream infections [15, 16] or, as life-threatening organ dysfunction caused by a deregulated host response to infection [17], review of clinical, laboratory and data . The clinical manifestations range from subclinical infection to severe manifestations of focal or systemic disease. [18]. Diagnosing newborns with RDS suspected of sepsis is both challenging and complex. Biomarkers can play an important role in providing a timely diagnosis of sepsis, helping the differential diagnosis with non-infectious SIRS and the decision-making in the initial management[19]. Biomarkers have been shown to be useful in the diagnosis of infection and a good predictor of mortality, severe sepsis and septic shock in newborn with sepsis before organ dysfunction has advanced too far.

MATERIAL AND METHODS

The study was designed as a prospective, and we included 100 newborns with respiratory distress syndrome (RDS) suspected for sepsis admitted in the Intensive Care Unit at the PHI University Clinic for Children Diseases – Skopje in period of December 2019 till 31 May 2020 y . Symptoms and signs of newborns with RDS include: labored, rapid, grunting respirations that occur immediately or a few hours after birth with flaring of the nasal alae and substermal and suprasternal retraction, tachypnea. Tachypnea is due to an attempt to increase minute ventilation to compensate for a decreased tidal volume and increased dead space. Retractions occur as the infant is forced to generate a high intrathoracic pressure to expand the poorly compliant lungs. The levels of PCT was ≥ 2ng/ml. A sample for blood culture, PCT obtained by peripheral venous puncture was taken at the first admission in the ICU, the second on 3 day and the third on day 7.

Medical data records of admitted newborns with RDS suspected for sepsis injury were analyzed. The laboratory were done in the Clinical Laboratory at the PHI University Children's Hospital–Skopje.Procalcitonin levels was measurement by immunoassay: automated Vidas Biomerieux immunoassay (ng/ml) patented ELFA (Enzyme-linked fluorescent assay) technology. Blood culture media were incubated at 37°C for 5days in BactAlert 3D 360.Positive blood culture was detected with the new multiplex polymerase chain reaction–based rapid diagnostic test (BioFire FilmAray Blood Culture Identification).

Statistical analysis. Data analysis is performed in a Statistic program 7.1 for Windows and SPSS Statistics 23.0,to compare the means of the variables, one-way ANOVA test. For all analyses p value $< 0,05$ was taken for statistical significance.A P-value< 0.05 was considered as significant.

RESULTS

In this study who was designed as a prospective, we included 100 (M:F=59:41) newborns with respiratory distress syndrome (RDS) suspected for sepsis admitted in the Intensive Care Unit at the PHI University Clinic for Children Diseases – Skopje in period of December 2019 till 31 May 2020 y.The newborns with RDS suspected for sepsis have been divided into two groups The first group included 50 newborns with RDS and positive blood culture and the second group included 50 newborns with RDS and negative blood culture. In first group we isolated twenty one with two or three bacteria at the same time.The identified bacteria included Staphylococcusaureus (n=37) mecA, Streptococcus (n=3), Acinetobacter baumannii (n=5), Serratia marcescens (n=4) and Entrobacteriaceae (n=35) .

The average gestational age of the newborn with RDS and positive blood culture was 36,01± 3,1 weeks and the newborn with RDS and negative blood culture 36,26± 3,2 weeks. There is no statistically significant difference in average gestational age between the two groups($p<0.01$). In the first group of newborn with RDS and positive blood culture was 64,2 % preterm newborns and 35,8% term newborns. The comparable values in the second group were 58,2 % preterm newborns and 41,8% term newborns. Preterm newborns in both groups dominated (64,2% and 58,2%).The tested difference in relation to this parameter is statistically in significant ($p<0.01$).The average birth weight of the newborn with RDS and positive blood culture was 2490,5 ±791,6 grams, and the newborn with RDS and negative blood culture was 2690,2±788,5grams. There is no statistically significant difference in average birth weight between the two groups ($p<0.01$).In the first

group of newborn with RDS and positive blood culture was 54% mechanical ventilation BCPAP was 26%and 20% of oxygen therapy. The comparable values in the second group were 44% mechanical ventilation BCPAP was 32%and 24% of oxygen therapy. The tested difference in relation to this parameter is statistically in significant (p<0.01).

Statistical analysis confirmed significantly different values of PCT in the analyzed time period in first group newborns with RDS and positive blood culture p<0.001(figure.1). The highest average values (42.37±43.59) were measured during admission with a subsequent sharp jump. After the second measurement at day 3, the average values of PCT slowly decreased(39.05±41.29), so that after the third measurement on day 7,they slowly began to normalize (9.76±15.58).

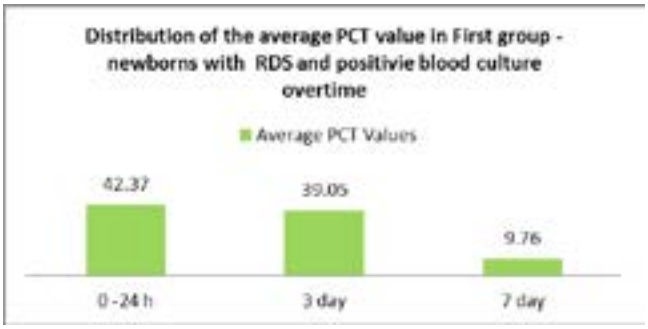

Figure1. Distribution of the average PCT value in newborns with RDS and positive blood culture over time

Statistical analysis confirmed significantly different values of PCT in the analyzed time period in second group with RDS and negative blood culture p<0.001(figure.2). The highest average values (42.37±43.59) were measured during admission with a subsequent sharp jump. After the second measurement at day 3, the average values of PCT slowly decreased(39.05±41.29), so that after the third measurement on day 7,they slowly began to normalize (9.76±15.58).

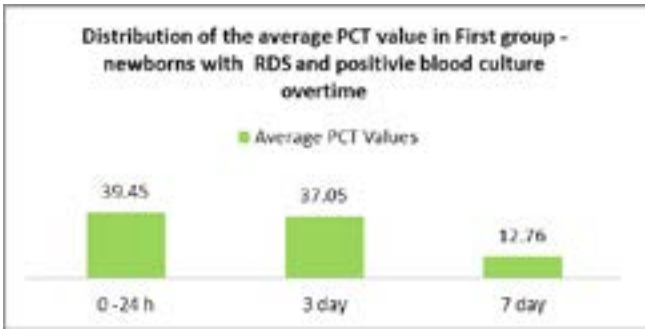

Figure2. Distribution of the average PCT value in newborns with RDS and negative blood culture over time

There is statistically significant difference in average PCT between the two groups overtime (p<0.05).

Statistical analysis confirmed significantly different values of PCT in the analyzed time period in first group newborns with RDS and positive blood culture with MV and BCPAP p<0.001(figure.3). The highest average values (38.31±52.50) were measured in newborns with RDS and positive blood culture with MV and BCPAP during admission, with a subsequent sharp jump compared to newborns with RDS and positive blood culture with oxygen mask. After the second measurement at day 3, the average values of PCT slowly decreased(37.61±42.85), so that after the third measurement on day 7,they slowly began to normalize(27.87±32.67).

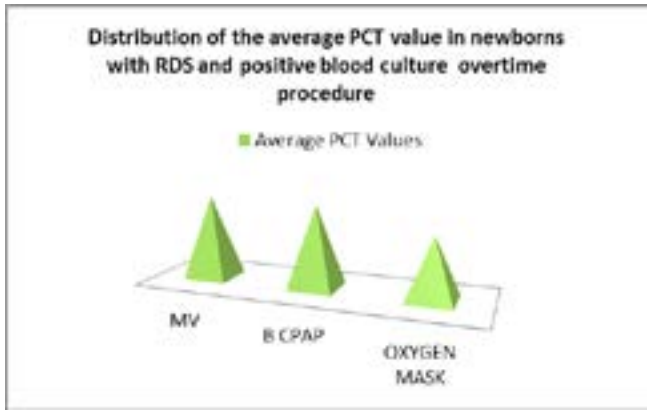

Figure 3. Distribution of average PCT value in newborns with RDS and positive blood culture over time compared to procedure (MV , BCPAP, OXYGEN MASK)

Statistical analysis confirmed significantly different values of PCT in the analyzed time period in first group newborns with RDS and negative blood culture with MV and BCPAP p<0.001(Figure.4). The highest average values (36.35±42.51) were measured in newborns with RDS and positive blood culture with MV and BCPAP during admission, with a subsequent sharp jump compared to newborns with RDS and positive blood culture with oxygen mask. After the second measurement at day 3, the average values of PCT slowly decreased(33.71±42.75), so that after the third measurement on day 7,they slowly began to normalize(21.77±32.67).

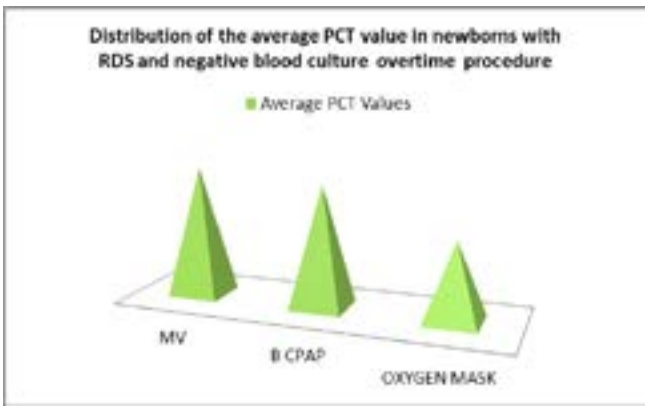

Figure 4. Distribution of average PCT value in newborns with RDS and positive blood culture over time compared to procedure (MV , BCPAP, OXYGEN MASK)

There is statistically significant difference in average PCT between the two groups overtime procedure (MV , BCPAP, OXYGEN MASK) ($p<0.05$).

DISCUSSION

Respiratory distress syndrome is a common cause of hospitalization in the intensive care unit. It is the leading cause of death in preterm newborns . Respiratory distress syndrome [RDS] remains the major cause of mortality and morbidity in preterm newborns. Respiratory distress syndrome most commonly occurs in preterm newborns as a result of surfactant deficiency and lung underdevelopment. [20,21].Risk factors for sepsis in the postnatal period include: male gender, hypogammaglobulinemia, birth weight <1000 grams, central venous catheters, prolonged duration of mechanical ventilation and intravenous alimentation. Another condition associated with prematurity and severe sepsis is necrotic enterocolitis [22,23,24].Mechanical ventilation can effectively improve the arterial oxygen partial pressure and reduce the mortality of newborns with RDS.

Sepsis in newborns with RDS is essential for life-threatening condition and is an unusual systemic reaction to what is sometimes an otherwise ordinary infection, and it probably represents a pattern of response by the immune system to injury[25,26]. A hyper-inflammatory response is followed by an immunosuppressive phase during which multiple organ dysfunction is present and the patient is susceptible to nosocomial infection. Early biomarkers to diagnose sepsis in ICU are widely used in clinical practice and they are useful for monitoring the infectious process, and can reduce the risk of death in newborns with RDS[27,28]. The diagnostic performance of PCT in numerous studies from literature has suggested PCT to be a useful marker in the diagnosis of sepsis [29,30] in newborns with RDS . In our study, we examined PCT values , in newborns with RDS suspected for sepsis. Preterm newborns in both groups dominated (64,2% and 58,2%).Statistical analysis confirmed significantly different values of PCT in the analyzed time period in first group newborns with RDS and positive blood culture $p<0.001$The highest average values (42.37±43.59) were measured during admission with a subsequent sharp jump. Statistical analysis confirmed significantly different values of PCT in the analyzed time period in second group with RDS and negative blood culture $p<0.001$. The highest average values (42.37±43.59) were measured during admission with a subsequent sharp jump. There is statistically significant difference in average PCT between the two groups overtime ($p<0.05$).Statistical analysis confirmed significantly different values of PCT in the analyzed time period in first group newborns with RDS and positive blood culture with MV and BCPAP $p<0.001$. The highest average values (38.31±52.50) were measured in newborns with RDS and positive blood culture with MV and BCPAP during admission, with a subsequent sharp jump compared to newborns with RDS and positive blood culture with oxygen mask. Statistical analysis confirmed significantly different values of PCT in the analyzed time period in first group newborns with RDS and negative blood culture with MV and BCPAP $p<0.001$.The highest average values (36.35±42.51) were measured in newborns with RDS and positive blood culture with MV and BCPAP during admission, with a subsequent sharp jump compared to newborns with RDS and positive blood culture with oxygen mask. There is statistically significant difference in average PCT between the two groups overtime procedure (MV,BCPAP, OXYGEN MASK) ($p<0.05$).

CONCLUSION

Rapid treatment of sepsis is of crucial importance for survival of patients. Specific and rapid markers of bacterial infection have been sought for early diagnosis of sepsis. From our study we can conclude that PCT is promising sepsis markers in newborns with RDS, capable of complementing clinical signs and routine lab parameters suggestive of severe infection at the time of ICU admission. PCT measurement appears to be a better predictor to distinguish newborns with RDS and positive blood culture and newborns with RDS and positive blood

culture when compared to clinical sign and procedure (MV, BCPAP and OXYGEN MASK). Thus, our data raise the possibility that the addition of serum PCT to the standard work-up of critically ill patients with suspected sepsis could increase diagnostic certainty and improve patient management.

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Original scientific paper

THE ROLE OF PRO-INFLAMMATORY CYTOKINES IN INFLAMMATORY BOWEL DISEASES IN CHILDREN

Sonja Bojadzieva, Aco Kostovski, Aspazija Sofijanova, Olivera Jordanova, Filip Duma

PHI University Clinic for Children Diseases - Skopje.

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ABSTRACT

Objective: Inflammatory bowel disease (IBD), including ulcerative colitis (UC) and Crohn's disease (CD) are idiopathic chronic diseases of the gastrointestinal tract.The cytokines produced by T–lymphocytes, monocytes, intestinal macrophages, granylocytes, endothelial and fibroblast cells play a central role in the modulation of the intestinal immune defense. Cytokines with proinflammatory function which have main role in pathogenesis of disease are: Interleukin 1 (IL-1), Tumor necrosis factor alpha (TNF-α), IL-6, IL-8, IL-12. The aim of our study was to examine pro-inflammatory cytokines in patients with IBD and their correlation with phenotypic characteristics of disease. Methods:We have examined 46 children with IBD, (25 with CD and 21 with UC). Cytokines were determined with the ELISA (Enzyne-linked immunosorbent assay) method. Diagnosis was confirmed after the realisation of all diagnostic protocols provided by the European Society for Pediatric Gastroenterohepatology and Nutrition (ESPGHAN).Results: The IL-1, IL-6 and TNF- α values were increased in patients with CD and severe forms of disease. Correlation has been found between the phenotypic characteristics and the cytokines profile through increased TNF-α and IL-6 values in patients with CD with disease of terminal ileum, stenosis, fistulas and severe forms of IBD. Proinflammatory cytokines levels significantly decreased during therapy.Conclusion: Proinflammatory cytokines, especially the key cytokine TNF-α are very important in determing the disease activity, as well as in deciding when to implement biological therapy.

Key words: Cytokines, Inflammatory Bowel Disease, Crohn's disease, ulcerative colitis

INTRODUCTION

Inflammatory bowel disease (IBD), which includes ulcerative colitis (UC) and Crohn's disease (CD) is an idiopathic chronic disease of the gastrointestinal tract. Ulcerative colitis is a nonspecific chronic inflammation of the mucosa of the colon, while Crohn's disease can affect the entire gastrointestinal tract.The incidence of inflammatory bowel disease (IBD) ranges from 0.3 - 0.8% in the general world population [1-3]. It is believed that 20-30% of patients manifest the disease in childhood, adolescence and before the age of 18 [2-4] and only 5 % by the age of five [5].Although the disease can occur at any age, the peak occurrence of IBD ranges from 15 to 30 years of age, and the second, but less frequent between 50-70 years. The etiology and pathogenesis of UC and CD is still unknown, but the abundant research indicates simultaneous influence of the immunological, genetic, environmental factors and an imbalance between proinflammatory and antiinflammatory cytokines [6-8]. Recent studies suggest that the basic mechanisms of inflammation and tissue damage during IBD are too complex [9].

Immunopathogenesis of IBD is too complex and not yet fully explained, but there are several theories and mechanisms that partially indicate the possible occurrence of the disease.The cytokines produced by T –lymphocytes (T1 and T2), monocytes, intestinal macrophages, granylocytes, endothelial and fibroblast cells play a central role in the modulation of the intestinal immune defense. Cytokines with pro-inflammatory function which have main role in pathogenesis of disease are: Interleukin 1 (IL-1), Tumor necrosis factor alpha (TNF-γ), IL-6, IL-8, IL-12. Cytokines with pro-inflammatory function: Interleukin 1 (IL-1), tumor necrosis factor alpha

(TNF-á), IL-6, IL-8, IL-12, while the anti-inflammatory role cytokines are: IL-1 receptor antagonist, IL-4 IL-10 and IL-11 [10,11]. In CD, there is an imbalance between proinflammatory and antiinflamatory cytokines, particularly of complex receptor antagonist IL-1/IL-1 [12-14]. Inflammatory bowel disease is disrupts the integrity of the intestinal mucosa resulting in impairment of the function of the barrier which can lead to easier and increased passage of bacteria into the surrounding tissues and the bloodstream. Crohn's disease involves the Th1 T cell immune response [15], and the humoral immune response against bacteria. Inclusion criteria. The Porto ESPGHAN Criteria. According to the Porto criteria, clinically suspected IBD all children who have a history of persistent (≥ 4 weeks) or recurrent (≥ 2 episodes within six months), symptoms such as abdominal pain, diarrhea, rectal bleeding and reducing weight [3]. The classic triad (abdominal pain, diarrhea and body weight loss) are suspected to be affected by CD, as well as younger children that have mild lower abdominal pain and nonclasical onset of the disease. Other symptoms may include fever, failure to thrive, malnutrition, nausea and / or vomiting, psychiatric symptoms, arthropathy, erythema nodosum, amenorrhea, disturbed pubertal development or perianal disease. In particular, in clinical presentation of CD, extraintestinal symptoms that may represent a diagnostic problem may be dominant. Approximately 25-35% of patients with CD manifest extraintestinal symptoms, and in the pediatric population this may be the only dominant symptom, especially in patients with CD [2,3,16,17]. The existence of different phenotypical characteristics in IBD in adults and children indicates the need for prepearing additional criteria that will be used for children.For that reason, the ESPGHAN working group outlined the new guideline in 2005, the Porto criteria [3,16].The Porto criteria includes realization of endoscopy of the upper gastrointestinal tract (GIT) and it is important that it be implemented in all patients with CD, whether there is presence or absence of upper gastrointestinal symptoms in order to detect possible gastric or duodenal pathology, ulcers, but can also be obtained by biopsies [3]. The aim of our study was to examine pro-inflammatory cytokines in patients with IBD and their correlation with phenotypic characteristics of disease.

MATERIAL AND METHODS

In this study, we have examined 46 children with IBD, (25 with CD and 21 with UC) at the University Children's Hospital Skopje in the period of fifteen years (2003-2018y). In terms of gender distribution. 21 children were female and 25 male. The age of patients ranged from 4-20 years, main age was 10.6 years. The control group consisted of 40 healthy children, without anamnestic and clinical signs of IBD. Cytokines were determined with the ELISA (Enzyne-linked immunosorbent assay) method.

In the study from the cytokines profile, the following types of pro inflammatory cytokines were analyzed: TNF-γ, IL-1, IL-6. Diagnosis was confirmed after the realisation of all diagnostic protocols provided by the European Society for Pediatric Gastroenterohepatology and Nutrition (ESPGHAN).

Statistical analysis . Statistical analysis was performed on a personal computer (PS) using an adequate statistical program. Descriptive and analytical methods were used in the statistical processing of the results. ANOVA POST Hoz Test was used for multiple comparison of samplesThe level of specificity in accordance with international standards in biomedical sciences is 0.05 -0.01.

RESULTS

In our study we have examined total 46 patients (M:F=25:21), (25 with CD and 21 with UC) (figure 1).

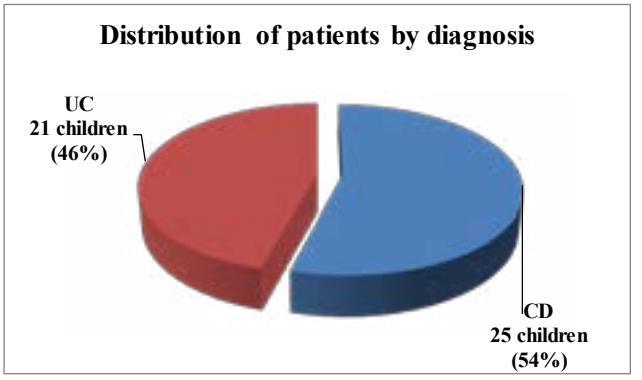

Figure 1 Distribution of patients by diagnosis.

In terms of age group, patients were divided into three age groups, younger than 8 years, 8–10 years, and older than 10 years (figure 2). In our study, 35 (76%) of all patients surveyed were older than 10 years.

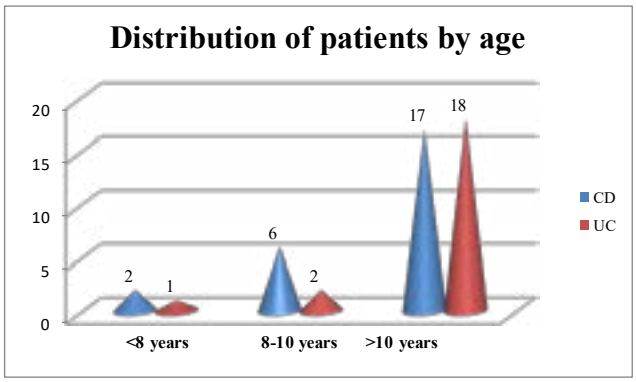

Figure 2. Distribution of patients by age divided into three age groups .

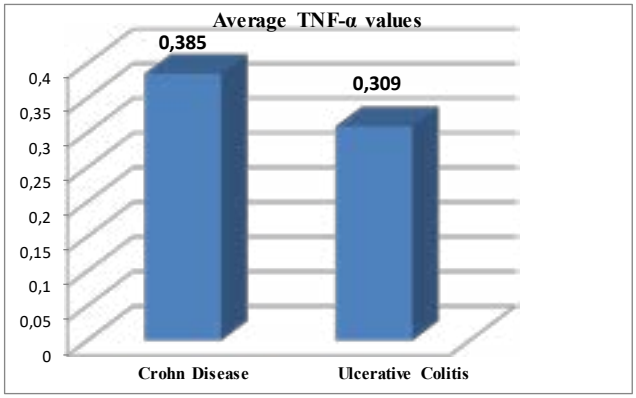

Figure 3. Average values of TNF-γ (pg/l) from patients with Crohn's Disease and Ulcerative Colitis.

Anova post Hoc Test, there is no statistically significant ($p>0.05$)

The diagnosis of inflammatory bowel disease is placed on the implementation of the diagnostic protocol "Porto criteria" by the European Society for Pediatric Gastroenterohepatology and Nutrition , including in it, despite clinical and laboratory investigations, and endoscopy of the upper gastrointestinal tract and flexible colonoscopic procedures, multiple biopsies and histopathological confirmation. According to the phenotypic characteristics of children with CB, we divided them into several groups (figure 4).

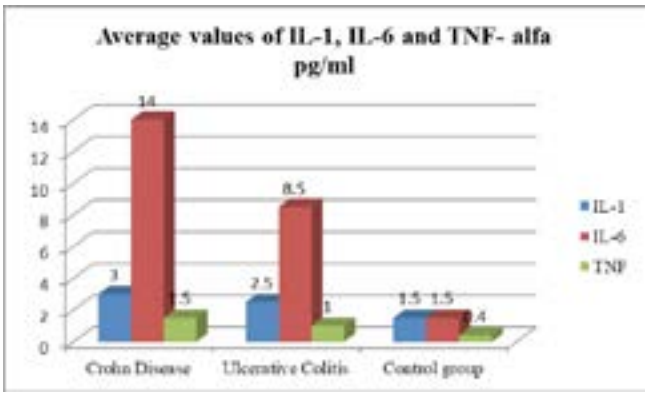

Figure 4 Average values of IL-1, IL-6 and TNF-alfa pg/ml

The Post-Hoc Test of multiple comparation showed that IL-1, IL-6 and TNF-γ values were statistically significant ($p<0.1$) increased in patients with CD. There were correlation between increased values of cytokines profile and the structural and fistulous phenotypic manifestations in children with CD.The IL-1, IL-6 and TNF-γ values were increased in patients with CD and severe forms of disease. Correlation has been found between the phenotypic characteristics and the cytokines profile through increased TNF-γ and IL-6 values in patients with CD with disease of terminal ileum, stenosis, fistulas and severe forms of IBD (figure 5). Pro-inflammatory cytokines levels significantly decreased during therapy.

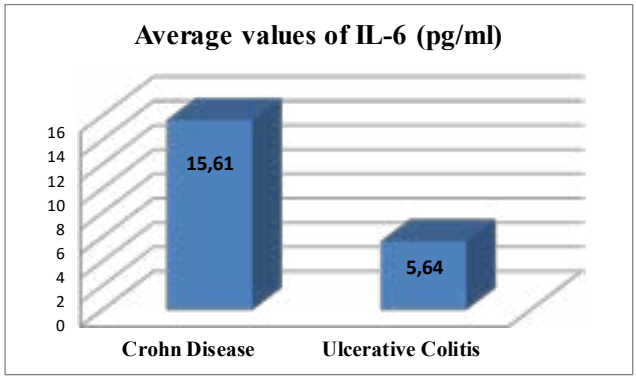

Figure 5 Average values of IL-6 (pg/ml) from patients with Crohn's Disease and Ulcerative Colitis. ANOVA Post Hoc Multiple Comparison Test was performed, which was statistically significant for Crohn's disease in relation to the group of patients with UC $p < 0.01$.Various phenotypic features of CD had different cytokine values. IL-6 elevated values are noteworthy, especially in stenosis and fistula forms of the disease (figure 6).

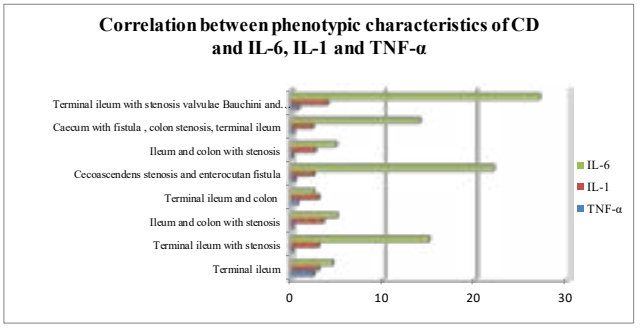

Figure 6 Correlation between phenotypic characteristics of CD and IL-6, IL-1 and TNF-γ

DISCUSSION

In our study of the total 46 patients, with CD were 25 (54%) children and 21 (46%) with UC. In terms of gender distribution 21 (36%) female and 25 (54%) male. With Crohn's Disease F:M=11:14 and UC F:M=10:11. Male gender was slightly elevated in CD as a as compared to some studies from Canada SAD and UK showing an increased incidence of male children with CD [18]. Gender distribution in our study was not statistical significant and not determine dominant incidence in one of the genders which is in correlation with data obtained in the literature [18,19].In terms of age group, patients were divided into three age groups, younger than 8 years were 3 (6.5%) children, from 8 to10 years were 8 (17.3%), and older than 10 years 35 (76%) Figure 2. Only 10 (24%) children were younger than 10 years which is in correlation with the data from the literature. Heyman, in his study shows that 47% of children were at the age 6-12 years old and 36.9% older than 13 years. It is believed that 20-30% of patients manifest the disease in childhood, adolescence and before the age of 18 (2-4) and only 5 % by the age of five [16, 20, 21].From clinical aspect, the intestinal manifestation of the disease was dominant 65% of the examined patients. Classic triad for Crohn's Disease (abdominal pain, diarrhea and weight loss), manifested 31% of patients.

Correlation between the mean TNF-γ values in CD and UC patients were not statistically significant. Elevated values of pro-inflamatory cytokines profil IL-1, Il-6 and TNF- γ in the severe and structural and fistulous phenotypic manifestations in children with CD would be explained by their direct role in disease inflammation, which is in correlation from literature data (2014 Porto [16]. This suggests that the immune mechanisms that play a role in the pathogenesis of the disease are different for UC and CD in the beginning and in the course of the disease and for the development of new therapeutic agents[16,22]. Revolutionary progress has been made in the treatment flow of patients with IBD using some TNF-γ antibodies. Nowadays, several types of anti TNF-γ antibodies approved for the treatment of refractory forms of CD and UC. This includes anti TNF-γ agent, infliximab, adalimumab, certolizumap adhesion molecule natalizumap. Infliximab is an IgG4 chimeric monoclonal antibody that targets the tumot necrosis factor alpha (TNF-γ). Randomized clinical trials have proven the effectiveness of drug application in heavy active luminal forms of CD and CD fistulas [23]. Infliximab is the first biological agent with proven efficacy through its clinical use. With the introduction of anti TNF-γ agents, the treatment of refractory forms of IBD has been changed. Clinical efficacy of anti TNF-γ suggests that cytokines have a powerful potential therapeutic ability in IBD [22,24] . It is approved for the treatment of fistulizing forms of CD and the UC, and in cases where the effect is not achieved with another form of therapy [25-28] .

CONCLUSION

Overall, phenotypic, serological and immunological aspects are key parameters and have an important role in the diagnosis and therapy in children with IBD. The implementation of the entire diagnostic protocol ESPGHAN .including clinical and laboratory investigations, and upper gastrointestinal endoscopy and flexible colonoscopic procedures, with multiple biopsies and histopathological confirmation is important in the diagnosis IBC in childhood.

We see their importance in the clinical and therapeutic monitoring of patients with IBD. Pro-inflammatory cytokines IL-1, Il-6 and TNF- γ, especially the key cytokine TNF-γ are very important in determine the disease activity, as well as in deciding when to implement biological therapy. Probably, in the future, even the most effective drugs will be replaced by the use of biological therapy .

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Original scientific paper

TREATMENT OF NERVES INJURIES ASSOCIATED WITH PEDIATRIC SUPRACONDYLAR HUMERAL FRACTURES-OUR EXPERIENCE

Todorovic L[1], Kamiloski M[1], Memeti Sh[1], Cokleska N[1], Mikjunovikj Lj[2], Racaj A[1]

[1]University Clinic for Pediatric Surgery, Skopje

[2]University Clinic for Traumatology, Orthopedics, Anesthesiology, Reanimation, Intensive Care and Emergency Center, Skopje

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ABSTRACT

Background: Supracondylar fractures of the humerus are the most common type of elbow fracture in children. Nerve injury is the most common complication. Our study aims to determine the risk of traumatic nerve injury associated with supracondylar fracture, to compare the risk in flexion-type compared with the extension type fractures, and to note any iatrogenic nerve injury after pin fixation.

Material and methods: The target group in this study is consisting of pediatric population (90 cases) presented with a displaced supracondylar fracture of the humerus (Gartland type II and III). All patients were treated at the University Clinic of Pediatric surgery-Skopje in the period of time from 2010 to 2020. The children were 2 to 14 years old. All of them were evaluated for nerve injury before and after the operation in order to determine if the nerve injury is traumatic or iatrogenic. Type of fracture, flexion or extension type was noticed.

Results: According to the data from 90 children treated for displaced supracondylar fracture of the humerus, traumatic nerve injury occurred in 9 patients (10%). 4 (44,4%) of the referred nerve injuries involved the ulnar nerve. All ulnar nerve injuries were result of a flexion type supracondylar fracture. 3 (33,3%) injuries involve the median nerve. All of them were result of an extension type of supracondylar fracture. The anterior interosseous nerve, as a branch of a median nerve was injured in all 3 cases. 2 (22.2%) were injuries of the radial nerve, all of them as a result of an extension type of supracondylar fracture.

Conclusions: According to our results, among all nerve injury associated with supracondylarar fractures, ulnar nerve injury predominates. Ulnar neuropathy occurred most frequently in flexion-type injuries. All 9 neuropathies were directly related to the injury itself and were noted at the time of admission. Spontaneous neurological recovery occurred in all 9 patients at a mean of 7.7 months (3 to 15) after injury.

BACKGROUND

Supracondylar humerus fractures (SCHF) are the most common type of elbow fractures in children. Extension-type represents approximately 96% to 98% of all pediatric supracondylar fractures of the humerus. Flexion-type represents approximately 2% to 4%.

As the median and radial nerves lie anterior to the supracondylar humerus region they are at a great risk for injury, primarily as a result of trauma: stretching, piercing or impinging at the fracture ends or being entrapped between two fracture fragments (traumatic or primary nerve injury) and the ulnar nerve injury is usually secondary to treatment (iatrogenic or secondary nerve injury).

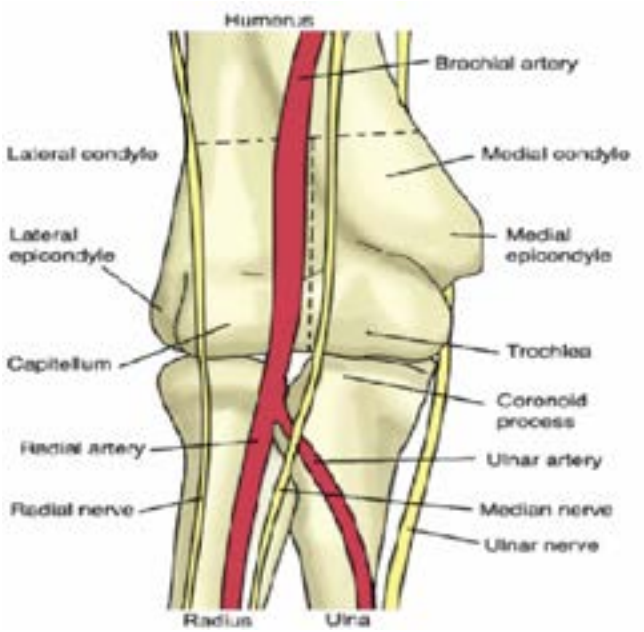

Image 1: Anatomy of the arm nerves

The incidence of primary nerve injury in SCHF is 7 – 10% and about 6% for secondary nerve injury. In the extension-type of SCHF, postero-medial displacement of distal fragment usually causes injury to the radial nerve and postero-lateral placement is more likely to cause median nerve injury. In the flexion-type of SCHF, the ulnar nerve injury predominates.

The standard operative treatment for displaced extension-type and flexion-type supracondylar humeral fractures is reduction followed by percutaneous pin fixation. The use of a medial pin may unnecessarily risk ulnar neurapraxia, whereas the use of lateral pins alone may demonstrate less biomechanical strength. Of all complications associated with supracondylar humeral fracture, nerve injury is the highest. The anterior interosseous nerve is at greatest risk of . The ulnar nerve is the most often injuried nerve in flexion-type fractures.

The treatment of nerve injury varies greatly depending on the severity and underlying cause. In either case, the goal of treatment is to manage or relieve symptoms and correct the underlying cause when possible.

Symptoms of a nerve injury include pain, numbness, and loss of muscle strength and coordination in the arm and hand.

Common symptoms of nerve injury are: burning feeling in hand, arm or finger, increased arm numbness or tingling while typing or writing, increased finger numbness or tingling while typing or writing, “pins and needles” sensation (prickling) in the hand, arm or fingers, tingling or other unusual sensations in the hands, weakness (loss of strength) in the hand, arm or fingers.

Image 2:

A: extension-type supracondylar fracture B: flexion-type supracondylar fracture

AIM

The purpose of our study was to determine the risk of traumatic neurapraxia in extension-type as compared with that of flexion-type supracondylar fractures and to perform subgroup analysis to assess the risk of iatrogenic neurapraxia caused by pin fixation.

MATERIAL AND METHODS

The target population in this study is consisting of pediatric population presented with a displaced supracondylar fracture of the humerus. All patient are treated at the University Clinic of Pediatric surgery-Skopje in the period of time from 2009 to 2019. The children are at age 2 to 14 years old. All of them were evaluated for nerve injury before and after the operation in order to determine if the nerve injury is traumatic or iatrogenic.

Children with other injuries to the elbow, such as condylar fractures and physeal injuries, were excluded from the study.

We identified 90 patients with 90 fractures and 9 nerve injuries. There were 50 boys and 40 girls with a mean age of 8.1 years. The mechanism of injury in 47 patients was a fall from a height, 27 during a sport activity and 16 as a result of a traffic accident. All the fractures were closed and displaced. The fractures were classified using the Gartland classification. 54 fractures were classified as Gartland type II and 36 as Gartland type III. 4 fractures had been treated by closed reduction and above-elbow casting, 70 by closed reduction and percutaneous cross Kirschner (K) wire fixation and 16 by formal open reduction and cross K-wire fixation.

The operative findings and details of the surgical procedure were recorded. Post-operative follow-up was carried out at six weeks, three months and subsequently every three months until full recovery. The clinical outcome at the last follow-up was assessed according to the criteria of Birch, Bonney and Wynn Parry13 and graded as excellent, good, fair or poor.

RESULTS

We report for 9 patients (10%) with traumatic nerve injury after a supracondylar humerus fracture. There was no a case of iatrogenic nerve injury. 4 (44,4%) of the referred nerve injuries involved the ulnar nerve. All ulnar nerve injuries were result of a flexion type supracondylar fracture.

3 (33,3%) injuries involve the median nerve. All of them were result of an extension type of supracondylar fracture. The anterior interosseous nerve, as a branch of a median nerve was injured in all 3 cases. 2 (22.2%) were injuries of the radial nerve, all of them as a result of an extension type of supracondylar fracture. All 9 neuropathies were directly related to the injury itself and were noted at the time of presentation. There was no case of compartment syndrome. Spontaneous neurological recovery occurred in all 9 patients at a mean of 7.7 months (3 to 15) after injury, with 8 patients having an excellent and 1 a good outcome. Surgical exploration wasn't indicated in the presented cases.

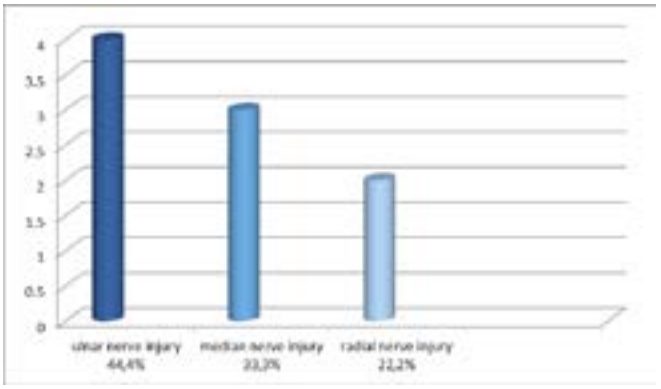

Table 1: Incidence of nerve injury.

DISCUSSION

Nerve injuries after supracondylar humeral fractures occur primarily due to tenting or entrapment of the nerve on the sharp proximal humeral fragment. The median or anterior interosseous nerves are most commonly damaged by extension-type injuries, while the less common flexion-type injuries affect the ulnar nerve more often.

Most studies in the orthopaedic and traumatology literature have reported a good to excellent prognosis for nerve injuries associated with supracondylar fractures in children.

Birch and Achan reported 118 cases of repaired nerve lesions "associated with fractures and dislocations at the elbow displayed at operation", of which 91 were in conjunction with supracondylar fractures. Of these, 43 involved the median, 35 the ulnar and 13 the radial nerve. They specified that 22 of the 91 injured nerves associated with supracondylar fractures were found to be entrapped within the fracture or impaled on a bone spike, while the remainder were compressed by swelling or fibrosis at or distal to the fracture, the latter showing uniformly good recovery after decompression. No reference was made to the need for grafting.

As pointed out by Lyons et al. the observation of nerve injury post-operatively does not imply that it occurred as a result of the intervention – it is possible that it had simply not been recognised at the time of presentation. Similarly, the trauma associated with the reduction may injure the nerve irrespective of whether percutaneous wiring techniques are used.

CONCLUSION

Nerve injuries associated with supracondylar humerus fracture is a frequent occurrence. The surgeon should have high degree of suspicion about it and a careful pre-operative clinical examination is needed to report it. Median nerve injury is the most common nerve injury associated with extension type of fractures. Ulnar nerve injury is the most common nerve injury in flexion type fractures. All of the nerve injuries were neuropraxias and they spontaneously resolve by 7,7 months (average).

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Original scientific paper

INCIDENCE OF POSTPARTUM HAEMORRHAGE IN "QUEEN GERALDINE" UNIVERSITY HOSPITAL FROM 2010-2019

Demaliaj, E. ; Ismaili, B. ; Elmasllari, A. ; Balla, F.

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ABSTRACT

Introduction: Postpartum haemorrhage (PPH) is defined as a blood loss of 500 mL or more within 24 hours after birth.

Objectives: Demonstrating the incidence of PPH, the most common cause of it, the incidence of emergency hysterectomy, the mean age of women complicated with postpartum haemorrhage, maternal and newborn morbidity and mortality rate.

Materials and Methods: We retrospectivily reviewed data from registry in "Queen Geraldine" University Hospital from January 2010 to December 2019. There were found 689 women diagnosed with postpartum haemorrhage.

Results: The incidence of postpartum haemorrhage was 1.64% in 2010, 1.51% in 2011, 0.54% in 2012, 1.07% in 2013, 1.04% in 2014, 0.87% in 2015, 0.94% in 2016, 0.73% in 2017, 0.76% in 2018, 1.05% in 2019. The most common cause of postpartum haemorrhage is placenta previa with 52.24% of all patients with PPH. Maternal mortality rate is 0. Emergency hysterectomy is performed in 7.54% of patients with PPH. The mean age range of women with PPH is 25-34 years old. There were 21% preterm births and 7.6% of preterm babies died after birth.

Conclusion: The highest incidence in the last 10 years in Queen Geraldine University Hospital was in 2010, 1.64%. The most common cause of PPH is placenta previa with 52.24% of PPH cases. Placenta previa was also the most common pathology complicated with hysterectomy. The preterm births were in 32-33 week of pregnancy and 7.6% of these babies died after delivery.

INTRODUCTION

Postpartum Haemorrhage (PPH) is commonly defined as a blood loss of 500 ml or more within 24 hours after birth. PPH is the leading cause of maternal mortality in low-income countries and the primary cause of nearly one quarter of all maternal deaths globally. Most deaths resulting from PPH occur during the first 24 hours after birth: the majority of these could be avoided through the use of prophylactic utero-tonics during the third stage of labour and by timely and appropriate management (1,3).

It is verified in approximately 5-17% of cases, while in about 1.1% post-partum massive haemorrhage occurs, defined by a loss of over 1000 ml or by such a blood loss that makes it necessary to transfer a certain amount of blood over 10 units of blood / 24 hours.

It occurs with a frequency ranging from 5-22% of the total number of births and occurs in a mortality ratio equal to 1: 1000 / 5: 5000 births in developing countries, equal to 3-5 cases per 1,000,000 births in industrialized countries (2,8).

Causes of postpartum haemorrhage include uterine atonia, lacerations, placentar retension, placenta acreta,uterine inversion coagulopathy which includes inherited coagulopathy that can lead to amniotic emboly, disruption of placenta or severe preeclampsia.

Uterine atony is the most common cause of PPH, but genital tract trauma (i.e. vaginal or cervical lacerations), uterine rupture, retained placental tissue, or maternal coagulation disorders may also result in PPH. Although the majority of women who experience PPH

complications have no identifiable clinical or historical risk factors, grand multiparity and multiple gestation are associated with an increased risk of bleeding after birth. PPH may be aggravated by pre-existing anaemia and, in such instances, the loss of a smaller volume of blood may still result in adverse clinical sequelae.

OBJECTIVES

This study aims to document the incidence of PPH in the last ten years in "Queen Geraldine" University Hospital, the causes of PPH, maternal and fetal outcome. We have also compared our data with different studies in Europe and worlwide.

METHODS AND MATERIALS

This is a retrospective descriptive study carried out in "Queen Geraldine" University Hospital Tirana, Albania. Data were obtainde fom labor ward birth registry from January 2010 to December 2019. The case notes were retrieved and the demographic, clinical, and outcome data were gathered. The data included the age of women, cause of postpartum haemorrhage, age of pregnancy, baby outcome, complications ecc. There were found 689 women diagnosted with postpartum haemorrhage in the last 10 years.

RESULTS

There were 66976 deliveries from January 1, 2010 to December 31, 2019. There were 689 cases of PPH during the study period. The incidence of PPH was 1.03 %. The spread of incidence year by year is: 1.64% in 2010, 1.51% in 2011, 0.54% in 2012, 1.07% in 2013, 1.04% in 2014, 0.87% in 2015, 0.94% in 2016, 0.73% in 2017, 0.76% in 2018, 1.05% in 2019. The highest incidence in the last 10 years in "Queen Geraldine" University Hospital was in 2010, 1.64%. The mean age range of women was 25-34 years old. Most of the cases have had lower segment cesarian section. Luckily the mortality rate is 0. The mean gestational age for preterm births was 32.6 weeks gestation.The most common cause of PPH in our hospital is placenta previa with 52.24% of PPH cases. Placenta previa was also the most common pathology that ended in hysterectomy. 7.54% of all cases were complicated with hysterectomy. 144 of cases were preterm births, which means 4.2 % of all preterm births in the last ten years (3426). 7.6% of preterm cases died after delivery.

CONCLUSIONS

The incidence in the last 10 years in "Queen Geraldine" university hospital was 1.03 %, lower than that reported elsewhere in similar setting in the literature. This study is importmant because it reports the incidence and the common causes of postpartum haemorrhage. 52.24 % of all cases had placenta previa as the cause of PPH. This is different from other countries (9) who reported uterine atony as the most common cause of PPH. It is important to emphasize that in ten years the maternal mortality rate was 0%, and a good maternal and newborn outcome with a low maternal morbidity rate and a low fetal mortality rate (7.6% of preterm cases or 1.54% of PPH cases).

DISCUSSIONS

The incidence of PPH in "Queen Geraldine" Hospital in Tirana was 1.03%. The most common cause of postpartum haemorrhage was placenta previa. According to WHO statistics and other countries in development, uterine atony is the most frequent cause. I have compered this study with a systematic review and meta-analyze from 1148 obtained studies and 11 included meta-analyzes, published in 2017 in PubMed (5,6,7) .

Several studies have estimated the incidence of PPH among pregnant women with placenta previa in different countries. However, there was a wide variation in the results of the conducted studies. The incidence of PPH was reported to be approximately 18% in a Canada population-based retrospective cohort study among 308 cases of placenta previa, 21% in a Italy retrospective singleton pregnancies cohort between January 2003 and August 2008 and 59% in a USA retrospective singleton births cohort that occurred between 1976 and 2001 among the 230 placenta previa women(4,5,6). So the statistics from our study can be compared with studies in other developed countries in world.

Future studies should involve the classification, other risk factors of PPH, prevention and treatment.

The results will be important for informing efforts to prevent, treat, and identify causes of PPH among pregnant women with placenta previa and would be contribute to the planning and implantation of relevant public health strategies.

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Original scientific paper

КЛИНИЧКА ПРИМЕНА НА РАЗЛИКИТЕ ВО БАЗИЧНИТЕ КАРАКТЕРИСТИКИ КАЈ ПАЦИЕНТИ КАЈ КОИ СЕ ИЗВЕДУВА АНГИОГРАФСКИ И ИВУЗ-ВОДЕНО СТЕНТИРАЊЕ НА ДОЛГИ ЛЕЗИИ

Никола Бакрачески[1], Виолета Мојсовска[1], Резеарта Елези[2], Невзат Елези[3], Никола Оровчанец[4]

[1]Специјална болница за превенција, лекување и рехабилитација на кардиоваскуларни заболувања – Охрид

[2]Клиничка болница - Тетово

[3]Државен Универзитет - Тетово

[4]Институт за епидемиологија и биостатистика, Скопје

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АБСТРАКТ

Вовед: Повеќе клинички студии покажаа дека Перкутаните Коронарни Интервенции (ПКИ) водени со Интраваскуларен Ултразвук (ИВУЗ) водат кон подобрување на краткорочните и долгорочните исходи во однос на ангиографски водените ПКИ. Голем број студии ја докажаа клиничката важност и влијанието на базичните карактеристики, во однос на успешноста на интервнецијата и можните компликации од истата.

Цели: Компарација на базичните клинички карактеристики кај две одделни групи на пациенти, кои ќе послужат како основен предиктор на исходот од ИВУЗ воденото и ангиографски воденото стентирање на долги коронарни лезии третирани со зотаролумус-обложени стентови, во тек на едногодишно следење на пациентите.

Материјал и методи: Во студијата се вклучени 60 пациенти со ангиографски докажана коронарна артериска болест за перкутана коронарна интервенција: стентирање на долга коронарна лезија. Пациентите се поделени во две групи: I група: Ангиографски-водено стентирање и II група: ИВУЗ-водено стентирање.

И кај двете групи ќе биде иследувана застапеноста на следните базични клинички карактеристики: возраст, пол, хипертензија, хронична бубрежна инсуфициенција (ХБИ), дијабет, иперхолестеролемија, пушење, прележан миокарден инфаркт (МИ), ретходна перкутана коронарна интервенција (ПКИ), претходен коронарен артериски бајпас (CABG), акутен коронарен синдром (АКС), истисна фракција на левата комора (ЕФ);

Заклучок: Евидентирањето и статистичката обработка на базичните карактиеристики на пациентите ќе ни овозможат подобро разбирање на настаните кои би ги очекувале од самата интервенија и ќе ни даде можност за максимална подготвеност за справување со компликациите кои би се јавиле.

Клучни зборови: Базични карактеристики; ангиографски водените ПКИ; ИВУЗ водени ПКИ; долги лезии;

ВОВЕД

Иако коронарна ангиографија претставува златен стандард и е широко користена метода за дијагностицирање на корорнарна артериска болест и за водење на перкутана коронарна интервенција (ПЦИ), кога се работи за дифузни долги коронарни лезии сè уште останува предизвик затоа што преваленцата на интензивна рестеноза и тромбоза на стент останува висока во споредба со кратките коронарни лезии.

Кај овие пациенти интраваскуларниот ултразвук (ИВУЗ) може да биде корисна алатка за да добиеме информации за разбирање на коронарната артериска болест преку нејзиниот капацитет да ни овозможи визуелизација на ѕидот на крвниот сад и неговата интеракција со коронарните материјали во живо. Како дополнување ИВУЗ игра клучна улога во полето на перкутаните коронарни интервенции, прикажувајќи ни ги недостатоците од аплицирањето на стентовите, што следствено води кон подобрување на техниките на стентирање. Овој исчекор драматично ги намали перипроцедуралните компликации како и значајно намаливање на MACE компликации кај пациенти кај кои се употребува ИВУЗ споредено со пациети кај кои е направена само коронарна ангиографија.

Токму импактот на базичните клинички карактеристики кај пациентите кај кои се изведува коронарна ангиографија или ИВУЗ водена интервенција, има значајна улога во предвидување на текот на интервенцијата, очекуваниот резултат и можните компликации во тек на интервентиот и постинтервентниот период.

ЦЕЛ

Компарација на базичните клинички карактеристики кај две одделни групи на пациенти, кои ќе послужат како основен предиктор на исходот од ИВУЗ воденото и ангиографски воденото стентирање на долги коронарни лезии третирани со зотаролумус-обложени стентови, во тек на едногодишно следење на пациентите.

МАТЕРИЈАЛ И МЕТОДИ

Изведена е проспективна студија во Специјална болница за превенција, третман и рехабилитација на за кардиоваскуларни заболувања "Св.Стефан" – Охрид во траење од една година. Во студијата се вклучени 60 пациенти со ангиографски докажана коронарна артериска болест за перкутана коронарна интервенција: стентирање на долга коронарна лезија. Пациентите се поделени во две групи: I група: Ангиографски-водено стентирање и II група: ИВУЗ-водено стентирање. Пациентите ќе бидат вклучени доколку имаат неостијална стеноза на коронарната артерија, поголема или еднаква на 20 mm во должина, со референтен дијаметар кој ќе дозволи имплантација на стентови со дијаметар ≥2.0 mm, без инволвираност на сигнификантна бочна гранка (дијаметар ≥2.0 mm). Исклучувачки критериуми ќе бидат: акутен миокарден инфаркт, кардиоген шок, ЛВЕФ <25%, напредната тешка валвуларна мана, напредната/тешка хронична бубрежна болест, крвавечки улкус на ГИТ, постоење на тотална оклузија, TIMI <3 по стентирањето, постоење на контраиндикација за користење на двојна антиагрегациона терапија (ацетил-салицилна киселина+клопидогрел).

Во основа кај двете групи ќе биде иследувана застапеноста на следните базични клинички карактеристики:

- Возраст
- Пол
- Хипертензија
- Хронична бубрежна инсуфициенција (ХБИ)
- Дијабет
- Хиперхолестеролемија
- Пушење
- Прележан миокарден инфаркт (МИ)
- Претходна перкутана коронарна интервенција (ПКИ)
- Претходен коронарен артериски бајпас (CABG)
- Акутен коронарен синдром (АКС)
- Истисна фракција на левата комора (ЕФ);

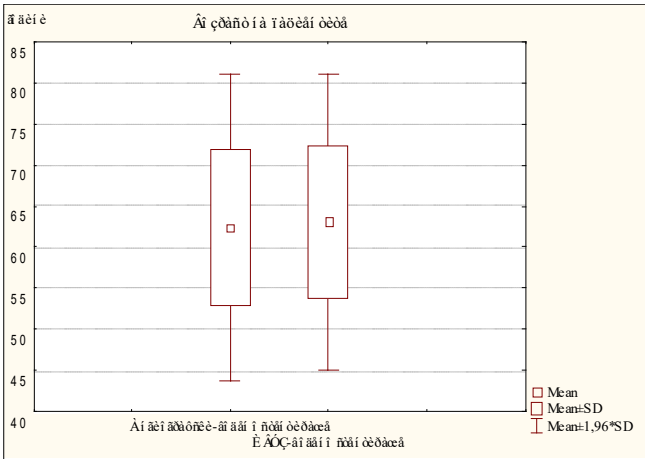
СТАТИСТКА

Анализата на податоците изведена е во статистички програми Statistica 7.1 for Windows и SPSS Statistics 23.0

РЕЗУЛТАТИ

Базичните клинчки карактеристики се евидентираа кај секој пациент од групата на ангиографски-водено стентирање и групата со ИВУЗ-водено стентирање. Кај 30 пациенти кај кои е изведено ангиографски-водено стентирање, возраста варира во интервалот 62,33±9,53 години; ±95,00%CI: 58,78-65,89; минималната возраст изнесува 46 години, а максималната возраст изнесува 79 години, додека кај 30 пациенти кај кои е изведено ИВУЗ-водено стентирање, возраста варира во интервалот 63,03±9,21 години; ±95,00% CI: 59,59-66,47; минималната возраст изнесува 45 години, а максималната возраст изнесува 77 години.

Графикон 1: Дескриптивна статистика за возраста на пациентите



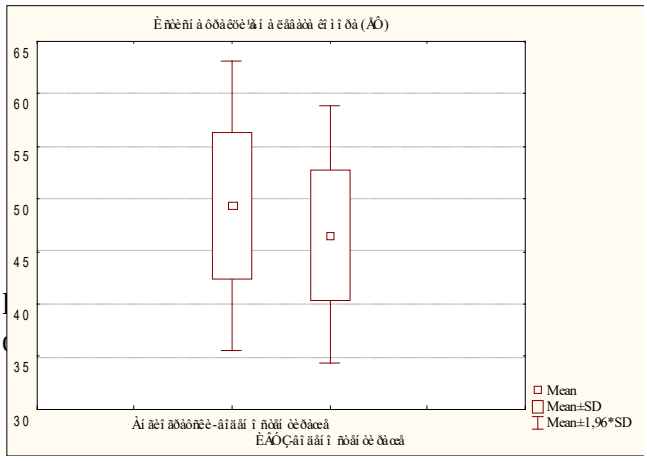
За t= -0,29 и p>0,05(p=0,77) пациентите кај кои е изведено ИВУЗ-водено стентирање имаат незначајно поголема возраст од пациентите кај кои е изведено ангиографски-водено стентирање (табела 1.1).

Табела 1.1 Разлика / Возраст на пациентите

Variable	Mean АВИ	Mean ИВУС	t-value	df	p	Valid N АВИ	Valid N ИВУС	Std.Dev. АВИ	Std.Dev. ИВУС
Возраст	62,33	63,03	-0,29	58	0,77	30	30	9,53	9,21

АВИ / Ангиографски-водено стентирање; ИВУС / ИВУЗ-водено стентирање

Во однос на застапеноста според пол на пациентите, од 30 пациенти кај кои е изведено ангиографски-водено стентирање, 10(33,30%) се жени а 20(66,70%) се мажи, а од 30 пациенти кај кои е изведено ИВУЗ-водено стентирање, 4(13,30%) се жени а 26(86,70%) се мажи. За Pearson Chi-square=3,35 и p>0,05(p=0,13) / Monte Carlo Exact Sig.(2-sided) нема значајна разлика помеѓу двете групи на стентирани пациенти земајќи ја во обзир дистрибуцијата на пациентите по пол. Анамнестички податок за дијагностицирана и третиерана хипертензија од 30 пациенти кај кои е изведено ангиографски-водено стентирање, 6(20,00%) пациенти немале хипертензија а, 24(80,00%) пријавија претходно дијагностицирана хипертензија и во групата на ИВУЗ-водено стентирање од 30 пациенти, 1(3,30%) нема хипертензија, а 29(96,70%) се со претходно дијатностицирана хипертензија на редовна антихипертензивна терапија. Во прикажаната кростабулација во релацијата група хипертензија за Fisher's Exact Test p>0,05(p=0,10) / Monte Carlo Exact Sig.(2-sided) нема значајна разлика помеѓу двете групи на стентирани пациенти во однос на присуството на хипертензија. Од резултатите кои се однесуваат на пушење кај стентираните пациенти и во двете групи (ИВУЗ-водено стентирање и ангиографски водена интервенција) регистрирани се еднаков број на пациенти, односно по 17(56,70%) не пушеле ,а 13(43,30%) се пушачи, со кростабулација во релацијата група пушење за Pearson Chi-square=1,07 и p>0,05(p=0,44) / Monte Carlo Exact Sig.(2-sided), без значајна разлика помеѓу двете групи на стентирани пациенти. Во групата на ангиографски водена интервенција евидентирани се 18(60,00%) пациенти кои не дадоа анамнестички податок за претходен миокарден инфаркт, а кај 12(40,00%) пациенти е дијагностициран претходен миокарден инфаркт, без значајна разлика помеѓу двете групи на стентирани пациенти во однос на присуството на претходен миокарден инфаркт, Pearson Chi-square=0,07 и p>0,05(p=1,00) / Monte Carlo Exact Sig. (2-sided). Последователно со извшена перкутана коронарна интервенција (ПКИ) во ангиографски воденатa група од 30 пациенти, кај 17(56,70%) е направена ПКИ, а 13(43,30%) не даваат податок за претодна ПКИ и во групата на ИВУс-водено стентирање, 22(73,30%) без претодна ПКИ, а 8(26,70%) пациенти претходно се подложени на ПКИ. По статистичка обработка на дадените податоци нема значајна разлика помеѓу двете групи на стентирани пациенти во однос на ПКИ (Pearson Chi-square=1,83 и p>0,05(p=0,28) / Monte Carlo Exact Sig. (2-sided). Според податоците на застапеност на ХБИ во групата на ангиографски-водено стентирање, 29(96,70%) немале ХБИ а 1(3,30%) имал ХБИ, додека во групата кај ИВУЗ-водено стентирање, 29(96,70%) немале ХБИ а 1(3,30%) имал ХБИ. Во однос на претходен коронарен артериски бајпас (CABG) во групата на ангиографски-водено стентирање, 29(96,70%) пациенти немаат претоден CABG, а 1(3,30%) пациент дава анамнестички податок за претходна хируршка реваскуларизација на миокардот (CABG), а во групата на ИВУЗ водена ангиографија сте 30 пациенти се без претходен CABG. Во прикажаната кростабулација во и во релацијата група ХБИ и во релацијата група CABG за Fisher›s Exact Test p>0,05(p=1,00) / Monte Carlo Exact Sig.(2-sided) нема значајна разлика помеѓу двете групи на стентирани пациенти. Од резултатите кои се однесуваат на акутен коронарен синдром (АКС) од 30 пациенти кај кои е изведено ангиографски-водено стентирање, 25(83,30%) пациенти не е евидентиран АКС, а 5(16,70%) пациенти се со АКС, додека во групата со ИВУЗ-водено стентирање, 27(90,00%) од пациентите немаат АКС, а 3(10,00%) даваат анамнестички податок за АКС. Во однос на иститсната фракција на левата комора (ЕФ), дескриптивната статистика евидентира кај 30 пациенти кај кои е изведено ангиографски-водено стентирање, ЕФ варира во интервалот 49,33±7,04 %; ±95,00%CI: 46,71-51,96; минималната вредност изнесува 35 % а максималната вредност изнесува 60 %, а од 30 пациенти кај кои е изведено ИВУЗ-водено стентирање, ЕФ варира во интервалот 46,57±6,23 %; ±95,00%CI: 44,24-48,89; минималната вредност изнесува 30 % а максималната вредност изнесува 60 %.



За Z= 1,35 и p>0,05(p=0,18) пациентите кај кои е изведено ангиографски-водено стентирање (АВИ) имаат незначајно поголема ЕФ од пациентите кај кои е изведено ИВУЗ-водено стентирање (табела 2.1).

Табела 2.1 Разлика / Истисна фракција на левата комора (ЕФ)

Variable	Rank Sum АВИ	Rank Sum ИВУС	U	Z	p-level	Valid N АВИ	Valid N ИВУС
ЕФ (%)	1006,50	823,50	358,50	1,35	0,18	30	30

АВИ / Ангиографски-водено стентирање; ИВУС / ИВУЗ-водено стентирање

ДИСКУСИЈА

Оваа студија ќе ја потврди користа и предноста на темелната обработка на базичните податоци кај пациентите кои ќе подлегнат на ИВУЗ-воденото стентирање на долги лезии и ангиографски-воденото стентирање , потенцирајќи ја зависноста на раните и доцните клинички исходи од употребата на овие податоци и во двете групи на пациенти. Тоа ќе доведе до подобро разбирање причините кои се резултат на разликите во базичните податоци кај одредена група на пациенти, а кои придонесуваат за зголемување, односно намалување на успешноста на интервенцијата, разлика во однос на очекуваниот резултат и можната појава на непредвидени комликации при изведување на коронарната ангиографија без и со ИВУС проценка.

Имајќи ги во предвид статистичките разлики кои ги евидентиравме во однос на базичните карактеристики кај нашите пациенти, планот за припрема и третман на пациентот во прединтервентниот, интервентниот и постинтервентниот период ќе биде прилагоден врз основа на групата во која е евидентиоран пациентот, а ќе биде базирана врз нашето претходно искуство со можни компликации и студии со кои е потврдена корелацијата помеѓу одреден ризик фактор и очекуваните компликации од коронарна интервенција.

Оваа студија претставува предиктор на текот на интервенцијата, мајорните несакани срцеви збиднувања (MACE) кои би ги очекувале при изведување на коронарна ангиографија и ИВУЗ водено стентирање, која ќе ја очекуваме во групите на пациенти кај кои е евидентирана значајна статистичка разлика во податоците, во нашата студија тоа се групите на хиперлипидемија и срцева слабост.

ЗАКЛУЧОК

Фокусот на современата интервентна кардиологија се пренесе кон подобрувањето на безбедноста на коронарните интервенции, како на ангиографски водените, така и на ИВУЗ водени интервенции. Токму евидентирањето и статистичката обработка на базичните карактиеристики на пациентите ќе ни овозможат подобро разбирање на настаните кои би ги очекувале од самата интервенија и ќе ни даде можност за максимална подготвеност за справување со компликациите.

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Profesional paper

ДЕГЕНЕРАТИВНО ЗАБОЛУВАЊЕ НА ЦЕРВИКАЛНИОТ СЕГМЕНТ ОД ‘РБЕТОТ КАЈ ПАЦИЕНТИ СО ЦЕРВИКОБРАХИЈАЛЕН СИНДРОМ

Јаневски Петар[1], Митреска Н[1], Арсовска А[2], Јаневски Г[3]

[1]Универзитетски институт за радиологија, Скопје, Р.С.Македонија
[2]Универзитетска клиника за неврологија, Скопје, Р.С.Македонија
[3]Универзитетска клиника за гастроентерохепатологија, Скопје, Р.С.Македонија

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АБСТРАКТ

Вовед: Една од главните причини за рефракторна вратна болка е дегенеративното заболување на цервикалниот сегмент од `рбетот. Наша цел е да го прикажеме типот на дегенеративното заболување на цервикалниот сегмент од `рбетот кај овие пациенти.

Материјали и методи: Студијата е аналитичка-трансверзална студија во која беа користени МР прегледите на цервикалниот `рбет и податоците од прашалниот дизајниран за оваа студија. Фокусната група се состои од 98 испитаници на возраст од 35-70 год. со рефракторна вратна болка.

Резултати: Нашата студија покажа дека кај 77 испитаници постои надув на еден или повеќе интервертебрални дискови додека кај 50 испитаници резултатите од МР на цервикалниот сегмент од ‘рбетот покажаа дека постои протрузија на еден или повеќе интервертебрални дискови. Ваквиот наод незначајно е асоциран и со трауматска повреда на вратот (Chi-square=0,54 df=1 p=0,46).

Заклучок: Надув на интервертебрален диск на цервикалниот сегмент од ‘рбетот како патолошка промена е чест кај симптоматските пациенти и се регистрира кај 78,57% од испитаниците. Од друга страна појавата на дискус херниј не е толку честа и се јавува кај нешто повеќе од половина од испитаниците (51,02%).

Клучни зборови: МР, надув, дискус херниј, рефракторна вратна болка, `рбет.

ВОВЕД

Здравјето е еден од најважните елементи и атрибути на нашиот живот, предуслов за извршување на секојдневните активности и водење на среќен живот воопшто. Во 1948 година СЗО го формализира модерното разбирање на здравјето, па истото го дефинира како: „Здравјето е состојба на целосна физичка, психичка и социјална благосостојба, а не само отсуство на болест и инвалидитет”[1]. Болести на современиот живот се незаразните состојби кои станаа водечка причина за морбидитет и морталитет во развиените земји. Ова епидемиолошко поместување сé повеќе зема замав и во земјите во развој[2]. Болката во вратот е многу честа појава. Кај скоро 70% од популацијата се јавува болка во вратот во некој период од животот. Анамнезата е од голема помош во диференцијацијата на различната патологија на цервикалниот ‘рбет. Повеќето испитаници со болка вовратот имаат отсуство на неуролошки симптоми при неуролошки преглед како резултат на бенигна болка во вратот за која не е потребна понатамошна клиничка евалуација[3]. Кај 35% од индивидуите без симптоми во вратот, постои абнормален наод (надув на дискот, фасетна дегенерација, спинална стеноза). Кај асимптоматските индивидуи на магнетна резонанца е најдено 52% надув, 27% протрузија и 1% екструзија [4].Главна причина на цервикалниот синдром се дегенеративните промени на цервикалниот ‘рбет. Радиолошките наоди на цервикална спондилоартроза, како редукција на И.В. просторот, формирање на остеофити и склероза на апофизните зглобови се чести. Вертебралната спондилоза е евидентирана од

патолозите пред повеќе од еден век. Цервикалната спондилоза е пронајдена при аутопси на 30 годишни кадавери и е докажано дека прогредира за околу 70% и 90% кај 70 годиши жени и мажи. Цервикалната радикулопатија од дегенеративни заболувања може да се дефинира како болка која се шири во еден или во обаатаа горни екстремитети како резултат на компресија и/или иритација на еден или повеќе цервикални нервни корени [5]. Цервикалната радикулопатија се јавува кај 85 во 100.000 индивидуи, многу помалку од лумбалната радикулопатија. Најчесто зафатени цервикаални нервни корени се Ц7 (60%) и Ц6 (25%) [6].

ЦЕЛИ

Главна цел

Да се направи радиолошка анализа на дегенеративните заболувања на цервикалниот сегмент од ‘рбетот кај пациентите со рефракторната цервикобрахијална болка.

Специфични цели

Да се прикажат демографските карактеристики на испитаниците со дегенеративно заболување на `рбетот (пол, возраст);

Да се прикаже типот на дегенеративното заболување на цервикалниот сегмент од ‘рбетот;

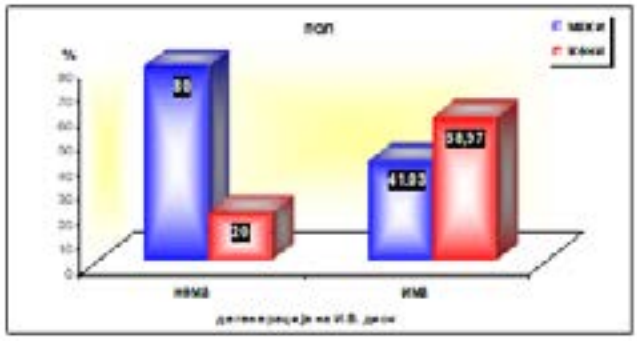
МАТЕРИЈАЛ И МЕТОДИ

Истражувањето претставува проспективна аналитичка - трансверзална (cross-sectional) студија. Се спроведуваше на ЈЗУ Универзитетскиот институт за радиологија - Скопје каде што се вршеше прибирањето на резултати од испитаниците и анализа на наодите. Како извор на податоци се користеа МР прегледите на цервикалниот сегмент од `рбетот и специјалистичките радиолошки извештаи, како и податоците добиени од прашалникот дизајниран за потребите на истражувањето за истите испитаници.

Фокусната група се состои од испитаници на возраст од 35-70 год. со рефракторна вратна болка. Испитуваната група ја сочинуваат испитаници со работна дијагноза цервикобрахијален синдром или цервикална радикулопатија, упатени на Универзитетскиот институт за радиологија во Скопје, заради МР преглед на цервикалниот сегмент од ‘рбетот. Големина на примерокот ја сочинуваат гропа од 98 испитаници.

РЕЗУЛТАТИ

Во нашата студија според резултатите од МР на цервикалниот сегмент од ‘рбетот дегенерација односно дехидратација на интервертебрален диск или дискови се регистрира кај 78 (79,59%) испитаници, со прилично рамномерна половата дистрибуција од 48 (48,98%) машки и 50 (51,02%) женски испитаници. Резултатите од истражувањето покажуваат дека дегенерацијата на интервертебралните дискови на цервикалниот дел на ‘рбетот сигнификантно зависи од полот на испитаниците (Chi-square=9,68 df=1 p=0,0019), што се должи на значајно почест наод на оваа патолошка состојба кај жените. Во оваа серија на испитаници, дегенерација на интервертебралните дискови на цервикалниот дел на ‘рбетот имаат 32 (41,03%) машки испитаници и 46 (58,97%) женски испитаници.



Просечната возраст на испитаниците со дегенерација на интервертебралните дискови на цервикалниот дел на ‘рбетот изнесува 35,35±4,2 години, додека просечната возраст на групата без наод за дегенерација изнесува 25,6±5,4 години. Разликата во просечната возраст од 9,75 години меѓу испитаниците без и со наод за дегенерација и статистички се потврди како сигнификантна (t=8,68 p<0,001). Зголемување на возраста за една година за 35,9% (95% CI 1,203 - 1,535) пати ја зголемува шансата за појава на дегенеративни промени на цервикалниот дел на ‘рбетот.

Во однос на појава на надув на интервертебрален диск, односно дискови, резултатите од МР на цервикалниот сегмент од ‘рбетот покажаа дека таква патологија постои кај 77 (78,57%) испитаници.

Надув	N (%)
нема	21 (21,43%)
има	77 (78,57%0
вкупно	98 (100%)

Полот на испитаниците нема сигнификантно влијание на појавата на надув на интервертебралните дискови

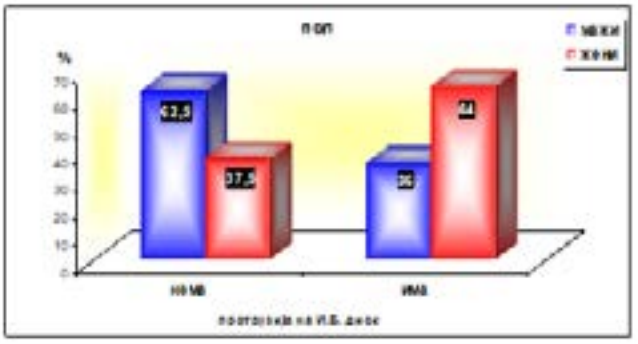
на цервикалниот дел од ‘рбетот (Chi-square=1,27 df=1 p=0,26). Во МР наодот од цервикалниот дел од ‘рбетот се забележува надув кај 40 (51,95%) машки и 37 (48,05%) женски испитаници.

Појавата на надув на И.В диск од цервикалниот дел од ‘рбетот сигнификантно се зголемува со зголемување на старосната група на испитаниците. Испитаниците со наод за надув на интервертебралните дискови на цервикалниот дел од ‘рбетот имаат сигнификантно поголема просечна возраст од испитаниците без ваков наод (34,26 ± 5,2 вс 30,05 ± 7,5 t=2,99 p=0,0035).

Резултатите од МР на цервикалниот сегмент од ‘рбетот кај 50 (51,02%) испитаници одат во прилог на протрузија или екструзија на интервертебрален диск, односно интервертебрални дискови.

ДИСКУС ХЕРНИЈА	N (%)
нема	48 (48,98%)
има	50 (51,02%)
вкупно	98 (100%)

Резултатите од истражувањето покажуваат дека појавата на хернијација на интервертебралните дискови на цервикалниот дел на ‘рбетот сигнификантно зависи од полот на испитаниците (Chi-square=6,88 df=1 p=0,009), што се должи на значајно почест наод на оваа патолошка состојба кај жените. Во оваа серија на испитаници, хернијација на интервертебралните дискови на цервикалниот дел на ‘рбетот имаат 18 (36%) испитаници од машки пол и 32 (64%) женски испитаници.



Просечната возраст на испитаниците од групата со хернијација на интервертебралните дискови на цервикалниот дел на ‘рбетот изнесува 35,02 ± 4,42 години, и сигнификантно (t=2,93 p=0,0042) е повисока од просечната возраст на испитаниците од групата без дискус хернија, која изнесува 31,62 ± 6,83 години.

ДИСКУСИЈА

Како резултат на оваа студија добивме престава за застапеноста на дегенеративните заболувања на цевикалниот сегмент од ‘рбетот кај популација во Р.Македонија. Според податоците на Институтот за јавно здравје во Скопје, од сите мускуло-скелетни заболувања во Р.Македонија, заболувањето на интервертебралните дискови е на прво место по дијагностицирани случаи, со стапка од 6,45 случаи на 10.000 жители, со просечно траење на лекувањето во болнички стационар од 13,74 денови [7].

Цели на оваа студија беа да се направи анализа на дегенеративните заболувања на цервикалниот сегмент од `рбетот кај популацијата во Р.Македонија, и да се прикажат демографските карактеристики на испитаниците со дегенеративно заболување на `рбетот (пол, возраст). Дегенерацијата или дехидратацијата на интервертебралниот диск познато е дека настанува како резултат на природниот процес на стареење под влијание на различни надворешни и генетски фактори. Дискус хернијата со помош на магнетна резонанца може да биде дијагностицирана кај 10% од асимптоматските индивидуи помлади од 40 години и кај 5% од оние кои се постари од 40 години. Дегенерацијата на И.В. дискот може да биде детектирана кај 25% од асимптоматските индивидуи помлади од 40 години и 60% од оние постари од 40 години. Разни студии покажале дека од 51 - 67% од возрасните чувствуваат болка во вратот и раката во некој период од животот, од кои кај 54% таа болка е присутна и во последните 6 месеци. Во една ваква студија во која учествувале 497 асимптоматски здрави индивидуи е забележано дека инциденцата на дегенерација на И.В. дискот се зголемува со годините, пропратено со намалување на сигналот на МР кај 17% од машките и 12% од женските испитаници од 20 до 29 години и 86% од машките и 89% од женските испитаници на возраст од 60 до 69 години. Хернијација на И.В. диск претежно се јавува кај помлади испитаници односно помади од 40 години. Додека дегенерација на И.В. дискот претежно се јавува кај индувидуи постари од 40 години како дел од процесот на природно старење. Овие индивидуи постари од 40 години имаат поголем ризик од цервикална радикулопатија (8). Овие резултати во однос на прогредирањето на патологијата на цервикалните И.В. дискови со годините се во согласност со нашата студија односно зголемувањето на возраста за една година ја зголемува шансата за појава на дегенерација на еден или повеќе

И.В. дискови за 36%.

Врз основа на резултатите добиени од нашето истражување за инциденцата на патолошките состојби на И.В. дисковите од цервикалниот сегмент од ‘рбетот во испитуваниот промерок се доаѓа до заклучок дека кај 78 (79,59%) испитаници во нашата студија постои дегенерација (дехидратација) на еден или повеќе И.В. дискови. Надув на интервертебрален дискус или дискови на цервикалниот сегмент од ‘рбетот се прати кај 77 (78,57%) испитаници, додека повеќе од половина од испитаниците во студијата 50 (51,02%) имаат некој степен на хернијација на интервертебрален диск, односно интервертебрални дискови од цервикалниот сегмент на ‘рбетот. Во популациската студија во Рочестер, Минеаполис, С.А.Д., годишната документирана појава на цервикална радикулопатија кај мажи и жени била 107,3 и 63,5 случаи следствено, на 100.000 популација. Кај 21,9% од испитаниците причината за цервикалната радуколапатија била протрузија на И.В. диск, додека 68,4% била резултат на спондилоза, дискус херниј, или двете [9]. Друга студија за ризик факторите во С.А.Д. открива дека од 13.000.000 индивидуи од војската на С.А.Д. инциденцата на појава на цервикална радикулопатија е 1,79 случаи на 1.000 индивидуи годишно. Во истата студија забележано е дека индивидуите постари од 40 год., женските индивидуи и белата раса имаат поголем ризик од цервикална радикулопатија[10]. Друга студија во Италија открила инциденца на цервикална радикулопатија од 3 случаи на 1.000 индивидуи [11].

Половата дистрибуција е различна во зависност од патологијата на И.В. дискот. Резултатите од истражувањето покажуваат дека дегенерацијата и појавата на дискус хернии на интервертебралните дискови на цервикалниот дел на ‘рбетот сигнификантно зависи од полот на испитаниците, што се должи на значајно почест наод на овие патолошки состојби кај жените. Во оваа серија на испитаници, дегенерација на интервертебралните дискови на цервикалниот дел на ‘рбетот имаат 32 (41,03%) испитаници од машки и 46 (58,97%) женски испитаници, а хернијација на интервертебралните дискови на цервикалниот дел на ‘рбетот имаат 18 (36%) машки и 32 (64%) женски испитаници. За разлика од тоа полот на испитаниците нема сигнификантно влијание на појавата на надув на интервертебралните дискови од цервикалниот дел на ‘рбетот. Кинли предлага дека половата дистрибуција на дискус херниите е приближно еднаква нај двата пола[12]. Марчиони и Хендерсон забележуваат дека жените имаат поголема инциденца на појава на дискус хернија отколку мажите(11), додека Шоенфилд заклучил дека женскиот пол има сигнификантно поголем ризик за појава на дискус хернија (10). Заклучоците од овие студии се во согласност со резултатите и заклучокот од нашата студија дека припадничките на женскиот пол имат поголем ризик од појава на дегенерација или дискус хернија на цервикалниот сегмент од ‘рбетот.

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Profesional paper

IMPACT OF SYSTEMATIC PELVIC LYMPHADENECTOMY ON SHORT TERM POSTOPERATIVE QUALITY OF LIFE IN PATIENTS WITH EARLY STAGE ENDOMETRIAL CANCER

Tanturovski Mile[1], Jovanovska Viktorija[1], Stojovski Marjan[1], Tanturovski Dragan[1], Stojchevski Sasho[1], Aluloski Igor[1]

[1]Department of gynecologic oncology, University clinic of gynecology and obstetrics, University "Ss. Cyril and Methodius", Skopje, Republic of North Macedonia

[2]Institute of epidemiology, biostatistics and medical informatics, University "Ss. Cyril and Methodius", Skopje, Republic of North Macedonia

[3]Univeristy clinic of psychiatry, University "Ss. Cyril and Methodius", Skopje, Republic of North Macedonia

CORRESPONDENCE
Mile Tanturovski, MD
Department of gynecologic oncology,
University clinic of gynecology and obstetrics, University "Ss. Cyril and Methodius", Skopje, Republic of North Macedonia
Adress: Majka Tereza Blvd. No. 17, 1000, Skopje, Republic of North Macedonia
e-mail: mile.tanturovski@gmail.com
phone: +38978485585

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ABSTRACT

Objective: to determine the potential impact of systematic lymphadenectomy vs. no lymphadenectomy on the perioperative change in QoL in patients undergoing surgical treatment for early stage endometrial cancer.

Patients and methods: Patients scheduled for surgical treatment of clinically early stage endometrial cancer at the Department of gynecological oncology at the University Clinic of Gynecology and Obstetrics in Skopje, in the period January – December 2018 were approached for participation. Eligible subjects were divided into two groups: Group 1 (no LND) consisted of 60 patients who had hysterectomy plus bilateral salpingo-oophorectomy without lymph node dissection (LND); Group 2 consisted of 24 patients who had hysterectomy plus salpingo-oophorectomy plus systematic pelvic LND. Quality of life was quantified using a standardized and validated questionnaire (FACT-G) preoperatively and 30 days after surgical treatment.

Results: The patients in the LND group exhibited statistically significantly lower postoperative scores for FACT-G (87.7 vs 75.8 for the no LND and LND groups respectively, p=0.002), as well as for the physical wellbeing domain (23.4 vs. 20, p=0.004) and emotional wellbeing domain (20.7 vs 17, p=0.008). Twelve patients from the group with no lymphadenectomy (20%) experienced a clinically significant decline in the postoperative QoL, compared to 12 patients (50%) in the lymphadenectomy group (p=0.006).

Conclusion: There was a significant decrease in the postoperative QoL 30 days after surgery in patients that undergo systematic pelvic lymphadenectomy for early stage endometrial cancer compared to patients that do not.

Key words: quality of life, endometrial cancer, lymphadenectomy

INTRODUCTION

Endometrial cancer is the most common gynecologic malignancy in the developed world and the sixth most common malignant disorder worldwide accounting for up to 6% of all malignancies. Approximately 320000 new cases are identified each year [1]. The highest incidence rates are registered in the developed countries of North America and Europe, where endometrial cancer is the most common malignant neoplasm of the female genital tract and the fourth most common location in women after breast, lung and colorectal cancer [2]. Endometrial cancer is the second most common malignant neoplasm in women (after breast cancer) in The Republic of North Macedonia with an estimated 400 new patients diagnosed annually [1], and a corresponding age-standardized incidence rate of 24.3 per 100000 women.

Traditionally, endometrial cancers have been classified into two types, based on histopathology: type 1 are low-grade estrogen related endometroid adenocarcinomas that are usually diagnosed early and have a favorable prognosis, while type 2 endometrial cancers are high grade endometroid adenocarcinomas, papillary serous and clear cell carcinomas and carcinosarcomas [3]. The latter group of cancers are hormone independent and are associated with a more aggressive tumor behavior and poorer prognosis.

Metastatic spread, be it regional or through the vascular and/or lymphatic systems, is the most important prognostic factor that influences the overall patient survival. The most frequent location for metastatic spread of endometrial cancers are the pelvic lymph nodes. The uterus drains through three main lymphatic trunks: utero-ovarian (infundibulopelvic), parametrial and presacral trunk which drain into the external iliac, common iliac, internal iliac, presacral and para-aortic lymph node basins [4]. Although theorized and described, direct lymphatic metastasis to the para-aortic lymph nodes with negative pelvic nodes occurs rarely in endometrial cancer patients [5]. Systematic pelvic and/or para-aortic lymph node dissection (LND) has been well recognized as a cornerstone of surgical staging of endometrial cancer ever since the International Federation of Gynecology and Obstetrics (FIGO) moved from clinical to surgical staging of endometrial cancer [6]. The comprehensive FIGO surgical staging algorithm for endometrial cancer recommends a procedure that includes total hysterectomy and bilateral salpingo-oophorectomy, peritoneal washing and pelvic and/or para-aortic lymphadenectomy. The therapeutic benefits of lymphadenectomy, however, remain controversial and a matter of scientific debate, especially in patients with early stage endometrial cancer. Patients undergoing systematic pelvic and para-aortic lymphadenectomy experience longer operative times and are exposed to greater risk of intraoperative and postoperative complications than patients treated with hysterectomy with bilateral salpingo-oophorectomy alone [7], which in turn, negatively impacts the quality of life (QoL).

OBJECTIVE

The aim of the study was to determine the potential impact of systematic lymphadenectomy vs. no lymphadenectomy on the perioperative change in QoL in patients undergoing surgical treatment for early stage endometrial cancer.

PATIENTS AND METHODS

The study was designed as a prospective cohort study and was conducted at the Department of gynecologic oncology at the University clinic of gynecology and obstetrics, University "Ss. Cyril and Methodius", Skopje, Republic of North Macedonia. Eligible consecutive patients scheduled for surgical treatment of endometrial cancer at the Department between January and December 2018 were approached for participation in the study. Inclusion criteria were: presence of a histologically verified endometrial cancer that was presumed early stage based on preoperative evaluation. Patients that were unfit for surgical treatment were excluded from the study. Written consent for participation was obtained from all patients and the study was approved by the Ethical committee of the Medical faculty at the University "Ss. Cyril and Methodius", Skopje, Republic of North Macedonia.

Contrast CTs of the abdomen and chest were performed to exclude lymphadenopathy and/or extrauterine disease. Patients were than classified into two groups, based on the ESMO-ESGO-ESTRO recommendations for endometrial cancer treatment [8]: group 1 (no LND) were patients with low risk endometroid endometrial cancer (clinically stage I, grade 1/2, myometrial invasion <50%) and were treated with total abdominal hysterectomy with bilateral salpingo-oophorectomy without lymph node dissection; group 2 (LND) were patients with intermediate/high risk endometrial cancer (clinical stage I of endometoid cancer grade 3 and/or myometrial invasion ≥50%, patients with clinical stage II and all patients with non-endometroid

histology) which were treated with total abdominal hysterectomy with bilateral salpingo-oophorectomy and systematic pelvic lymph node dissection.

All surgeries were performed via laparotomy by five surgeons from the Department in a standardized fashion. The lymphadenectomy included dissection of the external iliac, internal iliac, obturator, presacral and common iliac nodes up to the bifurcation of the aorta in accordance with the Department's protocol. No para-aortic lymph node dissection was performed given that all patients were early stage and the risk of para-aortic involvement was low [5].

The main endpoint of the study was the postoperative change in quality of life, measured by the Functional Assessment of Cancer Therapy-General (FACT-G) score [9], version 4. The FACT-G questionnaire consists of 27 questions, grouped in four domains: physical well-being (PWB), social well-being (SWB), emotional well-being (EWB) and functional well-being (FWB). The PWB, SWB and FWB domains have 7 questions and score 0-28, while EWB has 6 questions and scores 0-24. The answers in the FACT-G questionnaire are formulated as a 5-point Likert scale (0- "not at all" to 4 – "very much"), and the values are summed up to form a total score of 0-108.

The questionnaire was translated in Macedonian and was self-administered by the patients, with a researcher available, should the patient have any questions or issues. Patients filled out the questionnaire on admission and approximately 30 days post-surgery, during the first follow-up visit at our Outpatient department.

To assess the postoperative change in the quality of life, the study used the "minimally important difference" (MID) concept [10]. The MID concept is defined as the lowest difference in the overall score or any domain sub-score that is perceived by the patient as an improvement or deterioration, consequently influencing the management of the patient [10]. The study employed a distribution-based method to calculate MID. For the purposes of this study, QoL one-month post-surgery was categorized as "deteriorated" if the postoperative FACT-G (or relevant domain) score was at least 5 points lower than the preoperative score (MID=5). The data was used to transform the raw scores into a categorical dichotomous variable indicating a decline in overall QoL (or relevant domain).

We also recorded and analyzed the following variables: body mass index (BMI), level of education (high school or lower vs. university degree), marital status (married/living with a partner vs. divorced/widowed), place of residence (urban vs. rural), comorbidities and smoking. The following comorbidities were recorded: diabetes, history of a major thrombotic event, chronic renal failure, history of immunosuppression and chronic cardio-vascular conditions (excluding hypertension).

The data was digitized and entered into a database. The statistical analysis was carried out using the SPSS statistical software package version 23 (IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp.). Standard descriptive statistics were done and data was displayed using frequencies, percent, mean and standard deviation (SD), where appropriate. The difference in the FACT-G score and the associated domains pre- and postoperatively were compared using the Mann Whitney's U test for independent samples. The differences in the distributions of the listed categorical variables in the two groups of patients were tested using the Chi square test and Fisher's exact test, depending on the group size. A value of $p<0.05$ was considered statistically significant.

RESULTS

A total of 91 patients were recruited in the study. Of those, 7 patients (7.7%) were excluded from statistical analysis: 6 (6.6%) patients with incomplete questionnaires and one patient (1%) who was unavailable for evaluation one month after surgery. The remaining 84 patients (92.3%) were selected for analysis, 60 patients in group 1 (no LND) and 24 patients in group 2 (LND).

The demographic and clinical characteristics of the patients included in the study are summarized in Table 1. The groups were homogenous. The average age of patients in group 1 (no LND) was 60.9±8, while the average age of patients in group 2 (LND) was 62.5±7.8. The mean BMI were 33.7±7.8 and 31.5±6.4 for group 1 (no LND) and group 2 (LND), respectively. Most of the patients had a high school degree or lower education (95% and 79.2% for the no LND and LND groups, respectively), were married/living with a partner (80% and 95.8% for the no LND and LND groups, respectively), came from urban communities (66.7% for both groups) and were non-smokers (95% and 95.8%, respectively). Approximately half of the patients in both groups had at least one comorbidity (53.3% vs. 45.8% for the no LND and LND groups, respectively). Thirty-two patients (53.3%) from the no LND group were Stage IA, 24 (40%) were Stage IB and 4 patients (6.7%) were

upstaged to Stage II on the final pathology report. Seven (29.2%) patients from the LND group were surgical Stage IA, 5 (20.8%) were Stage IB, 8 (33.3%) were Stage II, while 4 (16.7%) patients had pelvic node involvement and were Stage IIIC1. The pathology report confirmed endometroid histology in the vast majority of patients in the no LND group (96.7%), and only two patients (3.3%) had a revised diagnosis of mixed histology on the final pathohistology report. The following histologic types were recorded in the LND group: poorly differentiated endometroid in 14 patients (58.3%), mixed in 4 (16.7%) and serous and clear cell carcinomas in 3 (12.5%) of the patients each. The median number of retrieved lymph nodes in the LND group was 14 with a range of 6-27.

Table 1. Summary of the relevant demographic and clinical patient characteristics

Parameter	Group 1 (no LND) n=60	Group 2 (LND) n=24
Age, mean±SD	60.9±8	62.5±7.8
BMI, mean±SD	33.7±7.8	31.5±6.4
Degree of education, n (%) High school or lower University diploma	 57 (95%) 3 (5%)	 19 (79.2%) 5 (20.8%)
Marital status, n (%) Married/living with a partner Divorced/widowed	 48 (80%) 12 (20%)	 23 (95.8%) 1 (4.2%)
Employment status, n (%) Employed/retired Unemployed	 40 (66.7%) 20 (33.3%)	 15 (62.5%) 9 (37.5%)
Place of residence, n (%) Urban community Rural community	 40 (66.7%) 20 (33.3%)	 16 (66.7%) 8 (33.3%)
Comorbidities, n (%) Absent Present	 28 (46.7%) 32 (53.3%)	 13 (54.2%) 11 (45.8%)
Smoking, n (%) Non-smoker Smoker	 57 (95%) 3 (5%)	 23 (95.8%) 1 (4.2%)
Surgical stage, n (%) IA IB II IIIC1	 32 (53.3%) 24 (40%) 4 (6.7%)	 7 (29.2%) 5 (20.8%) 8 (33.3%) 4 (16.7%)
Final histology, n (%) Endometroid Mixed Serous Clear cell	 58 (96.7%) 2 (3.3%)	 14 (58.3%) 4 (16.7%) 3 (12.5%) 3 (12.5%)
Number of nodes, median (range)		14 (6-27)

The comparison between the preoperative and postoperative QoL in both groups is presented in table 2. No statistically significant differences were identified in the preoperative overall and domain scores (p=0.28, 0.4, 0.77, 0.41 and 0.1 for FACT-G, PWB, FWB, SWB and EWB respectively). The patients in the LND group exhibited statistically significantly lower average scores for FACT-G (87.7 vs 75.8 for the no LND and LND groups respectively, p=0.002), as well as for the physical wellbeing domain (23.4 vs. 20, p=0.004) and emotional wellbeing domain (20.7 vs 17, p=0.008). The differences for the scores on the functional wellbeing and social wellbeing scales were not statistically significant (p=0.09 and 0.07, respectively).

Table 2. Comparison of pre- and postoperative FACT-G and domain scores*

	Group 1 (no LND) (mean ±SD)	Group 2 (LND) (mean. ±SD)	p†
Preoperative			
FACT-G	87.8±14.3	82.3±20.7	0.28
PWB	23.5±4.4	22.2±5.7	0.4
FWB	20.9±4.6	20.2±5.5	0.77
SWB	22.8±3.8	21.5±5.1	0.41
EWB	20.5±3.2	18.5±5.8	0.1
Postoperative			
FACT-G	87.7±17.3	75.8±22.6	0.002
PWB	23.4±5.1	20±6.1	0.004
FWB	20.8±5.4	18.4±6	0.09
SWB	22.8±4.7	20.3±6.1	0.07
EWB	20.7±4.9	17 ±6.6	0.008

*LND – systematic lymph node dissection; PWB-physical wellbeing; FWB-functional wellbeing; SWB-social wellbeing; EWB-emotional wellbeing. †Mann Whitney U test

The clinical significance of the difference in postoperative QoL was evaluated using the MID concept. Twelve patients from the group with no lymphadenectomy (20%) experienced a clinically significant decline in the postoperative QoL, compared to 12 patients (50%) in the lymphadenectomy group and the difference was statistically significant (p=0.006, Table 3).

Table 3. Comparison of patients with clinically significant decline in postoperative QoL*

Postoperative QoL	Group 1 (no LND) n (%)	Group 2 (LND) n (%)	p†
FACT-G Unchanged	48 (80%)	12 (50%)	0.006
FACT-G Diminished	12 (20%)	12 (50%)	

*LND–systematic lymph node dissection; QoL–quality of life. †Chi square test

DISCUSSION

Nodal assessment in patients with newly diagnosed endometrial carcinoma is an important aspect of the initial management of these patients. This prospective study evaluated the impact of lymphadenectomy on the early postoperative QoL in patients with clinically early stage endometrial cancer. The average FACT-G scores one-month post-surgery were significantly lower in patients undergoing lymphadenectomy compared to patients that underwent hysterectomy with bilateral lymphadenectomy alone. Additionally, 50% of the patients in the lymphadenectomy group experienced a clinically significant decrease in quality of life, physical and emotional wellbeing, compared to 20% in the no lymphadenectomy group.

Published data on the impact of systematic lymph node dissection on the QoL is scarce. A population-based retrospective study in the Netherlands evaluated the health-related QoL in patients with FIGO Stage I/II endometrial cancer receiving lymphadenectomy, external beam radiotherapy (EBRT) or both [11]. Lymphedema, gastrointestinal tract symptoms, diarrhea, back and pelvic pain, and muscular joint pain were the most commonly reported symptoms. The lymphadenectomy cohort had higher lymphedema scores (7%) and the cohort who received radiotherapy had higher bowel symptom scores (15%). The group that received lymphadenectomy and radiotherapy had the highest symptom scores (21%). The authors showed that, despite different symptom patterns, in patients who had pelvic lymphadenectomy (e.g. lymphedema), radiotherapy (e.g. diarrhea) or both, no clinical differences in overall QoL were observed compared with women not receiving adjuvant therapy, lymphadenectomy or both. Angioli et al [12] compared patients undergoing lymphadenectomy for endometrial cancer vs. patients who received hysterectomy with bilateral salpingo-oophorectomy alone. In their series of 95 patients, only lymphedema interfered with patients' QoL, while other associated morbidities from the surgery did not impact QoL and global health status was not statistically significantly different between the groups. Both studies were retrospective by design and evaluated long term impact of lymphadenectomy on QoL at least 12 months after surgery when other factors such as adjuvant therapy might influence the results.

In a recent study of QoL in endometrial cancer patients [13], authors found that the global health scores were lower and pain scores were higher in women who received EBRT. Given that no patients in that series underwent pelvic lymph node dissection, the authors used SEER data for lymph node metastases to identify patients that could safely forego EBRT and found that EBRT could be avoided in 39.5% of their patients with no difference in survival, noting that that increase in lymphedema is a tradeoff to avoid symptoms from EBRT, accepting that a small percentage of patients will have worse symptoms owing to a combination of treatments. The authors concluded that performing lymphadenectomy to triage patients for adjuvant treatment can improve (QoL) and lower health provider costs with no difference in survival. In our series, adjuvant EBRT was avoided in 29.2% of the node-negative patients with high-risk endometrial cancer.

Systematic lymphadenectomy in patients with endometrial cancer increases the operative times and are the risk of intraoperative and postoperative complications compared to hysterectomy and bilateral salpingo-oophorectomy alone [14, 15]. Indeed, the extent of the surgical procedure and the associated increase in perioperative morbidity could explain the decline in the short term postoperative QoL and physical wellbeing. Aljabri et al [16] studied a cohort of 76 patients undergoing major aortic surgery and detected a significant decrease in the physical well-being 5 weeks post-surgery. The extent of surgical resection was found to negatively influence the short term postoperative physical wellbeing in patients surgically treated for gastric and colorectal cancer [17,18], and similar data was published in a longitudinal study of a series of patients with hepatic resections [19]. The statistically significant postoperative deterioration of the physical QoL after extensive surgical procedures could be due to the acute systemic inflammatory response after major surgery, including "sickness behavior" [20] and the unattainability of complete postoperative rehabilitation in certain cases [21].

The therapeutic role of lymphadenectomy remains a matter of scientific debate. A large retrospective analysis of the US National Cancer Institute's Surveillance, Epidemiology, and End Results program (SEER) databases [22] included 39396 patients treated for endometrial cancer from 1988 to 2001. The authors compared the therapeutic outcomes of 12333 patients undergoing systematic lymph node dissection vs 27063 patients that had no lymph node dissection and found that the extent of lymph node resection was associated with improved survival among women with intermediate- or high-risk endometrial cancer.

Two randomized control trials [14, 15] have disputed the impact of lymphadenectomy on the survival of patients with endometrial cancer. Between both studies, a total of 1922 patients were randomized to systematic lymph node dissection vs no lymph node dissection in addition to standard hysterectomy with bilateral salpingo-oophorectomy to evaluate the possible survival benefit of lymphadenectomy. The cumulative results of these studies reported that lymphadenectomy did not improve disease-free survival (pooled HR, 1.23; 95% CI 0.96–1.58) and overall survival (pooled HR, 1.07; 95% CI, 0.81–1.43). The results of the of these studies have been widely disputed due to methodological inconsistencies, mainly the large proportion of low-risk cases and lack of clear protocols for adjuvant therapy especially in patients with nodal disease.

Lymph node assessment remains crucial for proper staging and adjuvant therapy tailoring in patients with endometrial cancer. Completely foregoing lymph node dissection would lead to improper staging and under- or over-treatment, with adjuvant therapy decisions based on patient and uterine features alone. For example, adjuvant chemotherapy has been shown to provide a significant improvement in overall survival in patients with extrauterine disease, including nodal involvement [8]. Sentinel lymph node (SLN) mapping has emerged as a viable, less-invasive alternative to comprehensive LND since its introduction in endometrial cancer in 1996 [23]. Two studies have demonstrated non-inferiority of sentinel lymph node mapping over systematic lymphadenectomy in endometrial cancer. The FIRES trial [24] was conducted on 385 patients with clinical stage I endometrial cancer. Patients underwent sentinel lymph node biopsy followed by a comprehensive LND and the authors demonstrated that the sentinel lymph node biopsy failed to identify lymph node involvement in 3% of node-positive patients yielding a false negative predictive value of 0.4% across all patients. The trial of Soliman et al. [25] recruited 123 patients with high-risk endometrial cancer and had a false negative predictive value of 1.4% across all patients. A recent study, focusing on the QoL aspect of sentinel lymph node mapping [26] concluded that the benefit of SLN mapping over comprehensive LND lies in the reduction of lymphatic morbidity and subsequent improvement in QoL.

This study is limited by the relatively small sample size, therefore all observed differences between the groups of patients with deteriorated and identical/improved postoperative QoL, should be interpreted with caution. The systematic lymphadenectomy group included only patients with presumed early stage disease with no evidence of nodal involvement on preoperative imaging to limit the confounding effect of the extensive surgical resection and/or para-aortic lymph node dissection that would be required in the treatment patients with extrauterine disease and/or bulky nodal disease. The MID concept in the study was used to identify only the subset of patients with deteriorated postoperative QoL, based on the valid evidence that QoL is diminished 30 days after surgery.

CONCLUSION

The evaluation of quality of life provides additional information from the patients' perspective related to the disease burden and treatment effectiveness. QoL is a multi-dimensional dynamic concept reflecting the patient's subjective perception of the influence of the disease and the associated treatment. The concept incorporates changes in physical, social, emotional and functional wellbeing that can present at any time beginning at moment the patient is diagnosed, during the treatment and long after the patient has finished the treatment.

Our study identified a clinically significant decrease in the postoperative QoL 30 days after surgery in patients that undergo systematic pelvic lymphadenectomy for early stage endometrial cancer compared to patients that do not. Systematic lymph node dissection is, certainly, not devoid of adverse effects. Although there might not be a discernable therapeutic benefit from LND, it remains the cornerstone of proper surgical staging, facilitating the tailoring of postoperative adjuvant treatment.

Women undergoing surgery for endometrial cancer should be counseled about the potential benefits of surgical staging including LND, which can influence their postoperative treatment in a significant manner, as well as the possible negative impact of the treatment on the short-term QoL. Sentinel lymph node mapping might be a viable alternative for these patients as it is associated with a better QoL and reduced perioperative morbidity, compared to comprehensive LND, without impeding the reliability of the staging procedure. QoL data may, in some cases, facilitate expectation management and coping strategies an enable endometrial cancer to patients to make better-informed decisions about the treatment about their treatment.

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Profesional paper

INTERVENIMI I HERSHËM NË ÇREGULLIMET E SPEKTRIT TË AUTIZMIT

Naser DURMISHI[1], Siëndrra MEHMETI[2], Bunjamin MEHMETI[2], Rrezearta Elezi[3]

[1]Departamenti i psikijatrisë të fëmijëve dhe adoleshentëve, Klinika Univers. e Psikijatrisë, Shkup, R. e Maqedonisë së Veriut

[2]Departamenti i Edukimit Special dhe Rehabilitimit, Fakulteti Pedagogjik, Universiteti i Tetovës, R. e Maqedonisë së Veriut

[3]Spitali Klinik, Tetovë

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ABSTRAKT

Çrregullimet e Spektrit të Autizmit kanë filluar të ngjallin interes, madje edhe krijojnë shqetësim kohëve të fundit me frekuencën gjithnjë në rritje në nivel ndërkombëtarë. Ndonëse shumë më tepër prindër - në krahasim me vitet e kaluara, kanë filluar të lexojnë rreth çrregullimeve zhvillimore të fëmijëve dhe të shfaqin shqetësime në lidhje me zhvillimin e fëmijëve të tyre, intervenimi vazhdon të mbetet problematik tek ne. Ky punim bazohet mbi përvojat e prindërve gjatë periudhës së intervenimit tek fëmijët e tyre që gjenden në spektër. Përmes këtij hulumtimi, në mënyrë specifike targetohen prindërit, kuadri mjekësor dhe ai arsimor në lidhje me përgatitjen e tyre për intervenim të hershëm. Metoda e shfrytëzuar për fitimin e rezultateve është pyetësori i cili përfshin pyetje rreth përvojës së përgjithshme gjatë intervenimit, poashtu qasjen e profesionistëve te përfshirë gjatë periudhës së intervenimit dhe procesit arsimor. Rezultatet e hulumtimit na tregojnë se nuk ekzistojnë resurse të mjaftueshme për intervenim të hershëm, gjithashtu prindërit deri diku janë të përgatitur për intervenim të hershëm, ndonëse kuadri mjekësor dhe kuadri arsimor kanë nevojë për më tepër përgatitje.

Fjalë kyçe: Çrregulimet e Spektrit Autik, Intervenimi i hershëm,

HYRJE

Çrregullimi i Spektrit të Autizmit apo i ashtuquajturi Autizëm janë dy terma të përgjithshëm për një grup të çrregullimeve komplekse të sistemit nervor qendrorë që janë të karakterizuara me vështirësi në shkallë të ndryshme të aftësisë të interaksionit social, komunikimit verbal dhe joverbal dhe manifestim të sjelljeve përsëritëse.

Dokumentimi më i hershëm i autizmit daton nga viti 1943 në letrën e Kanner-it "Çrregullimet autike në kontaktin afektiv", lidhur me pohimin e tij të identifikimit të fëmijëve autikë që nga viti 1938.

Intervenimi i hershëm si nocion nënkupton masa të ndërmara lidhur me inicimin e ekzaminimit, identifikimin e individëve nën rezik potencial, diagnostikimin, trajtimin si dhe evaluimin e gjendjes së fëmijëve të tillë që nga lindja deri në moshën 36 muajore të zhvillimit (zhvillimi i hershëm psikomotor). Intervenimi i hershëm rritë kapaciettin e përgjithshëm të zhvillimit të këtyre fëmijëve, duke u mësuar shkathtësi që bashkëmoshatarët e tyre i arrijnë në mënyrë të natyrshme. Gjithashtu nënkupton edukimin e familjes me fëmijë të tillë për mënyrë efektive të interaksionit me fëmijën dhe njëri tjetrin në çiftin prindëror, si dhe sigurimin e shërbimeve të targetuara që mbështesin këtë edukacion.

Objektivi kryesor në detektimin e hershëm të Çregullimeve të spektrit Autik (angl. Autistic Spektrum Disorders-ASD) në moshën e hershme është që t'i mundësohet fëmijës dhe familjes qasje në shërbimet e intervenimit sa më herët. Kjo objektiv buron nga disa qëndrime të rëndësishme që determinojnë suksesin e intervenimit:

Qëndrimi i parë qëndron në të kuptuarit tonë më të mirë rreth natyrës neuro-qendrore të ASD. Provat shkencore sugjerojnë se ASD është prezent që nga lindja - ka

komponentë të fortë gjenetike dhe simptomat shfaqen herët në jetë, kjo paraqet edhe kohën kur duhet të regjistrohen.

Qëndrimi i dytë i arsyetimit qëndron në ekzistimin e "periudhës kritike" kur truri është aftësuar për të mësuar gjuhën e hershme, shkathtësitë sociale, dhe konceptet kognitive. Intervenimi i hershëm përpiqet më tepër të intervenojë gjatë këtyre periudhave optimale të të mësuarit, se sa këto të kompenzohen më vonë në jetë. Ky fenomen është i lidhur me dukurinë e plasticitetit të trurit – gjegjësishtë kapacitetin e demonstruar të trurit përgjatë kohës kur përvojat e hershme formësojnë lidhjet dhe funskionet neurale.

Qëndrimi i tretë është se familja ka nevojë për shërbime po aq sa edhe vetë fëmija. Intervenimet bazuar tek fëmija përpiqen të ndërtojnë aftësitë e fëmijës, përderisa përfshirja e familjes është kruciale jo vetëm për të ndihmuar në përpjekjet që kanë në fokus fëmijën, por po me aq rëndësi për të ndërtuar shkathtësi të përfaqësimit (advokimit) si kujdestarë të fëmisë. Shkathtësitë e advokimit paraqesin aftësimin e prindërve të marrin vendime rreth nevojave të fëmijës së tyre, qasjen në resurse dhe në menaxhimin e sistemit të shëndetit, çrregullimeve dhe të edukimit të fëmisë të tyre.

Mosha në të cilën ASD mund dhe duhet të detektohet dhe diagnostikohet ka qenë një target i ndryshueshëm. Deri shumë vonë qëndrim konvencional ishte që të pritet deri moshën 3 vjeçare para se të përcaktohet që fëmija ka pengesë të dukshme të komunikimit ose intelektuale. Por, me theksimin e intervenimit të hershëm, teksa fokusi më i madh ra mbi autizmin dhe ASD, si dhe me zhvillimin e instrumenteve më të mira të skriningut dhe vlerësimit, është aritur një avancim në diagnostikimin e hershëm.

Qëndrimet aktuale ndërkombëtare janë që pjesa më e madhe e fëmijëve mund të diagnostikohej deri në moshën 24 muajshe (18 deri 20 muaj). Edhe pse orvatjet vazhdojnë, qëllimi i detektimit dhe fillimit me intervenim të hershëm të fëmijëve para moshës 3 vjeçare ende nuk është përmbushur përveçse në një pjesë të shteteve të zhvilluara ku ka koncentrim të lartë të resurseve.

METODI

Hulumtimi është realizuar nëpërmjet analizës dhe interpretimit të të dhënave të fituara përmes anketimit, ku pëaqësohen pyetje që kanë të bëjnë me kohën e intervenimit të hershëm tek fëmijët me ASD dhe kushtet e intervenimit të hershëm përgjatë gjithë eksperiencës. Anketa përmban 23 pyetje, prej të cilave 20 pyetje janë të mbyllura dhe 3 janë të hapura.

MOSTRA

Prindër të fëmijëve me ASD (Shoqata për Autizëm "URA BLU", Qendrën për Trajtim të Fëmijëve me Nevoja të Veçanta "AURA", në Shoqatën e Psikologëve të Maqedonisë dhe nxënës në klasat speciale të Shkollës Fillore "Liria" dhe nxënës në Shkollën Fillore "Kirili dhe Metodij" Tetovë).

Numri i përgjithshëm i të anketuarve është 18.

QËLLIMI

Hulumtimi përmes anketës së realizuar me prindër të fëmijëve me ASD, targeton të potencohet rëndësia e intervenimit të hershëm tek fëmijtë dhe familjet me fëmijëve me ASD. Duke marë parasyshë mungesën e përgjithshme të informatave dhe gjallësinë e ndryshimeve të informatave shkencore-profesionale të fushës, qëllimi dot bënte një avancim në gjendjen egzistente.

REZULTATET DHE PËRFUNDIMI

Hulumtimi na tregonë se nga numri i përgjithshëm i mostrës, 72.2% e fëmijëve kanë diagnozë të autizmit, gjithashtu përqindja më e madhe e prindërve me përqindje të njëjtë, gjegjësisht 77.6% kanë pritur 1-6 muaj ose më shumë se 12 muaj, kohë relativisht të gjatë, për të marrë përgjigje për gjendjen e fëmijës së tyre. Po ashtu, përqindja më e madhe e pjesëmarrësve, respektivisht 38.8% shprehin se shërbimet dhe burimet nuk janë të mjaftueshme për ndërhyrje të hershme. Fëmijët që janë të përfshirë në sistemin arsimor, me përqindje më të madhe, respektivisht 64.2% nuk kanë asistent personal dhe nga ata që kanë, asnjë prej tyre (0%) nuk ofrohet nga ministria. Përveç kësaj, 78.5% (11) nga numri i përgjithshëm i të anketuarve tregojnë se fëmija i tyre nuk ka asistent arsimtar.

Rezultatet e hulumtimit na tregojnë se resurset ekzistente janë të pamjaftueshme për intervenim të hershëm në ASD. Prindërit janë relativisht të përgatitur për intervenim të hershëm, ndonëse kuadri mjekësor si dhe kuadri arsimor kanë nevojë për avancim në përgatitjen e tyre.

Këto rezultate dëshmojnë se individët me spektër të autizmit të përfshirë në studim nuk janë të trajtuar adekuat normave dhe standardeve relevante lokale dhe ndërkombëtare, që dëshmon humbje të paarsyeshme të

kohës më frytdhënëse në trajtim, me çka edhe limiton dukshëm rezultatet e aritura në trajtimin aktual si edhe ate të mëtejshëm.

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Profesional paper

THE USE OF FRACTIONAL FETAL ARM VOLUME IN FETAL WEIGHT ESTIMATION

Sotir Nikolovski[1,2], Stefan Matik[1], Gordana Ristevska-Dimitrovska[2], Viktorija Jovanovska[3], Vesna Janevska[4]

[1]Private hospital Plodnost Bitola, Republic of North Macedonia,

[2]Higher Medical School, University St. Kliment Ohridski Bitola, Republic of North Macedonia,

[3]University Clinic of Obsterics and Gynecology, Faculty of Medicine, Ss. Cyril and Methodius University in Skopje, Republic of North Macedonia,

[4]Institute of Pathology, Faculty of Medicine, University Ss. Cyril and Methodius, Skopje, Republic of North Macedonia

Corresponding author:
Sotir Nikolovski, MD MSc Gynecology Obstetrics Specialist, Private hospital Plodnost, ASNOM 9, Bitola, Republic of North Macedonia tel. +389 78 477247, e-mail: sotirropi@gmail.com

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ABSTRACT

Introduction: Fetal weight estimation by using arm volume (VolA) obtained with three-dimensional ultrasound, as a new method that enables accurate measurement of fetal weight.

Aim: The main purpose of this study is to determine the accuracy of calculating the fetal weight based on arm volume (VolA) obtained by three-dimensional ultrasound in relation to actual birth weight.

Methods: 106 pregnant women admitted for delivery were included in this cross-sectional study. Using a three-dimensional ultrasound, the volume of the fetal arm (VolA) was recorded, and after birth the actual birth weight of the neonate was measured.

Results: Simple linear regression analysis revealed a regression equation of birth weight as: Estimated fetal weight = 49.785 x fractional volume of the arm + 1561.8, with a coefficient of determination R2=0.4702. To evaluate the precision of the obtained linear regression formula in birthweight prediction, a comparison among the new formula and other formulas was conducted, including Lee`s formula, Liang`s formula, Viera`s formula and the new formula. The mean absolute percentage errors (MAPE) were 8.79%, 28.23%, 33.42% and 7.98 %, respectively.

Conclusion: This study showed that fetal weight can be estimated using 3D ultrasound techniques, including fractional volumetry of the fetal arm.

Key words: 3-dimensional ultrasound (3DUS); Birth weight (BW); Arm volume (VolA)

INTRODUCTION

An accurate estimation of fetal weight is s requisite in obstetric management and is mostly based on standard formulas in which two-dimensional biometric parameters are included, namely: biparietal diameter (BPD), head circumference (HC), abdominal circumference (AC) and femur length (FL)(1). Unfortunately, estimated fetal weight (EFW) is not as precise as actual body weight (BW) and is typically associated with random errors ranging from 8.1 to 11.8%(2). This is accountable to several factors, among which is the unfavorable fetal position, thick fetal subcutaneous fat and maternal obesity(3).

Previous investigators have described the use of 3-dimensional (3D) volume parameters for improving fetal weight estimation.(4,5) As an example, fractional limb volume is a sub-volume of the arm or thigh that is used to evaluate soft tissue development as a proxy for fetal nutritional status (6).

Arm volume calculated using a three-dimensional ultrasound is a new tissue parameter that is supposed to overcome the technical limitations of two-dimensional ultrasound. This parameter is relatively easily obtained, quickly measured and it is highly reproducible both intra- and inter-observer (7). Changes in the volume of the fetal arm can detect subtle changes in the amount of fetal soft tissue during pregnancy (8).

Today, even greater progress has been made in calculating fetal weight based on three-dimensional ultrasound by the introduction of the concept of fractional fetal arm volume, with only five intersectional planes being measured within the volume of the limb(9). Therefore, the concept of fractional fetal arm volume has been implemented to solve these technical limitations(6). The soft tissue as a parameter is derived from the central part of the limb's diaphysis, because the transverse sections of the mid-limb are more likely to exhibit sharper soft-tissue borders. The measurement time has been significantly reduced because only five planes are taken into consideration within the fractional fetal arm volume and areas of acoustic shadowing are more likely to be seen. Measuring the fractional fetal arm volume is also far more reproducible among different examiners. In the future, with the aid of automated volumetric computer software, measurements would be far more objective(10).

The main purpose of this study is to determine the accuracy of calculating the fetal weight based on arm volume (VolA) obtained by three-dimensional ultrasound in relation to actual birth weight.

MATERIALS AND METHODS

In this cross-sectional study 116 pregnant women were included. The delivery was completed within the next 48 hours after admission at the department of gynecology and obstetrics at Dr. Trifun Panovski Clinical Hospital in Bitola.

The inclusion criteria for this study were: alive fetus, singleton term pregnancy and delivery in less than 48 hours after the 3D examination.

Exclusion criteria were: fetus demise, multiple pregnancies, delayed birth by more than 48 hours after 3D ultrasound examination and a newborn with any structural malformation.

Information about demographic characteristics of the mother, including nationality, maternal age, smoking status, body weight, social status, were taken at the moment of admission to the health facility.

The measurement of the newborns weight was conducted immediately after delivery on the ward, with the same weighting scale with ±5 g error.

The acquisition and storage of ultrasound volumes was done by placing the ultrasonic probe parallel to the longitudinal section of the fetal humerus and the volume of the fetal arm (VolA) was shown in three orthogonal planes: axial, sagittal and coronal (Fig.1). The markers were placed at the ends of the diaphysis. A transverse plane was then followed by a fractional lowering of the marker from one end of the bone to the other at a distance of 5.0 mm. The perimeter of the fetal arm in the transversal plane was manually drawn at each plane (Fig.2). At the end of the process, a three-dimensional arm volume (VolA) was stored on the ultrasound device.

4D view software (GE Medical Systems) already installed on the ultrasound device, was used for arm volume calculation using using automated modules for fetal arm volume (VolA).

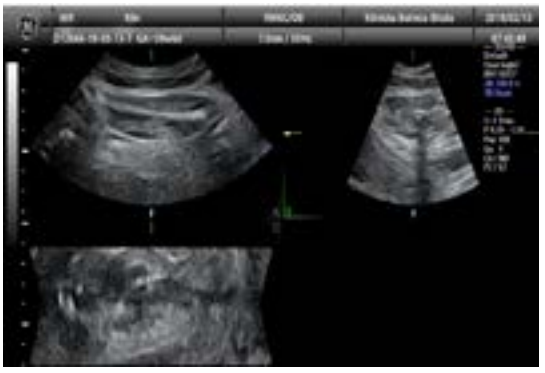

Fig.1. Fetal arm volume (VolA)

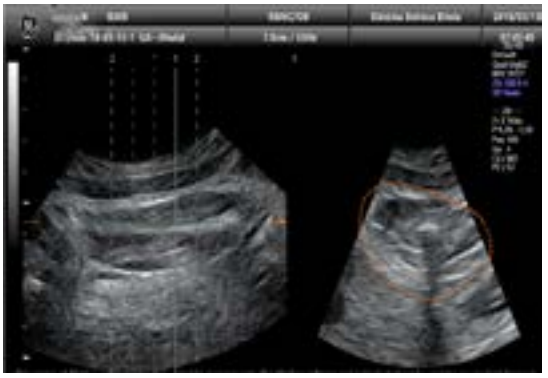

Fig.2. Perimeter drawing

Voluson E8 Expert ultrasound device with a BT10 software version with an abdominal volume matrix convex probe RM6C (2.1 to 6.1 MHz) was used for all ultrasound examinations that were performed transabdominally. The amount of amniotic fluid was not used as a selection criterion.

Statistical data processing was performed with SPSS for Windows ver. 17 by applying appropriate statistical methods: Descriptive statistics for describing quantitative variables, absolute and relative numbers and categorical variables. The linear regression (correlation) method utilized to determine the degree or strength of the existing dependency is used to determine the relationship, the dependence between two numerical series; P <0.05 was considered to be a statistically significant difference. Data are analyzed descriptively with ± standard deviation (SD), maximum and minimum values. Pearson's correlation coefficient (R) was used to estimate the relationship between VolA and BW.

The procedures of this study involving human participants are in concordance with the ethical standards of the Helsinki Declaration of 1964 and subsequent amendments, confirmed by a decision of the Ethics Committee of the Medical Faculty in Skopje.

RESULTS

A total of 106 patients were evaluated throughout the study period from 2018 until 2019. The patients' sociodemographic data are shown in Table 1. The analysis of the data showed that the average age of the women who gave birth in the study was 30.41 ± 4.8 years, with a median age of 30 years, a minimum of 16 and a maximum age of 45 years. All women were Caucasian, belonging to different nationality, Macedonian 81.8%, Albanian 3.4%, Turkish 2.5% and Roma 1.72%. The average gestational age in the study was 39 ± 1.17 gestational weeks, with a minimal gestation age of 33.6 and a maximal gestation age of 41.4 gestational weeks.

Table 1. Patients' sociodemographic data

Characteristics	Mean + SD (n = 116)	Minimum	Maximum
Age (yrs.)	30.41 ± 4.8	16	45
GA (weeks)	39 ± 1.17	33.6	41.4
Weight (kg)	77+8.5	61	95

Characteristics	Percentage	Characteristics	Percentage
Education		Nationality	
No education	1.72%	Macedonian	88.7%
Primary	11.2%	Albanian	5.1%
Secondary	36.2%	Turkish	2.58%
High	38.8%	Roma	1.72%
Other	0.86%	Others	1.9%
Social status		Smoking status	
Student	12%	Yes	63%
Employed	63%	No	37%
Unemployed	25%		

The average birth weight was 3253.2+ 435 g, with the smallest weight of 2150 g, and the largest weight of 4500 g. The mean volume of the arm was 33.975 ± 6.002 cm3. The minimal volume of the arm was 20.215 cm3, while the largest volume of the arm was 45.957 cm3.

Simple linear regression equation of birth weight on fractional AVol was generated from all the data from 106 fetuses that were analyzed. A positive correlation between arm volume and birth weight was shown with simple scatter plot of arm volume against birth weight (Fig. 3) and the Pearson correlation coefficient for fractional arm volume as the only sonographic parameter for the calculation of birth weight was r = 0.76, p < 0.001. With a simple linear regression analysis, a regression equation of birth weight was obtained: Estimated fetal weight = 49.785 x fractional volume of the arm + 1561.8. This regression model had a coefficient of determination (R2) = 0.4702. This new formula of arm volume by three-dimensional ultrasound had the values of error (-0.0125g ± 324.72g), percent error (-1.0445% + 10.6%), absolute error (262.12g + 191.65g), and absolute percent error (8.29% + 6.68%) in predicting birth weight.

To evaluate the precision of the new linear regression formula in predicting the actual birthweight, a comparison among the new formula and other formulas was conducted, including Lee`s formula (BW = 76.837xVolA+599.102) [5], Liang`s formula (BW=36.024xAVol+ 1088.60) [10], Vieira`s formula (BW = 43.23xAVol+681.59) [11] and New formula (BW=49.785*AVol + 1561.8) (Table 2). The mean absolute percentage errors (MAPE) were 8.79%, 28.23%, 33.42% and 7.98 %, respectively.

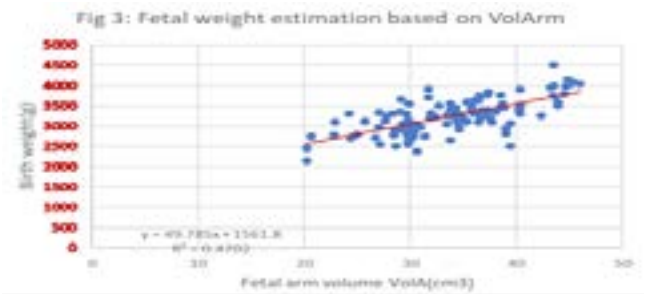

Table 2. Comparison of the mean error, mean absolute error, mean percentage error, and mean absolute percentage error and mean absolute percentage error with four different formulas (n = 116).

	LEE[5]	Liang[10]	Vieira [11]	New formula (AVol)
Mean Error (ME) (g)	43.61	940.74	1102.92	0.01
Mean Absolute Error (MAE) (g)	278.99	940.93	1102.92	251.40
Mean Percentage Error (MPE) (%)	0.83	28.22	33.42	-1.00
Mean Absolute Perecentage Error (MAPE) (%)	8.79	28.23	33.42	7.98

Error (E) = Estimated fetal weight (EFW) - Actual birthweight (BW)

Absolute error (AE) = Absolute ((EFW - BW)

Percentage error (PE) = (EFW - BW) / BW x 100%

Absolute percentage error (APE) = Absolute ((EFW - BW)/ BW x 100%

EFW = Estimated fetal weight

BW = Actual birth weigh

DISCUSSION

Birth weight prediction has traditionally relied upon anatomic measurements of the fetal head, limbs, and abdomen circumference (14). Hadlock and associates have reported predictive accuracy within 15% (±2 SD) of actual BW using functions containing fetal head circumference, abdominal circumference, and femur length (15). Other investigators, however, have suggested that an estimation of soft tissue mass (e.g., skin, fat, and muscle) may improve our ability to evaluate fetal intrauterine nutritional status and growth (16) and may be a reliable indicator of fetal growth abnormalities(17). Such abnormalities cannot be detected if soft tissue abnormalities, which represent the earliest manifestations of abnormal growth, are not taken into consideration unless these measurements are sensitive to the extend that they detect the subtle changes in the muscular or fatty tissue(18).

A review of the medical literature indicates that fractional limb volume has been used for EFW in relatively few countries, although when making these comparisons it is important to recognize that different prediction models have been variously applied (19–21). Most studies primarily examined late third-trimester fetuses and many reports acceptable reproducibility of these measurements.

The first studies in which fetal weight was calculated using the upper arm and thigh volume (VolArm and VolTh) with 3DUS reported more accurate birth weight results compared to calculations based on 2DUS formulas.

In the study of Liang et al. in 1997 the aim was to determine the usefulness and accuracy of fetal upper-arm volume in predicting birth weight. In a prospective study, 105 pregnant women were included, and the authors found that the upper arm volume correlated well with birth weight ($r = 0.92$, $n = 105$, $p < 0.0001$). Linear and polynomial regression was used, and a new formula was obtained, Birth weight = 1088.60 + 36.024 x Upper-arm volume. The accuracy of this new formula was compared with two previously developed Chinese equations predicting fetal weight, and other standard formulas which were formulas based on 2D biometric parameters. As a conclusion they found that their formula was more accurate in predicting birth weight than all the other formulas by traditional two-dimensional ultrasonography, either in error, percentage error, or absolute error (5).

Later, in the study of Lee et al. in 2001 where fractional limb volume as a new ultrasonographic parameter was introduced, new birth weight prediction model was used and they examined its practical validity for estimating fetal weight during late pregnancy. One hundred fetuses were scanned at a mean ± SD gestational age of 39.2 ± 1.2 weeks. Intraclass correlation indicated a significant degree of inter- and intra-observer reliability for fractional thigh and arm volumes. Fractional upper arm volume ($r = 0.83$) was strongly correlated with birth weight. The best prediction model (abdominal circumference and fractional thigh volume) gave weight estimates that deviated from actual birth weight by -0.025% ± 7.8%. They also used linear and polynomial regression, and thus obtained a new formula - Birth weight = 76.837 (ArmVol) + 599.102. This model generated a mean percent error of 0.1 ± 9.6, Absolute error in grams of –0.50 ± 359 and R2 was 0.68(6).

In the study of Vieira et al. in 2008 where the purpose was the evaluation of the accuracy of fetal upper arm volume, using three-dimensional ultrasound (3DUS), in the prediction of birth weight, with a prospective cross-sectional design, 25 pregnancies were evaluated. They found that fetal upper arm volume was strongly correlated to birth weight ($r=0.83$; $p<0.005$). Linear regression was the best equation [birth weight=681.59 + 43.23 x fetal upper arm volume]. The fetal upper arm volume mean error (0 g), mean absolute error (196.6 g) and mean percent absolute error (6.5%) were lower than using Shepard's formula; however, the difference did not reach significance ($p>0.05$). Birth weight predicted by fetal upper arm volume had a mean error lower than Hadlock's formula, but this difference was not statistically significant ($p>0.05$). Their conclusion was that the accuracy of fetal upper arm volume obtained through 3DUS is similar to the accuracy of bidimensional ultrasound in the prediction of birth weight(22).

In a prospective cross-sectional study, Chang et al. (2011) used 3D US to test the accuracy of fetal soft tissue volume of the upper arm measurement in predicting small for gestational age (SGA) fetuses. They concluded that fetal soft tissue volume of upper arm assessed by 3D US is a novel method to predict SGA fetuses(23).

In the study of Mack et al. in 2017 fetal soft tissue was assessed by using fractional limb volume as a proxy for in-utero nutritional status. They investigated automated fractional limb volume for rapid-estimate fetal weight assessment. Fifty neonates were delivered at 39.4 weeks' gestation. The Hadlock model generated the most accurate birth weight (0.31%) with a mean random error of ±7.9%. Despite systematic underestimations, the most precise results occurred with fractional arm volume (-9.1% ± 5.1%) and fractional thigh (-5.2% ± 5.2%) models. The size and distribution of these prediction errors were improved after correction for systematic errors. It was concluded that automated fractional limb volume measurements can improve the precision of weight predictions in third-trimester fetuses. Correction factors may be necessary to adjust underestimated systematic errors when using automated fractional limb volume with prediction models that are based on manual tracing of fetal limb soft tissue borders(24).

CONCLUSION

The upper-arm volume assessed by three-dimensional ultrasonography can accurately predict birth weight. Our study has at least validated the application of upper-arm volume by three-dimensional ultrasonography in estimating fetal weight. Further larger series are needed to confirm our findings.

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Profesional paper

PANDEMIA ME COVID 19 NË KLINIKËN UNIVERSITARE TË PSIKIATRISË – SHKUP DHE KËNAQËSIA E PACIENTËVE NGA PËRDORIMI I TELEMJEKËSISË GJATË MJEKIMIT TË TYRE NË SPITALIN DITOR.

Kadri Haxhihamza[1] , Slavica Arsova[1], Stojan Bajraktarov[1], Gjorgji Kalpak[1], Branislav Stefanovski[1], Antoni Novotni[1], Milos Milutinoviq[1].

[1]Klinika Universitare e Psikiatrisë – Shkup

Korrespondenca me:
Kadri Haxhihamza,
Klinika Psikiatrike Universitare, Shkup, Maqedonia e Veriut.
E-mail: kadrihadzihamza@gmail.com

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ABSTRAKT

Sfondi: Ekziston një interes në rritje për përdorimin e telemjekësisë si një mjet për ofrimin e kujdesit shëndetësor, veçanërisht në rrethana të pandemisë. Kjo është pjesërisht si rezultat i pajisjeve elektronike më të lira dhe më të thjeshtë për t'u përdorur dhe pjesërisht sepse rritja e kostove të kujdesit shëndetësor dhe pritjet e pacientëve kanë rritur nevojën për të gjetur mënyra alternative të kujdesit shëndetësor.

Parathënie: Telemjekësia dhe specifikisht, telepsikiatria, në mënyrë të shpejtë po bëhet një qasje e rëndësishme e kujdesit klinik. Në rastet kur efektivat mjekësore dhe pacientët e kanë shumë të vështirë për të kontaktuar në përputhje me udhëzimet kombëtare dhe rregullat e sjelljes në rast të pandemisë, telemjekësia (në këtë rast – telepsikiatria) është praktikisht i vetmi mjet adekuat për ofrimin e kujdesit efektiv klinik për pacientët por edhe për personelit mjekësor .

Materjalet dhe metodat: Një studim i kënaqësisë së pacientëve është ndërmarrë në Spitalin Ditor në Klinikën Universitare të Psikiatrisë në Shkup. Pyetësori vetë-raportues i modifikuar anonim (formulari i shkurtër i Pyetsorit për Kënaqësinë e Pacientëve (PSQ-18) që përfshin ndryshimet demografike, gjininë dhe moshën, u plotësua nga 28 pjesëmarrës. Mosha mesatare e subjekteve ishte 40.25 +/- 22 vjet, me një shumicë të vogël e meshkujve (18 pjesëmarrës) kundrejt femrave (11 pjesëmarrëse).

Rezultatet: Kënaqësia e përgjithshme me kujdesin psikiatrik ishte e lartë (80.22%). Asnjë nga variablat demografikë ose të tjera nuk tregon korrelacion relevant me kënaqësinë.

Diskutim: Punëtorët shëndetësorë kan obligim për të zvogëluar shkallën dhe kohëzgjatjen e kontakteve ballë për ballë me pacientët si rezultat i pandemisë, por duke i falenderuar telemjekësisë pacientat ishin në gjendje të kontaktojnë me mjekët e tyre praktikisht në çdo kohë.

Përfundim: Shumë profesionistë të shëndetit mendor janë duke përdorur gjerësisht, softuer komercial të shkarkuar nga Interneti për të siguruar kujdes direkt në shtëpinë e pacientit, por sqarimi i çështjeve kyqe dhe zgjidhjeve të mundshme janë të nevojshme për të informuar më mirë ata që duan të praktikojnë telemjekësinë me përgjegjësi.

Fjalët kyçe: telemjekësia, telepsikiatria, pacienti, kënaqësia.

HYRJE

Idea e telemjekësisë (TM) filloi me një grup mjekësh nga Maqedonia e Veriut që morën pjesë në seminarin e TM në SHBA (Alaska dhe Arizona) në vitin 2007. Disa seminare u organizuan në vitet në vijim në shtetet e rajonit të Ballkanit (Maqedonia e Veriut, Kosova, Mali i Zi dhe Shqipëria) për të siguruar njohuri themelore të TM për profesionistët mjekësorë dhe për të identifikuar palët e interesuara, dobësitë dhe pengesat e mundshme në shtetet përkatëse për krijimin e një sistemi të qëndrueshëm të TM. Për shkak të sfidave të ndryshme, disa shtete ishin të suksesshme në ndërtimin e një sistemi TM, ndërsa të tjerat jo. Ndër këto të fundit ishte Maqedonia e Veriut.1

Pandemia me COVID-19 ndryshoi mënyrën e ofrimit të kujdesit shëndetësor në të gjithë botën: njerëzit duhej të mbanin distancën e tyre, megjithatë ata duhej të merrnin trajtim shëndetësor. Në këto rrethana, kishte vetëm një metodë që mund të plotësonte të dy kërkesat: ruajtja e distancës fizike midis pacientit dhe mjekut ndërsa aplikohet trajtimi dhe mbrojtja maksimale e e shëndetit e të dyja palëve. Kjo ishte e mundëshme vetëm me përdorimin e TM.

Për shkak të specifikave të saja, telepiksiatria (TP) ishte edhe më e përshtatshme: falë zhvillimit të fundit të teknologjisë telekomunikuese, si psikiatrat ashtu dhe pacientët e tyre ishin në gjendje të kontaktojnë, të kalojnë përmes të procesit të psiko-diagnostikimit dhe madje të pranojnë rekomandimet mbi trajtimin farmakologjik dhe psikoterapinë, gjithnjë duke mbajtur distancën e nevojshme fizike gjatë procesit.2

METODAT

Një studim i kënaqësisë së pacientëve (e llojit të seksionit tërthor) është ndërmarrë në Spitalin Ditor (si departament i Klinikës Universitare të Psikiatrisë në Shkup) gjatë muajit prill të viti 2020. Pyetësori i aplikuar ishte anonim dhe vetë-raportues (forma i shkurtër e Pyetësorit të Kënaqësisë së Pacientit (PSQ-18) i modifikuar me variablat demografike, të gjinisë dhe moshës. Pyetsorin, i cili në esencë e kishte kënaqësinë e pacientëve me shërbimin në Spitalin ditor, u plotësua nga 28 pjesëmarrës.3

Mosha mesatare e subjekteve ishte 40.25 +/- 19 vjet, me një shumicë të vogël të meshkujve (18 pjesëmarrës) kundrejt femrave (11 pjesëmarrës). Shumica e pjesëmarrësve ishin nga kryeqyteti, Shkupi (26) dhe vetëm dy prej tyre ishin nga vendbanimet e afërta. Të gjithë ata ishin pacientë në repartin tonë gjatë disa muajve të fundit (4-6), si në periudhën e pandemisë CORONA 19 ashtu edhe para saj. Në këtë mënyrë pacientët ishin në gjendje të shohin ndryshimin midis trajtimeve "ballë për ballë" kundrejt TP.

Ekzistojnë shtatë nënklasa në PSQ-18: Kënaqësia e Përgjithshme, Cilësia Teknike, Mënyra Ndërpersonale, Komunikimi, Aspektet Financiare, Koha e kaluar me doktorin, Qasja dhe Komoditeti. Rezultatet e secilës nënklasë fitohen duke shtuar pikët e pyetjeve (artikujve) që e përbëjnë nënklasën dhe duke e ndarë me numrin e artikujve për të marrë një rezultat që do të krahasohet midis nënklasave. Për shkallën e përgjithshme, të gjitha rezultatet mblidhen. Nota më e lartë = kënaqësi më e madhe me trajtimin, për secilën nënklasë, si dhe për shkallën në tërësi.

Instrumenti, PSQ-18, përmban 18 artikuj duke përfshirë secilën nga shtatë dimensionet e kënaqësisë me kujdesin mjekësor të matur nga PSQ-III: kënaqësia e përgjithshme, cilësia teknike, mënyra ndërpersonale, komunikimi, aspektet financiare, koha e kaluar me mjekun , qasja dhe komoditeti. Rezultatet e nën-shkallëve PSQ-18 janë në thelb të ndërlidhura me homologët e tyre në shkallën e plotë (PSQ-III) dhe posedojnë besueshmëri të brendshme të përshtatshme. Për më tepër, si madhësia e koeficientëve të korrelacionit dhe modeli i përgjithshëm i korrelacioneve midis nënkallave PSQ-18 janë shumë të ngjashme me ato të vërejtura për PSQ-III. Këto analiza paraprake mbështesin përdorimin e PSQ-18 në situata kur nevoja për shkurtësi pamundëson administrimin e PSQ-III me gjatësi të plotë.

Rezultatet u paraqitën nga analiza sasiore përshkruese, në%.

Rezultatet

Të gjithë pacientët plotësuan pyetësorët e tyre. Kënaqësia e përgjithshme e pacientëve ishte e lartë-80.22%.

Përgjigjet për PSQ-18 në total janë paraqitur në tabelën 1.

	Jam shumë dakord (1)	Jam dakord(2)	Nuk jam i sigurtë (3)	Nuk jam dakord (4)	Fuqimisht nuk jam dakord (5)
Mjekët mirë e shpjegojnë arsyen e testeve mjekësore	20	2	1	2	3
Unë Mendoj se zyra e mjekut tim ka gjithçka që duhet të sigurojë kujdes të plotë mjekësor	18	4	2	1	3
Kujdesi mjekësor që kam marrë është pothuajse i përsosur	14	6	3	2	3
Ndonjëherë mjekët më bëjnë të pyes veten nëse diagnoza e tyre është e saktë	10	10	4	1	3
Ndihem i sigurt se mund të marr kujdesin mjekësor që më nevojitet pa u ngarkuar financiarisht	3	2	4	13	6
Kur shkoj për kontrollim mjekësor, ata janë të kujdesshëm për të kontrolluar gjithçka kur më trajtojnë dhe ekzaminojnë	14	9	1	0	4
Më duhet të paguaj më shumë kujdesin tim mjekësor sesa mund ta përballoj	2	3	4	11	8
Kam qasje të lehtë tek specialistët mjekësorë që më duhen	10	10	3	2	3
Aty ku marr kujdesin mjekësor, njerëzit duhet të presin shumë gjatë për trajtim urgjent	2	2	8	8	8
Mjekët veprojnë shumë afarist dhe jopersonal ndaj meje	4	1	6	7	10
Mjekët e mi më trajtojnë në një mënyrë shumë miqësore dhe të sjellshme	20	5	0	1	2
Ata që ofrojnë kujdesin tim mjekësor ndonjëherë nxitojnë shumë kur më trajtojnë	1	5	4	9	9
Mjekët ndonjëherë injorojnë ato që unë u them atyre	2	2	6	8	10
Kam disa dyshime për aftësinë e mjekëve që më trajtojnë	0	1	5	8	14
Mjekët zakonisht kalojnë mjaft kohë me mua	12	8	2	4	2
E kam të vështirë të marr një takim për kujdesin mjekësor menjëherë	2	3	4	10	9
Unë jam i pakënaqur me disa gjëra në lidhje me kujdesin mjekësor që marr	1	3	6	9	9
Unë jam në gjendje të marr kujdes mjekësor sa herë që kam nevojë	17	3	3	3	2

(Tabela 1)

Sa i përket nënshkallave të tjera, rezultatet janë paraqitur në tabelën2.

Nënshkallat	Mesatarja e këtyre moduleve
Kënaqësia e përgjithshme (p. 3, 17)	82
Cilësia teknike (p. 2, 4, 6, 14)	69
Mënyra (sjellja)ndërnjerëzore (p. 10, 11)	73
Komunikim me pacientin (p. 1, 13)	78
Aspektet financiare (p.5,7)	102.5
Koha e kaluar me mjekun (p. 12, 15)	82
Qasja dhe komoditeti (p. 8, 9, 16, 18)	86.25

(Tabela 2)

Në sistemin tonë shëndetësor është mjaft e vështirë për pacientët të bëjnë një takim me specialist posaçërisht nëse ai jeton jashtë Shkupit: është një detyrë ngarkuese, veçanërisht në aspektin financiar. Prandaj, nuk është për t'u habitur që nënkategoritë "Aspektet financiare (p.5,7)" dhe "Qasja dhe komoditeti (p. 8, 9, 16, 18)" kanë mesataren më të lartë.

Duke i analizuar variablat e shtuara (gjinia, mosha, vendi i jetesës), nuk është detektuar ndonjë ndryshim i rëndësishëm.

DISKUTIM

Pacientët zakonisht vijnë në Spitalin Ditor çdo ditë pune rreth orës 08.30 dhe largohen rreth orës 14.30. Gjatë kësaj periudhe kohore ata angazhohen për aktivitete të ndryshme në repartin tonë (punë në grup, terapi e punës krijuese, psikoterapi etj.). Por, për pjesën tjetër të ditës dhe në fundjavë ata janë vetë. Shpesh, pacientët shprehin dëshirën e tyre të paktën të jenë në kontakt me ne (mjekët) edhe kur janë jashtë repartit tonë. Për të përmbushur angazhimin tonë si mjekë, ne (mjekët Arsova, Vujoviç, Kalpak dhe unë) ramë dakord të jemi në dispozicion të pacientëve tanë me anë të TP pasdite nga ora 18.00 deri në orën 20.00. Kjo u përshëndet nga pacientët sepse kjo do të zvogëlonte frikën e tyre se "ata nuk do të dinin se çfarë të bënin nëse situata e tyre përkeqësohet në mbrëmje". Fatkeqësisht, përpjekjet tona u pritën me mosbesim.

Sistemi shëndetësor në Maqedoninë e Veriut ishte mosbesues ndaj TM për mjaft kohë, por pandemia COVID-19 i ndryshoi të gjitha, pasi ishte e qartë se vetëm TM mund të plotësonte kërkesat e OBSH në lidhje me pandeminë.

Dilema aktuale me të cilën përballen sistemet e kujdesit shëndetësor në të gjithë botën është se si të ruhet aftësia për të ofruar shërbim jo vetëm për ata të prekur me COVID-19, por edhe për pacientët që vuajnë nga sëmundje të tjera akute dhe kronike, ndërsa mbrojnë mjekët, infermierët dhe personelin tjetër shëndetësor ndihmës. Nuk është për t'u habitur që sistemet shëndetësore në të gjithë botën tani po përdorin telemjekësinë (pa dallim se si ata e quajnë) për të siguruar kujdesin gjatë mbajtjes së pacientëve në shtëpitë e tyre. Përdorimi masiv i telemjeksisë tregon dobinë e saj si një mjet efektiv për të respektuar të ashtuquajturën "distancë shoqërore" në mjediset klinike ose mjedise të tjera.4

Duhej të zvogëlonim shkallën dhe kohëzgjatjen e kontakteve tona me pacientët: dy herë në javë për rreth dy orë duke respektuar të gjitha masat paraprake (veshja e maskave për fytyrë, mbajtja e distancës etj). Sidoqoftë, falë sistemit TP, pacientët ishin në gjendje të kontaktojnë me mjekët e tyre praktikisht në çdo kohë. Nga pikëpamja e pacientëve, ata (ndoshta) humbën njëfarë kohe kontakti "të drejtpërdrejtë" (ballë për ballë) por ata fituan shumë kohë (TP) për të qenë me mjekët e tyre.

Ndoshta shembujt më të mirë se si ndjehen pacientët për këtë lloj trajtimi janë përgjigjet në pyetjen numër tetë ("Unë kam qasje të lehtë te specialistët mjekësorë që më duhen") dhe tetëmbëdhjetë ("Unë jam në gjendje të marr kujdes mjekësor sa herë që kam nevojë"): më shumë se 71% e pjesëmarrësve ishin "shumë dakord» ose «dakord» me këtë deklaratë të dhënë në pyetësor.

PËRFUNDIME

Profesionistët e shëndetit mendor sot janë duke përdorur teknologji të lira në dispozicion përmes përdorimit të gjërë të kompjuterave personal, Internetit, pajisjeve mobile dhe programeve videokonferencuese për të ofruar shërbime të shëndetit mendor. Për shembull, shumë profesionistë të shëndetit mendor janë duke përdorur gjerësisht, softuer komercial të shkarkuar nga Interneti për të siguruar kujdes direkt në shtëpinë e një pacienti ose në mjedis tjetër jashtinstitucional.2

Kjo është një fushë në zhvillim e zhvillimi të shpejtë, dhe rreziqet dhe përfitimet e shërbimeve shëndetësore telementale të ofruara duke përdorur teknologji videokonferencimi nuk janë diskutuar ose adresuar gjerësisht në trajnimin zyrtar të praktikuesve të shëndetit mendor. Prandaj, sqarimi cilësor i çështjeve kryesore dhe zgjidhjeve të mundshme janë të nevojshme për të informuar më mirë ata që duan të praktikojnë me përgjegjësi.

Përhapja e pajisjeve dhe softverëve relativisht të lirë lejon madje edhe shtetet në tranzicion, si Maqedonia e Veriut, me burime dhe kapacitete të kufizuara, të zhvillojnë veprimtari elementare por efektive të TP. Edhe duke pasur parasysh që ky sistem TP u soll në jetë nën presionin e pandemive me COVID-19, ai ende tregon gjallërinë e Sektorit të Shëndetit Publik të paktën, të reagojë ndaj kërcënimeve për shëndetin publik kur është e nevojshme.

Në planin afatgjatë, sistemi i ardhshëm shëndetësor duhet të inkurajojë pacientët për të përdorur TM por edhe për të dekurajuar përdorimin e papërshtatshëm të shërbimeve. Në mënyrë ideale, sistemi do të zbatohej në të gjithë shtetin ose rajonin e gjerë për efikasitet maksimal. Telemjekësia ofron mjete për zbatimin e trageteve në pikën e nevojës.5

Për momentin, bashkëpunimi midis Klinikës Universitare të Psikiatrisë, Fondit të Sigurimit Shëndetësor dhe Ministrisë së Shëndetësisë është në një nivel shumë të lartë, duke lejuar që Klinika të ketë konsultime për TP "nga shtëpia", si për pacientët ashtu edhe për stafin mjekësor.

Mund vetëm të shpresojmë se ky sistem do të vazhdojë të funksionojë (dhe, natyrisht, të përsoset) pasi të mbarojë

pandemia sepse një thënie e vjetër thotë: “Çdo e keqe, për të mirë “.

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Profesional paper

ПРОЦЕНКА НА ПРИСУСТВО НА АНКСИОЗНОСТ КАЈ РОДИТЕЛИТЕ НА ДЕЦА ВО ПУБЕРТЕТ НА ТЕРИТОРИЈА НА ОПШТИНА ГОСТИВАР

Емире Билали[1], Елена Ќосевска[2], Бети Зафирова Ивановска[3]

[1]Основно училиште "Перпарими", Гостивар, Република Северна Македонија

[2]Институт за јавно здравје на Република СеверналМакедонија, Медицински факултет, Универзитет „Св. Кирил и Методиј", Скопје, Република Северна Македонија

[3]Институт за епидемиологија и биостатистика со медицинска информатика, Медицински факултет, Универзитет „Св. Кирил и Методиј", Скопје, Република Северна Македонија

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ИЗВАДОК

Вовед. Анксиозност е природниот одговор на телото за стрес. Основна карактеристика на ова нарушување е несоодветно ниво на вознемиреност и страв што се манифестира во нормалното функционирање на детето. Анксиозноста на родителите може да има негативно влијание врз здравјето на децата особено во период на развој –пубертетот.

Цел на трудот: Да се одреди присуство на анксиозност, депресија и страв кај родителите на деца кои се во период на пубертет во општина Гостивар.

Материјал и методи: Во оваа пресечна студија беа анализирани 300 родители на 150 ученици од VIII-мо и IX-то одделение, и 150 ученици од средни училишта на територијата на општина Гостивар. Беше користена ДАСС (Скала за Депресивност, Анксиозност и Стрес), составена од 42 прашања кои вклучуваат три скали за самооценување. Секоја скала содржи 14 прашања, поделени во подскали од 2-5 прашања со слична содржина. Резултатот од секој испитаник, односно родител за секоја подскала се оценуваше според индексот за оценување на интензитетот на депресијата, анксиозноста и стресот. Податоците добиени од испитувањето беа анализирани со статистичкиот програм SPSS for windows 23,0. За споредување на полот на анксиозни и неанксиозни родители, депресивни и недепресивни родители, родители во стрес и без стрес, беше користен Chi-square test. За сигнификантни се сметани сите оние резултати каде вредноста на $p < 0,05$.

Резултати и дискусија: Според резултатите од ДАСС скалата, преваленцијата на депресија кај родителите беше 23.34%, односно 70 родители манифестираа депресивност, преваленцијата на анксиозност беше 28.7%, односно 86 анкетирани родители манифестираа анксиозно нарушување, додека преваленцијата на стрес беше 22%, односно кај 66 родители според одговорите на прашањата се препознава стресна состојба. Резултатите од истражувањето покажаа дека полот немаше сигнификантно влијание на појавата на депресија, анксиозност и стрес кај родителите на учениците ($p=0.074$, $p=0.12$, и $p=0.054$), консеквентно. Не беше најдена статистичка сигнификантна разлика меѓу родителите со и без депресија, со и без анксиозност, и со и без стрес, а во зависност од нивниот пол ($p>0.05$). Но незначајно почесто овие состојби се манифестираат кај мајките на учениците. Детството и адолесценцијата е основна фаза на ризик за развој на симптоми и синдроми на анксиозност што може да варира од минливи лесни симптоми до анксиозно пореметување. Анксиозноста се однесува на одговор на мозокот на опасност, стимули што организмот активно ќе се обиде да ги избегне. Овој одговор на мозокот е основна емоција која е веќе присутна во детството, при што изразите паѓаат на континиум од блага до тешка. Родителството и анксиозноста беа пронајдени како интеракција меѓусебно со текот на времето.

Заклучок: Согласно со резултатите од оваа студија се покажа присуство на депресија, страв и анксиозност кај родителите, со почеста застапеност на анксиозноста во споредба со депресијата и стресот и незначајно почеста манифестација кај мајките на децата во пубертет во општина Гостивар.

Клучни зборови: анксиозност, родители, деца, пубертет.

ВОВЕД

Развојната психологија е насочена кон истражување на однесувањето на децата во секој момент од нивниот живот, и промените кои се случуваат од еден во друг временски период. Во трудот вниманието е насочено кон согледување на влијанието на анксиозноста кај родителите врз здравјето на децата во период на пубертет. (1)

Анксиозност е природниот одговор на телото за стрес. Тоа е чувство на страв или страв за тоа што ќе дојде. Анксиозните нарушувања се меѓу најчестите ментални нарушувања во детството и адолесценцијата. Основна карактеристика на овие нарушувања е несоодветно ниво на вознемиреност и страв што се манифестира во нормалното функционирање на детето. (2)Постојат повеќе поврзани фактори кои се асоцираат со анксиозните растројства. Причините за одредено растројство се различни и не е секогаш лесно да се утврди причината за секој случај. (6)

За време на адолесценцијата, има и драматични промени во мотивацијата, социјалното однесување и стапката на психопатологија, особено кај девојчињата. Една од најзначајните општествени промени за време на адолесценцијата е зголемувањето на независноста од родителските личности и соодветното потпирање на блиски пријателства. Прекумерната заштита е ризик од анксиозни нарушувања.

Со набљудување на однесувањето на децата и родителите, забележано е дека само присуството на родителите кај некои деца може да има позитивен, неутрален и негативен ефект. Анксиозноста на родителите може да има негативно влијание врз здравјето на децата особено во период на развој, односно во периодот на пубертет.

ЦЕЛ НА ТРУДОТ

Да се одреди присуството на анксиозност, депресија и страв кај родителите на деца кои се во период на пубертет во општина Гостивар.

МАТЕРИЈАЛ И МЕТОДИ

Во оваа пресечна студија беа анализирани 300 родители на 150 ученици од VIII-мо и IX-то одделение, и 150 ученици од средни училишта на територијата на општина Гостивар. Како инструмент на истражување беше користена ДАСС (Скала за Депресивност, Анксиозност и Стрес), составена од 42 прашања кои вклучуваат три скали за самооценување, дизајнирани за мерење на негативните емоционални симптоми на депресија, анксиозност и стрес. Секоја скала содржи 14 прашања, поделени во подскали од 2-5 прашања со слична содржина. Од испитаниците се бараше да ја користат скалата на интензитет/фреквенцијата од 4 точки за да го оценат степенот до кој тие го доживеале секој од симптомите во текот на изминатата недела (0- Воопшто не се применила кај мене; 1- се применила кај мене до одреден степен, или неколку пати;2- се применила кај мене во значителна мера, или еден добар дел од времето; 3- многу се применила кај мене, или поголемиот дел од времето).

Резултатот од секој испитаник, односно родител за секоја подскала се оценуваше според индексот за оценување на интензитетот на депресијата, анксиозноста и стресот, како што е даден во табелата.

Табела 1. Скала за оценување на интензитетот на депресијата, анксиозноста и стресот

	Депресија	Анксиозност	Стрес
Нормален	0 - 9	0 - 7	0 - 14
Лесен	10 - 13	8 - 9	15 - 18
Просечен	14 - 20	10 - 14	19 - 25
Тежок	21 - 27	15 - 19	26 - 33
Многу тежок	28+	20+	34+

СТАТИСТИЧКА АНАЛИЗА

Податоците добиени од испитувањето беа анализирани со статистичкиот програм SPSS for windows 23,0. Коефициент на сигурност (Cronbach's alpha) беше пресметан за трите подскали на ДАСС за да се одреди степенот на внатрешна конзистентност меѓу прашањата од подскалите. Вредностите на Cronbach's alpha од 0.928 за подскалата за депресија, 0.92 за подскалата за анксиозност, и 0.915 за подскалата за стрес сугерираат на заклучок за висок степен на внатрешна конзистентност во трите субскали, односно дека ДАСС скалата е сигурна. Сите податоци од интерес за изработка на трудот се табеларно и графички прикажани. Дескрипцијата на податоците е направена со релативни и апсолутни броеви. За споредување на полот на анксиозни и неанксиозни родители, депресивни и недепресивни родители, родители во стрес и без стрес, беше користен Chi-square test. За сигнификантни се сметани сите оние резултати каде вредноста на $p < 0,05$.

РЕЗУЛТАТИ

Во оваа истражување беа анализирани 300 родители на 150 ученици од VIII-мо и IX-то одделение, и 150 ученици од средни училишта на територијата на општина Гостивар.

Табела број 2 ги прикажува резултатите од ДАСС скалата која се однесува на подскалата за депресивност. Како најчесто вистинити, односно применливи родителите ги акцентираа следните прашања: үТешко ми беше да преземам иницијатива за да правам нештоү – 16.67% (50), и ү Воопшто не можев да доживеам некое позитивно чувство ү - 15.33% (46). За овие две прашања беа добиени и највисоки просечни скорови – 0.567±0.88, и 0.55±0.82, консеквентно.

ДАСС – скала за депресивност

Табела 2. Симптоми на депресија

бр	варијабла	0	1	2	3	mean ± SD
3	Воопшто не можев да доживеам некое позитивно чувство	189 (63)	65 (21.67)	34 (11.33)	12 (4)	0.55 ± 0.82
5	Едноставно не изгледаше дека можам да продолжам	206 (68.67)	69 (23)	23 (7.67)	2 (0.67)	0.40 ± 0.66
10	Се чуствував како да немам ништо за да одам понатаму	210 (70)	50 (16.67)	26 (8.67)	14 (4.67)	0.48 ± 0.84
13	Се чувствував тажен и во депресија	212 (70.67)	55 (18.33)	19 (6.33)	14 (4.67)	0.45 ± 0.81
16	Се чувствував како да изгубив интерес за се	206 (68.67)	60 (20)	23 (7.67)	11 (3.67)	0.46 ± 0.79
17	Се чувствував како да не вредам многу како личност	216 (72)	52 (17.33)	19 (6.33)	13 (4.33)	0.43 ± 0.79
21	Чувствувам дека животот не вреди да се живее	223 (74.33)	39 (13)	28 (9.33)	10 (3.33)	0.42 ± 0.79
24	Изгледаше дека не можам да уживам во работите кои ги правев	194 (64.67)	73 (24.33)	20 (6.67)	13 (4.33)	0.51 ± 0.80
26	Се чувствував вознемирен и тажен	194 (64.67)	76 (25.33)	20 (6.67)	10 (3.33)	0.49 ± 0.76
31	Не бев во состојба да бидам ентузијаст за нешто	200 (66.67)	76 (25.33)	19 (6.33)	5 (1.67)	0.43 ± 0.69
34	Се чувствував како да сум сосема безвреден	226 (75.33)	41 (13.67)	18 (6)	15 (5)	0.41 ± 0.81
37	Не можев да видам ништо во иднина за да се надевам	216 (72)	52 (17.33)	23 (7.67)	9 (3)	0.42 ± 0.76
38	Се чувствував како животот да нема смисла	223 (74.33)	46 (15.33)	20 (6.67)	11 (3.67)	0.39 ± 0.77
42	Тешко ми беше да преземам иницијатива за да правам нешто	189 (63)	61 (20.33)	35 (11.67)	15 (5)	0.59 ± 0.88

0 воопшто не се применила кај мене Cronbach`s alpha = 0.928

1 се применила кај мене до одреден степен, или неколку пати

2 се применила кај мене во значителна мера, или еден добар дел од времето

3 многу се применила кај мене, или поголемиот дел од времето

ДАСС – скала за анксиозност

Табелата за анксиозност ги прикажува резултатите од ДАСС скалата која се однесува на подскалата за анксиозност. Како најчесто вистинити, односно применливи родителите ги акцентираа следните прашања: ү Бев свесен за сушењето на мојата устаү – 14% (42), „ Значително се потевү - 13.67% (41), и „ Се соочував со тресењеү - 13.67% (41) . Просечните скорови за овие прашања изнесуваа – 0.56±0.85, и 0.567±0.82, и, 0.557±0.82, консеквентно.

Табела 3. Симптоми на анксиозност

бр	варијабла	0	1	2	3	mean ± SD
2	Бев свесен за сушењето на мојата уста	189 (63)	69 (23)	27 (9)	15 (5)	0.56 ± 0.85
4	Имав потешкотии со дишењето (на пр. значително побрзо дишење, дишење во отсуство на физички напор)	203 (67.67)	66 (22)	22 (7.33)	9 (3)	0.46 ± 0.76
7	Имав чувсто дека се тресам (на пр. нозете ми се тресат)	184 (61.33)	86 (28.67)	16 (5.33)	14 (4.67)	0.53 ± 0.79
9	Се најдов себеси во ситуации кои ме правеа многу анксиозен и полесно ми беше штом завршеа	187 (62.33)	77 (25.67)	25 (8.33)	11 (3.67)	0.53 ± 0.79
15	Имав чувство на апатија	199 (66.33)	72 (24)	19 (6.33)	10 (3.33)	0.47 ± 0.76
19	Значително се потев (на пр: потење на раце) и во отсуство на високи температури и физички напор	182 (60.67)	77 (25.67)	26 (8.67)	15 (5)	0.57 ± 0.82
20	Се чувствував исплашено без некоја добра причина	211 (70.33)	61 (20.33)	17 (5.67)	11 (3.67)	0.43 ± 0.76
23	Имав потешкотии при џвакање	227 (75.67)	39 (13)	29 (9.67)	5 (1.67)	0.37 ± 0.73
25	Бев свесен за работата на срцето во отсуство на физички напор (на пр: чувство на зголемување на отчукувањата на срцето, срцето губеше едно отчукување)	196 (65.33)	71 (23.67)	19 (6.33)	14 (4.67)	0.51 ± 0.81
28	Се чувствував како да сум блиску до паника	197 (65.67)	63 (21)	27 (9)	13 (4.33)	0.52 ± 0.83
30	Се плашев дека ќе бидам „исфрлен“ од некои неважни и непознати работи	208 (69.33)	67 (22.33)	21 (7)	4 (1.33)	0.40 ± 0.68
36	Се чувствував преплашен	221 (73.67)	57 (19)	17 (5.67)	5 (1.67)	0.35 ± 0.67
40	Се нервирав за ситуациите во кои можев да испаничам и да изгледам како будала	206 (68.67)	64 (21.33)	15 (5)	15 (5)	0.46 ± 0.81
41	Се соочував со тресење (на пр: на рацете)	194 (64.67)	65 (21.67)	24 (8)	17 (5.67)	0.56 ± 0.85

0 воопшто не се применила кај мене Cronbach`s alpha = 0.92

1 се применила кај мене до одреден степен, или неколку пати

2 се применила кај мене во значителна мера, или еден добар дел од времето

3 многу се применила кај мене, или поголемиот дел од времето

ДАСС – скала за стрес

Табела број 4 ги прикажува резултатите од ДАСС скалата која се однесува на подскалата за стрес. Како најчесто вистинити, односно применливи родителите ги акцентираа следните прашања: ү Претерано реагирав на одредени ситуацииү – 18.33% (51), „ Бев нестрплив кога на некој начин ќе задоцнев- 19.33% (58), и „ Бев многу нервозенү - 21% (63) . Просечните скорови за овие прашања изнесуваа – 0.78±0.87, 0.76±0.93, и, 0.747±0.96, консеквентно.

Табела 4. Симптоми на стрес

бр	варијабла	0	1	2	3	mean ± SD
1	Се наоѓам себеси загрижен за прилично незначајни работи	184 (61.33)	62 (20.67)	34 (11.33)	20 (6.67)	0.63 ± 0.93
6	Претерано реагирав во одредени ситуации	137 (45.67)	108 (36)	39 (13)	16 (5.33)	0.78 ± 0.87
8	Ми беше тешко да се опуштам	185 (61.67)	75 (25)	27 (9)	13 (4.33)	0.56 ± 0.83
11	Сосема лесно се вознемирував	164 (54.67)	82 (27.33)	31 (10.33)	23 (7.67)	0.71 ± 0.94
12	Се чувствував како да користам нервозна енергија	176 (58.67)	77 (25.67)	28 (9.33)	19 (6.33)	0.63 ± 0.89

14	Бев нестрплив кога на некој начин ќе задоцнев (на пр:во лифтови, сообраќај, кога ме чекаа)	152 (50.67)	90 (30)	36 (12)	22 (7.33)	0.76 ± 0.93
18	Се чувствував како да сум премногу чувствителен	163 (54.33)	85 (28.33)	33 (11)	19 (6.33)	0.69 ± 0.90
22	Тешко ми беше да се одморам	177 (59)	87 (29)	26 (8.67)	10 (3.33)	0.56 ± 0.79
27	Бев многу нервозен	163 (54.33)	74 (24.67)	39 (13)	24 (8)	0.75 ± 0.96
29	Тешко ми беше да се смирам откако ќе се вознемирев за нешто	162 (54)	91 (30.33)	31 (10.33)	16 (5.33)	0.67 ± 0.87
32	Тешко ми беше да толерирам прекини во нешто што правев	181 (60.33)	77 (25.67)	32 (10.67)	10 (3.33)	0.57 ± 0.81
33	Бев во состојба на нервна напнатост	209 (69.67)	64 (21.33)	16 (5.33)	11 (3.67)	0.43 ± 0.76
35	Бев нетолерантен кон се што ме спречуваше да напредувам во она што го правев	202 (67.33)	60 (20)	30 (10)	8 (2.67)	0.48 ± 0.78
39	Се наоѓав себеси нервозен	179 (59.67)	86 (28.67)	23 (7.67)	12 (4)	0.56 ± 0.81

0 воопшто не се применила кај мене Cronbach`s alpha = 0.915

1 се применила кај мене до одреден степен, или неколку пати

2 се применила кај мене во значителна мера, или еден добар дел од времето

3 многу се применила кај мене, или поголемиот дел од времето

Според резултатите за ДАСС скалата, преваленцијата на депресија кај родителите беше 23.34%,односно 70 родители манифестираа депресивност,преваленцијата на анксиозност беше 28.7%, односно 86 анкетирани родители манифестираат анксиозно нарушување, додека преваленцијата на стрес беше 22%, односно кај 66 родители според одговорите на прашањата се препознава стресна состојба. Во табела број 5 презентиран е и степенот на овие нарушувања кај анкетираните родителите.

Табела 5. Скала за оценка на интензитетот на депресијата, анксиозноста и стресот

	Депресија	Анксиозност	Стрес
Нормален	230 (76.67)	214 (71.33)	234 (78)
Лесен	21 (7)	17 (5.67)	26 (8.67)
Просечен	17 (5.67)	26 (8.67)	19 (6.33
Тежок	23 (7.67)	11 (3.67)	17 (5.67)
Многу тежок	9 (3)	32 (10.67)	4 (1.33)

Резултатите од истражувањето покажаа дека полот немаше сигнификантно влијание на појавата на депресија, анксиозност и стрес кај родителите на учениците (p=0.074, p=0.12, и p=0.054), консеквентно. Сите три состојби незначајно почесто ги манифестираа мајките на учениците. Според дадените одговори, депресија беше препознаена кај 29.4% (30) испитанички, а кај 20.2% (40) испитаници; анксиозни беа 34.3% (35) испитаници од женски пол, и ј 25.8% (51) од машки пол; стрес манифестираа 28.4% (29) испитанички и 18.7% (37) испитаници.

Табела 6. Разлика меѓу родителите со и без депресија, со и без анксиозност, и со и без стрес, според пол

родители пол	Депресија		Анксиозност		Стрес	
	има	нема	има	нема	има	нема
машки	40 (20.20)	158 (79.80)	51 (25.76)	147 (74.24)	37 (18.69)	161 (81.31)
женски	30 (29.41)	72 (70.59)	35 (34.31)	67 (65.69)	29 (28.43)	73 (71.57)
p value	X2=3.2 p=0.074 ns		X2=2.4 p=0.12 ns		X2=3.7 p=0.054 ns	

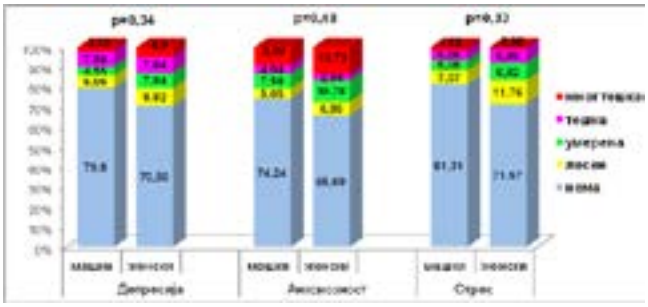
p value (Pearson Chi-square)

Не беше најдена статистичка сигнификантна разлика меѓу родителите со и без депресија, со и без анксиозност,

и со и без стрес, а во зависност од нивниот пол (p>0.05).

Многу тешка форма на депресија и анксиозност манифестираа преку своите одговори незначајно почесто испитаниците од женски пол – 4.9% (5) наспроти 2% (4), и 13.7% (14) наспроти 9.1% (18), консеквеентно, додека многу тешка стресна состојба кај 0.98% (1) една испитаничка и 1.5% (3) испитаници.

Слика 1. Форми на депресија, анксиозност и стрес според пол на родители



Pearson Chi-square: 4,64067, df=4, p=,326199 депресија

Pearson Chi-square: 3,45818, df=4, p=,484269 анксиозност

Pearson Chi-square: 4,57877, df=4, p=,333316 стрес

ДИСКУСИЈА

Кога се говори за психосоцијалниот развој на децата и адолесцентите, односите во семејството, пред сè односите меѓу родителите и децата, се покажува дека тие се како еден од најзначајните фактори. Имено, сите истражувања покажуваат дека односот помеѓу родителите и децата е важен за успешната социјализација на децата. Родители во состојба на стрес не се усогласени со потребите на детето и нивните емоции ги оставаат без поддршка. (8).

Анксиозноста е најчеста психијатриско нарушување и има долгорочни, компромитирачки ефекти врз односот мајка-новороденче и развојот на детето. Доенчето постојано се соочува со клима на негативно влијание што го нарушува интерактивното искуство на новороденчето и мајката. (13)

Анксиозноста е емоција, непријатно чувство на напнатост придружено со физиолошки промени, но и грижи и стравови, што значи дека неразбирањето на емоциите што се јавуваат во одредени ситуации, секако ќе придонесе за чувство на напнатост и несигурност на личноста. Според Мурис, епидемиолошките студии покажале дека анксиозните нарушувања се меѓу најчестите форми на психопатологија во детството / адолесценцијата и дека кај одреден процент од деца оваа вознемиреност може да биде хронична и да трае до зрелоста. Бројни фактори придонесуваат за појава на симптоми на вознемиреност, од генетика, темперамент и својства на личност, негативни животни искуства до семејни односи. Девојките обично имаат поизразена вознемиреност, што исто така беше добиено во нашата студија. (14)

Детството и адолесценцијата е основна фаза на ризик за развој на симптоми и синдроми на анксиозност што може да варира од минливи лесни симптоми до анксиозно пореметување. (3)

Адолесцентите кои се нервозни, напнати, вознемирени, раздразливи и тажни се повеќе склони кон развој на вознемиреност, која се карактеризира токму со загриженост и напнатост. Се покажа дека невротизмот е значително поврзан со вознемиреност и во истражувањето спроведено од Mohorić T., и сор. (14)

Родителството и вознемиреноста беа пронајдени како интеракција меѓусебно со текот на времето. На 4-годишна возраст повисоките нивоа на родителска непријателност доведоа до мало зголемување на вознемиреноста на возраст од 5 години, а зголемената вознемиреност на возраст од 5 години доведе до зголемено ниво на непријателство на родители од 6 години. Иако големината на овие откритија беше мала, тие укажуваат на тоа дека раниот третман на детска вознемиреност треба да вклучува и интервенција на родители и директен третман на симптомите на вознемиреност на детето.(5)

Проценките покажуваат дека приближно 10 до 20% од сите деца развиваат некаков вид анксиозни нарушувања. Тие се присутни кај деца од двата пола, иако се покажало дека некои анксиозни нарушувања се почести кај девојчињата. Нарушувања на вознемиреност може да се дијагностицираат по шестгодишна возраст. Раното откритие и соодветниот третман можат значително да помогнат во можните негативни ефекти што ги имаат овие нарушувања врз социјалниот и семејниот живот, како и врз перформансите на детето во училиште. (2)

Повеќето студии кои што го испитуваат односот на личноста на родителите и квалитетот на родителството се фокусираат на односот помеѓу нарушувања во психолошкото функционирање и родителско однесување. (10)

Резултатите од истражувањата покажуваат дека родителите доживуваат благ стрес, а главните извори на родителски стрес се приврзаност кон дете, комуникација со дете, дисциплина на детето и негова желба. Резултатите од истражувањето покажуваат дека најчестите практики за одгледување се прифаќање и хармонија и стимуланси за самореализација, додека авторитарните процедури се поретки, а казните се најретки. Родителите кои имаат повисоки нивоа на стрес се понегативни во комуникацијата со своите деца и помалку се вклучени во нивните секојдневни активности. Тие исто така користат повеќе авторитарни практики за родителство, што значи дека се порестриктивни, користат построги дисциплински мерки и покажуваат помалку љубов и топлина. (16)

Младите во когнитивна интервенција на однесувањето во семејната група пријавиле значително поголемо опаѓање на симптомите на анксиозност и депресија на 6-, 12- и 18-месеци споредено со младите во состојба на писмени информации. Младите со повисоки почетни нивоа на секој симптом (на пример, вознемиреност) пријавиле поголемо опаѓање на другиот симптом (на пр. депресија) од 0 до 6-месеци во когнитивна интервенција на однесувањето во семејната група. (9)

Според студијата на Факултетот за медицина на Универзитетот во Њујорк спроведена на повеќе од 20.000 семејства, 11% од децата со депресивни татковци, 19% од децата со депресивни мајки и 25% од децата во случаи кога и двајцата родители страдале од депресивно нарушување имало однесувања како проблематично и несоодветно емоционално функционирање, додека таквите деца кои потекнуваат од семејство во кое родителите не страдаат од депресивно нарушување, биле само 6%. (11)

Значајно е да се потенцира во кој степен родителската загриженост ја одразува родителската анксиозност или нивните проблеми со психичкото здравје. Освен на зголемување на загриженоста кај родителите, овие проблеми можат директно или индиректно да влијаат и на самото појавување на проблеми кај децата (12).

Во согласност со резултатите добиени од табелата за анксиозност најчести сиптоми кои биле присутни и за кои родителите беа свесни за тоа, кај 14% од родителите се јавило сушење на устата, 13.67% од родителите се појавило значително потење и кај 13.67% од родителите имало тресење.

Секојдневниот семеен живот се менува и станува покомплициран кога родителот страда од депресивно нарушување. Несигурноста поврзана со неизвесноста и за време на болеста влијае на секојдневниот живот на домаќинството. Таквото нарушување ја менува врската помеѓу родителите и децата, поради тешката комуникација. Оваа студија ја потенцира важноста за препознавање на анксиозноста кај децата и анксиозноста на родителите за тоа како анксиозноста влијае врз здравјето на децата.

Со околу една третина од младите кои доживеале клинички нарушувања на анксиозност до моментот кога ќе достигнат зрелост, ваквите нарушувања доведуваат до нарушување на личното, социјалното и академското функционирање. Кога не се лекуваат успешно, анксиозните нарушувања во детството може да предизвикаат долгорочно нарушување и зголемен ризик од дополнителни физички и ментални здравствени проблеми. (15)

Прекумерната заштита е ризик од анксиозни нарушувања. Во студија во Вашингтон за третман на анксиозноста, студијата ги учи родителите да ја намалат прекумерната заштита и да одговорат на симптомите на вознемиреност на детето со поддршка на начин што пренесува прифаќање на вистинскиот проблем на детето заедно со доверба во способноста на детето да се справи со анксиозноста.(15)

Психолошката, биолошката и социјалната дисфункција е најголем товар за една личност. Основата за добро ментално здравје е главно формирана во првите години од животот, а подобрувањето на менталното здравје на децата и младите е инвестиција во иднина. (2)

ЗАКЛУЧОК

Од добиените резултати се согледува дека родителите на децата од општина Гостивар покажуваат одредено ниво на анксиозност, депресија и страв. Од научната литература се согледува дека анксиозните родители значајно почесто од родителите без анксиозност имаат деца со панично растројство кое негативно се одразува врз нивниот пубертетски развој.

Потребно е родителите со анксиозност да ги следат активностите на своите деца, но да не искажуваат преголема загриженост, се со цел да не се развие појава на анксиозно растројство кај децата во нивниот пубертетски развој кое понатака може да има негативно влијание.

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Profesional paper

PACIENTËT E MJEKUAR ME ARTRIT URIK NË QENDRËN KLINIKE UNIVERSITARE TË KOSOVËS GJATË VITEVE 2014-2019

Shend Kryeziu, Shpresë Emini, Sellver Smaili, Yll Shala, Tonibler Gashi

Universiteti i Prishtines, "Hasan Prishtina", Fakulteti i Mjeksise- Prishtinë

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ABSTRAKTI

Artriti Urik, që në gjuhën angleze njihet si "Gout", është një formë progresive, e dhimbshme, dobësuese e inflamacionit të nyjeve. Është një nga sëmundjet më të zakonshme reumatike. Prevalenca e tij është në rritje dhe ka të ngjarë t'i atribuohet disa faktorëve, duke përfshirë faktorët e stilit të jetës dhe përdorimin e rritur të barnave shkaktuese. Qëllimi i punimit është që përmes tij të analizohet shpërndarja e të sëmurëve me artrit urik në bazë të gjinisë dhe moshës, të analizohet korelacioni në mes moshës dhe vlerave te acidit urik në gjak, raporti i të prekurve me artrit urik dhe konsumimit të alkoolit, si dhe bashkëshoqërimi i artritit urik me hipertension arterial. Punimi është i tipit deskriptiv, retrospektiv. Materiali për studim është marrë nga Klinika e Reumatologjisë të QKUK-së, ku të dhënat e pacientëve janë nxjerrë nga historitë e pacientëve të shtrirë në periudhën gjashtë vjeçare, nga viti 2014 deri në 2019. Janë përfshirë gjithsej 108 pacientë, mosha e të cilëve sillet prej 32 deri në 75 vjet. Për përpunimin e të dhënave janë përdorur metodat statistikore siç janë: mesatarja aritmetike dhe korelacioni linear. Nga 108 rastet e hulumtuara, 64 prej tyre apo 59,2% janë meshkuj, kurse 44 apo 40,8% janë femra. Grupmosha prej 60-69 vjet është më e prekura me gjithsej 37 raste, apo 34.24%, ndërsa me më pak raste është grupmosha prej 30-39 vjet, gjithsej me 6 raste ose 5.56%. Nga numri i përgjithshëm i pacientëve meshkuj, 44 prej tyre apo 68.75% janë përdorues të alkoolit. Nga të gjithë pacientët në studim, 79 ose 73.15% prej tyre vuajnë nga HTA, ndërsa 29 ose 26.85% nuk kanë HTA. Si përfundim mund të themi se: Artriti urik i prek të dy gjinitë, me predominim te meshkujt. Mosha më e atakuar është ajo mbi 50 vjeç, Nuk kemi gjetur korelacion ndërmjet moshës dhe vlerave të acidit urik në gjak. Konsumimi i alkoolit luan një rol me rëndësi si faktor rreziku për shfaqjen e sëmundjes sidomos te meshkujt, pasi te femrat nuk kemi gjetur asnjë paciente alooliste. Artriti urik bashkëshoqërohet shpesh me hipertension arterial.

Fjalët kyçe: Artriti urik, acidi urik, hiperurikemia, alkooli, hipertensioni arterial

HYRJE

Artriti Urik, që në gjuhën angleze njihet si "Gout", është një formë progresive, e dhimbshme, dobësuese e inflamacionit të nyjeve. Shkaktohet nga disa faktorë që ngrisin përqendrimin e acidit urik në serum (sUA), e që çon në hiperurikemi. Prevalenca e hiperurikemisë dhe Artritit Urik është rritur gjatë dekadave të fundit. Kjo për shkak të një popullsie në plakje, ndryshimeve në stilin e të jetuarit dhe të ushqyerit. Artriti Urik i patrajtuar ose i trajtuar në mënyrë të parregullt, mund të çojë në shfaqje kronike të sëmundjes, duke përfshirë inflamacion të vazhdueshëm, rritje të numrit të pezmatimeve akute, zhvillimeve të tofëve dhe dëmtimin strukturor të nyjeve. Të dhënat tregojnë se edhe kur pacientët janë asimptomatikë, mund ndodhë inflamacioni i vazhdueshëm dhe dëmtimi i mëvonshëm në nyje, lokalisht dhe në mënyrë sistemike. Qëllimi i trajtimit afatgjatë të artritit urik është që të zvogëlojë nivelet e sUA, të pengojë formimin e kristaleve të reja dhe të mundësoj shpërbërjen e kristaleve ekzistues. (1)

Nga një studim që u bë nga Departamenti i Biokimisë, Universiteti i Otago, Dunedin, Zelanda e Re dhe Departamenti i Mjekësisë, Universiteti i Otago, Christchurch, Zelanda e Re, thuhet se një qasje "trajtimi për të targetuar uratin e serumit" është thelbësor për menaxhimin efektiv të artritit urik. (2)

Studimi tjetër nga Universiteti i Parisit thotë se dieta dhe polimorfizmi gjenetik i transportuesve renal të urateve

duket se janë faktorët kryesorë shkaktarë të artritit urik primar. Artriti urik dhe hiperurikemia shoqërohen me hipertension arterial, diabet melitus, sindromën metabolike, sëmundjet renale dhe kardiovaskulare. (3)

Studimi në Departamentin e Terapisë Spitalore, në Kazan të Rusisë, thotë se në vitin 2015 janë caktuar kriteret e reja të diagnostikimit të artritit urik të zhvilluara nga Lidhja Evropiane Kundër Reumatizmit (EULAR) dhe Kolegji Amerikan i Reumatologjisë (ACR). Në vitin 2016 grupi EULARexpert ofroi strategjinë e trajtimit të pacientëve me artrit urik. Karakteristikat kryesore të strategjisë dhe hulumtimet e reja, që zbulojnë mundësitë më efektive dhe më të sigurta për trajtimin e artritit urik u përcaktuan në artikull. (4)

Studimi që është bërë nga Universiteti i Nottingham, UK, artriti urik është artriti inflamator mjaftë i përhapur dhe prek 2.5% të popullsisë së përgjithshme në Mbretërinë e Bashkuar. Eshtë gjithashtu i vetmi artrit që ka potencialin për tu kuruar me trajtime të sigurta, të lira dhe të tolerueshme, të cilat ulin acidin urik në serum duke frenuar xantin oksidazën ose duke rritur ekskretimin renal të acidit urik .(5)

Universiteti Mjekësor i Karolinës së Jugut, Charleston, SC, USA tregon se duhet inkurajuar konsumimi i perimeve dhe produkteve të qumështit me pak yndyrë ose pa yndyrë. Përdorimi i diuretikëve gjithashtu mund të rrisë nivelin e acidit urik në serum. Ulja e niveleve të acidit urik është thelbësore për të shmangur ndezjet e artritit urik.(6)

Studimi që u bë nga Departamenti i Farmacisë Klinike dhe Departamenti i Mjekësisë Familjare në Kolorado, thotë se terapitë shtesë që zvogëlojnë përqendrimin e urateve në serum përfshijnë agjentët tradicional urikosurik dhe një frenues të ri të reabsorbimit të urinës. Profilaksia e ndezjes akute me NSAIDs, kolchicine, ose kortikosteroide, rekomandohet në mënyrë universale me qëllim që të parandalohet artriti akut për një periudhë të paktën 6 muaj. (7)

Përveq studimeve të bëra në vendet e jashtme, tema e artritit urik është studiuar edhe nga profesionistë vendas. Sipas studimit të Dr. Avni Kryeziu, mr.sci, internist-reumatolog që është publikuar më 2009, artriti urik është sëmundje që shkaktohet nga çrregullimi i metabolizmit të acidit urik në organizëm, depozitimit të kristaleve të tij në inde dhe shfaqjen e episodeve inflamatore në nyjet përkatëse. Acidi urik është produkt i metabolizmit të purineve. Rritja e nivelit të tij, rrit riskun për artrite dhe kalkulozë renale. Rritja në gjak e përqendrimit të uratëve apo si quhet ndryshe, hiperurikemia, rezulton nga mbiprodhimi i urateve në organizëm, ulja e ekskretimit të acidit urik përmes veshkëve apo kombinimi i këtyre dy mekanizmave. Ekzistojnë edhe disa gjendje apo patologji që e bashkëshoqërojnë shfaqjen e kësaj sëmundje e që besohet se janë predispozitë e saj, siq janë obeziteti, diabeti melit, dislipidemia, etj. (8)

QËLLIMI I PUNIMIT

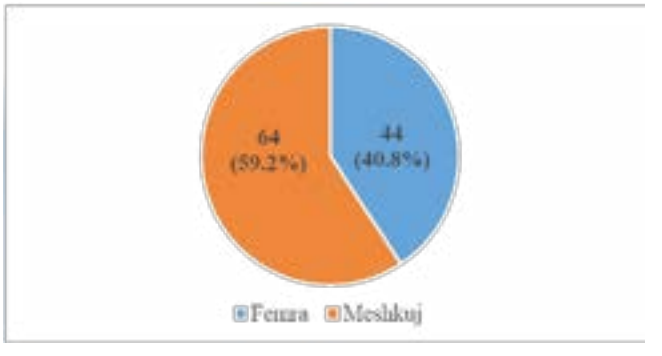
Qëllimi i punimit është që përmes tij të analizohet shpërndarja e të sëmurëve me artrit urik në bazë të gjinisë dhe moshës, të analizohet korelacioni në mes moshës dhe vlerave te acidit urik në gjak, raporti i të prekurve me artrit urik dhe konsumimit të alkoolit, si dhe bashkëshoqërimi i artritit urik me hipertension arterial.

MATERIALI DHE METODAT

Punimi është i tipit deskriptiv, retrospektiv. Materiali është marrë nga Klinika e Reumatologjisë të QKUK-së. Të dhënat e pacientëve janë nxjerrë nga historitë e pacientëve të shtrirë në periudhën gjashtë vjeçare, respektivisht nga viti 2014 deri në 2019. Janë gjithsej 108 pacientë, mosha e të cilëve sillet prej 32 deri në 75 vjeç. Të dhënat janë paraqitur me anë të tabelave dhe grafikoneve. Për përpunimin e të dhënave janë përdorur metodat statistikore siç janë: mesatarja aritmetike dhe korelacioni linear.

Rezultatet

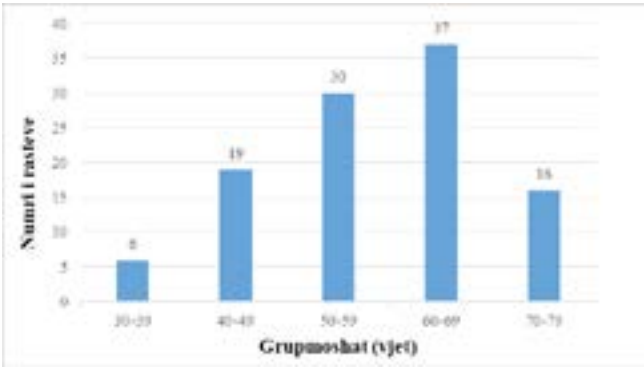
Pas marrjes së të gjitha të dhënave nga pacientët dhe pas përpunimit statistikor të tyre, përfituam rezultatet e mëposhtme:



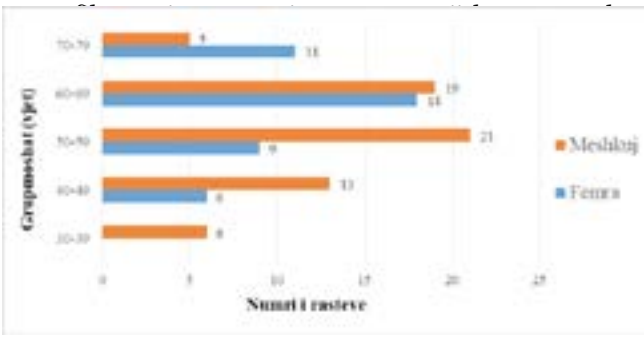
Grafiku 1. Raporti i të sëmurëve meshkuj ndaj atyre femra

Në grafikun 1 shihet se nga 108 rastet e hulumtuara, 64 prej tyre apo 59,2% janë meshkuj të sëmurë me artrit urik, kurse pjesa tjetër, 44 apo 40,8% janë femra të sëmura me

artrit urik.

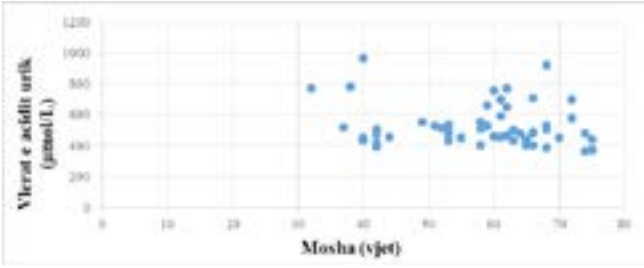


Grafiku 2. Numri i përgjithshëm i të sëmurëve sipas grupmoshave



Grafiku 3. Shpërndarja e rasteve sipas gjinisë nëpër grupmosha

Grupmosha më e atakuar te femrat është ajo 60-69 vjet me gjithsej 18 raste apo 40.91%, përderisa te meshkujt është grupmosha prej 50-59 vjet me gjithsej 21 raste apo 32.81%. Në grupmoshën 30-39 vjet nuk kemi pasur asnjë rast të gjinisë femër të sëmurë, përderisa te meshkujt i kemi pasur 6 raste apo 9.38%.



Grafiku 4. Shpërndarja e vlerave të acidit urik te të sëmurët me artrit urik sipas moshës

Nga grafiku vërejmë se në rastin tonë nuk ka korelacion ndërmjet moshës dhe vlerave të acidit urik në gjak te të sëmurët me artrit urik (r = - 0.16473).

Tabela 1. Të sëmurët femra dhe konsumimi i alkoolit

Grupmoshat (vjet)	Femra alkooliste				Totali	%
	Jo	%	Po	%		
30-39	...	...	...	...	...	...
40-49	6	13.64	...	...	6	13.4
50-59	9	20.45	...	...	9	20.45
60-69	18	40.91	...	...	18	40.91
70-79	11	25.00	...	...	11	25.00
Gjithsej	44	100.00	...	...	44	100.00

Nga tabela 1 shihet se asnjëra nga femrat paciente të studimit tonë nuk ka qenë përdoruese e alkoolit!

Tabela 2. Të sëmurët meshkuj dhe konsumimi i alkoolit

Grupmoshat (vjet)	Meshkuj alkoolist				Totali	%
	Jo	%	Po	%		
30-39	2	10	4	9.09	6	9.38
40-49	3	15	10	22.73	13	20.31
50-59	5	25	16	36.36	21	32.81
60-69	6	30	13	29.55	19	29.69
70-79	4	20	1	2.27	5	7.81
Gjithsej	20		44	68.75	64	100.00

Në tabelen e mësipërme vërejmë se nga numri i përgjithshëm i pacientëve meshkuj, 44 prej tyre apo 68.75% janë përdorues të alkoolit. Në grupmoshën 50-59 vjet kemi më së shumti përdorues të alkoolit me 21 raste ose 32.81%.

Tabela 3. Të sëmurëve me artrit urik të bashkëshoqëruar me HTA

Grupmoshat (vjet)	Pa HTA		Total	%	Me HTA		Total	%	Gjithsej	%
	F	M			F	M				
30-39	...	5	5	17.24	...	1	1	1.27	6	5.56
40-49	2	5	7	24.14	4	8	12	15.19	19	17.59
50-59	...	6	6	20.69	9	15	24	30.38	30	27.78
60-69	2	8	10	34.48	16	11	27	34.18	37	34.26
70-79	...	1	1	3.45	11	4	15	18.99	16	14.81
Gjithsej	4	25	29	26.85	40	39	79	73.15	108	100.00

F – Femra ; M – Meshkuj ; HTA – Hipertension arterial

Nga tabela e mësipërme shihet se nga numri i përgjithshëm i rasteve, 79 ose 73.15% prej tyre vuajnë nga HTA, ndërsa 29 ose 26.85% nuk kanë HTA. Grupmosha më e atakuar me HTA është ajo nga 60-69 me 27 raste apo 34.18%, ndërsa më së paku raste ka në grupmoshën 30-39 vjet me vetëm 1 rast ose 1.27%.

DISKUTIMI

Hiperurikemia është mjaft e zakonshme, me prevalencë të ranguar në mes 2.6% dhe 47.2% në popullata të ndryshme.(9,10)

Kjo rrjedhë nga fakti se artriti urik është një sëmundje e kohës moderne, e cila edhe në vendin tonë ka pësuar rritje viteve të fundit, përkatësisht dekadës së fundit.

Në nivel botëror që nga viti 1990 deri në vitin 2013, rasti i të prekurve me gout është dyfishuar.(11)

Artriti urik shfaqet më shpesh te meshkujt sesa te femrat. Meshkujt zakonisht preken në mes moshës 20 dhe 50 vjeçare, ndërsa femrat pas menopauzës. Te fëmijët dhe të rinjtë është sëmundje e rrallë.(12)

Edhe në studimin tonë, gjinia mashkullore është më e prekur me artrit urik, me 64 raste nga gjithsej 108. Nga pacientët meshkuj, grupmosha më e prekur është ajo mbi 50 vjet, për dallim nga të dhënat e literaturës së sipërme. Ky dallim vie nga fakti se te ne presupozohet se grupmoshat më të shtyra i ekspozohen më shumë sëmundjeve që janë shkaktarë të rritjes së vlerave të acidit urik në gjak, si bie fjala sëmundjet e veshkave, të gjakut, mbipesha, sëmundja e sheqerit etj...

Vlerat e acidit urik në gjak rriten me rritjen e moshës si te femrat ashtu edhe te meshkujt.(13)

Në punimin tonë nuk ka korelacion në mes moshës dhe vlerave të acid urik në gjak, gjë e cila nuk përputhet me të gjeturat e punimit në fjalë. Mendojmë që kjo mospërputhje rrjedh nga shkaku që pacientët e studimit tonë kanë qenë nën ndikimin e terapisë dhe vlerat e acidit urik kanë pësuar rënie.

Ndërlidhja ndërmjet konsumimit të alkoolit dhe artritit urik ka qenë e njohur për shekuj me radhë. Rreziku i zhvillimit të gout varion nga tipi i konsumit të alkoolit. (14)

Në një punim të punuar nga Zhao Li me bashkpunëtorë, nga 11039 pjesëmarrës të punimit, 4997 prej tyre ishin meshkuj, kurse 6042 femra. Nga ky punim u konstatua se konsumimi me doza të larta të alkoolit, e rritë rrezikun për hiperurikemi te meshkujt, por jo te femrat.(15)

Në gjetjet tona, nga grupi i femrave nuk ishte asnjë alkooliste, ndërsa te meshkujt ishin 44 nga 64 gjithsej, që do të thotë se alkooli ishte një shkaktar i rëndësishëm në paraqitjen e artritit urik te meshkujt. Për shkak të kulturës sonë të të jetuarit, femrat ende nuk i ekspozohen faktorit të rrezikut nga pirja e alkoolit, gjë që vërtetohet edhe në punimin tonë. Andaj, ndikimi i alkoolit te femrat është i pamatshëm në gjetjet tona.

Sëmundja paraqitet te meshkujt më shumë sesa te femrat, tradicionalisht për shkak të stilit të të ushqyerit. Sëmundja bashkëshoqërohet edhe me sëmundje përcjellëse si HTA, dislipidemi dhe obezitet.(16)

Nga një studim i radhës i bërë te të rriturit e Bangladeshit, janë marrë mostra të gjakut nga 140 meshkuj dhe 115 femra. Janë analizuar vlerat e acidit urik si dhe vlerat e yndyrës në gjak. Poashtu është bërë edhe matja e tensionit të gjakut dhe është definuar në këtë formë: SBP ≥ 140 mmHg dhe DBP ≥ 90 mmHg (çdo vlerë që i përshtatet kushtit konsiderohet jonormale, dhe personi konsiderohet me HTA). Nga të dhënat, prevalenca për hipertension te meshkuj është 63%, kurse te femrat 39%. (17)

Në studimin tonë, pacientet femra pothuajse të gjitha janë të shoqëruara me HTA, përkatësisht 40 nga 44 në total, ose 90.9%. Sa i përket meshkujve, prevalenca e rasteve është më e vogël, ku nga 64 meshkuj gjithsej, 39 prej tyre apo 60.9% kanë HTA si sëmundje bashkëshoqëruese. Nga studimi i mësipërm vërejmë ngjashmëri të madhe të numrit të meshkujve të prekur me HTA me punimin tonë, kurse sa i përket femrave, dallimi i madh në mes punimit tonë dhe punimit të mësipërm qëndron në faktin se pacientet femra të punimit tonë i takojnë moshës së shtyrë, përkatësisht pjesa më e madhe e tyre i takon moshës prej 60-69 vjet, 18 në total apo 40.91%.

PËRFUNDIMI

Pas analizës së rezultateve , krahasimit me literaturën dhe autorët tjerë, kemi ardhur në përfundimet si në vijim:

Artriti urik i prek të dy gjinitë, me predominim te meshkujt.

Mosha më e atakuar është ajo mbi 50 vjet, respektivisht te femrat më shumë sëmuret grupmosha 60-69 vjet, dhe te meshkujt ajo 50-59 vjet.

Nuk kemi gjetur korelacion ndërmjet moshës dhe vlerave të acidit urik në gjak.

Konsumimi i alkoolit luan një rol me rëndësi si faktor rreziku për shfaqjen e sëmundjes sidomos te meshkujt, pasi te femrat nuk kemi gjetur asnjë paciente alkooliste.

Artriti urik bashkëshoqërohet shpesh me hipertension arterial ngase nga numri i përgjithshëm, 73.15% kanë pasur edhe HTA.

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Profesional paper

КАРАКТЕРИСТИКИ НА ДЕНТАЛНИОТ ТУРИЗАМ - СТОМАТОЛОШКИ КАПАЦИТЕТИ И ТРЕТМАН НА ПАЦИЕНТИТЕ ОД СТРАНСТВО

Наташа Павлоска[1], Весна Велиќ Стефановска[1], Ќиро Ивановски[2], Влатко Коколански[2]

[1]Институт за епидемиологија и биостатистика со медицинска информатика, Медицински факултет, Универзитет "Св.Кирил и Методиј", Скопје

[2]Универзитет "Св. Кирил и Методиј", Стоматолошки факултет, Скопје

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АПСТРАКТ

Вовед: Новиот, 21 век, не соочува со неопходноста од прифаќањето на фактот дека добивањето на медицинскиот третман секојденевно ги преминува границите во потрага по достапност, подобра услуга и поголем квалитет. Денталниот туризам е една од најбрзорастечките гранки на здравствениот туризам. Во текот на светската економска рецесија, денталниот туризам е единствена гранка во туризмот, која не забележала негативен тренд. Опстојувањето и функционирањето на овој вид на туризам преставува куриозитет не само за економските туку пред се за здравствеите експерти. Цел: Оваа студија има за цел да укаже на одредени карактеристики на денталниот туризам во Република Северна Македонија од аспект на стоматолошките капацитети и третманот на пациентите од странство. Материјал и метод: Истражувањето преставува квантитативна аналитичка студија на пресек (cross sectional study) спроведена во периодот 2018-2019 година. За целите на истражувањето, примерокот беше добиен по метод на случаен избор, согласно однапред утврдени инклузиони критериуми. Беше користен нестандардизиран анкетен прашалник со вкупно 59 прашања групирани во пет целини. Прашалникот беше аплициран со Google Forms услугата, а беше пополнуван преку интернет прегледник. Резултати: Беа опфатени вкупно 232 доктори на дентална медицина од кои 53,02% од машки, и 46,98% од женски пол. Просечната возраст изнесуваше 38,4±8,2 години со мин/мак возраст од 24/ 61 година. Третина од анкетираните стоматолози, 32,3% беа специјалисти/ специјализанти во одредена област на денталната медицина. Кај најголемиот дел 37,3% искуството во лекување странци изнесуваше 0-5 години, следено со 28,1% - помеѓу 6-10 години и 19,8% со искуство од 11-15 години. Најголемиот број од денталните туристи беа од западните европски земји и тоа 85,3% следено со 49,6% од прекуокеанските земји, 32,8% Грција и Косово и Албанија со консеквентно 16,4% и 15,9%. Утврдивме сигнификантна асоцијација на водењето на досие/ картон (p=0,0042) во прилог на сигнификантно почесто негово водење во поликлиниките и специјалистичките ординаци споредено со ординациите за општа стоматологија. За p<0,05, утврдивме дека денталниот туризам резултирал со сигнификантно поголем број на вработувања во поликлиниките споредено со општите и специјалистичките стоматолошки ординации. Стоматолозите сметаат дека 51,7% од нивните пациенти од странство доаѓаат само за лекување, 28,4% сметаат дека тие стоматолошките услуги ги комбинираат со одмор, а 12,9% дека лекувањето е комбинирано со посета на роднини. Заклучок: Согледавме дека голем дел од докторите по стоматологија имаат искуство во давањето на дентални услуги на пациенти од странство, што укажува на неоспорна традиција за постоење на дентален туризам во нашата земја. Неопходно е поопсежно научно докуметирање на оваа дејност во нашата земја со што ќе се овозможи промоција во пошироки рамки како и поттик за подобра организациона структира и соодветна законска регулатива за развој и меѓународна етаблираност.

Клучни зборови: дентален туризам, пациент, дентален турист, здравствена услуга

ВОВЕД

Под здравствен туризам (health tourism), некои автори ги означувале сите форми на туризам поврзани со зачувување и унапредување на здравјето. Уште во 2005 година, Connell се спротивставил на оваа терминологија, со неологизмот «medical tourism», тврдејќи дека станува збор за нов сектор во подем, кој вклучува медицински зафати (1). Во последните две децении, впечатливо е интензовното нотирање на развојот на медицинскиот туризам, и неговата секција - денталниот туризам, како тренд на глобализација на медицинската и стоматолошката дејност. Во литературата се среќаваат и инвентивни синоними на денталниот туризам како: «dental vacation» и «dental holidays».

Нема единствена дефиниција на медицинскиот туризам. Според Светската здравствена Организација тоа подразбира прекугранично патување, со цел да се добијат медицински услуги. Најчесто барани здравствени услуги во друга држава се стоматолошките третмани, естетската хирургија, елективната хирургија и лекување на стерилитет (2). Аналогно на тоа, Американската Дентална Асоцијација (ADA) со резолуцијата 28Н-2008, го дефинира денталниот туризам како чин на патување во туѓа држава, заради добивање стоматолошки третмани (3).

Чинителите на денталниот туризам се делат на push (потискувачки) и pull (привлекувачки) фактори. Првите го одбиваат, а вторите го привлекуваат пациентот, односно денталниот турист (4). Најважни push фактори се високите цени на стоматолошките услуги во сопствената земја, немањето здравствено дентално осигурување и јазичната бариера на емиграциското население. Pull фактори се квалитетот на услугата во туѓата земја, краткото време на чекање, поевтините цени, познавањето на заеднички јазик, условите за одмор, политичката клима и друго (5).

Главни фактори на денталниот туризам во ЕУ се: пониската цена, пократкото време на чекање и довербата во стручноста и здравствениот систем (6). Примерот со американскиот континент, укажува дека факторите што го одредуваат денталниот туризам се: однос цена/ услуга, капацитет за давање на услуги, технологија, време на чекање, доверба во здравствен систем и урбан имиџ (7). За американското население кое жевее вдолж границата со Мексико, немањето здравствено осигурување е главен принуден мотив за дентален туризам (8).

Согласно улогата во рамките на денталниот туризам, авторите укажуваат на рецептивни и емитивни земји. Во првите доаѓаат државјани на вторите, заради добивање стоматолошки услуги кои се редовно повеќекратно поскапи во нивната матична земја (4). Во Европа, водечка рецептивна дестинација за дентален туризам е Унгарија, која учествува со 39% во овој пазар, Полска со 32%, Шпанија со 7%, Бугарија со 7% и Турција со 15% (9). Во Унгарија, прекуграничната мобилност стихијно започнала во деведесетите години на минатиот век, со доаѓање на пациенти од соседните држави, Австрија и Германија, а денес, емитивни земји се и другите богати држави од Западна Европа (9-11). Оваа експанзија се должи и на споредни мотивирачки фактори за европските дентални туристи, а тоа се културно-историските знаменитости и нискобуџетните летови до главниот град, поради што Будимпешта се нарекува «дентална престолнина» на Европа (9,10).

Во сегментот на давање стоматолошки услуги, според едни автори, Индија е супериорен лидер на глобално ниво, а потоа се посочуваат Костарика, Мексико, Унгарија, Полска, Романија, Литванија, Хрватска и Србија. Денталните туристи, најчесто се пациенти од развиените западни земји (12). Речиси истовремено, според други автори, приматот во денталниот туризам го има Мексико, поради близината со САД, од каде доаѓаат 25% од вкупниот број дентални туристи во светот. Второто место го делат Индија и Унгарија. Додека Унгарија ги опслужува европските пациенти, Индија ја посетуваат азиските, а обете земји делат и дел од денталните туристи од САД (13).

Денталниот туризам е една од најбрзорастечките гранки на здравствениот туризам. Постојат примери, како Лос Алгодонес, т.н Моларсити, мало гратче во северниот дел на Мексико, каде здравствениот, односно медицинскиот туризам е застапен исклучиво преку денталниот (14-17). Во овој град живеат 6000 луѓе, а ординираат 500 стоматолози. Во текот на светската економска рецесија, денталниот туризам е единствена гранка во туризмот, која не забележала негативен тренд. Опстојувањето и функционирањето на овој вид на туризам преставува куриозитет за економските и здравствеите експерти (16-17). Овој туризам расте со годишна стапка поголема од 15%, и на годишно светско ниво ги надминува приходите од 120 милијарди долари (14). Оваа студија има за цел да укаже на одредени карактеристики на денталниот туризам во Република

Северна Македонија од аспект на стоматолошките капацитети и третманот на пациентите од странство.

МАТЕРИЈАЛ И МЕТОДИ

Истражувањето преставува квантитативна аналитичка студија на пресек (cross sectional study) спроведена во периодот од февруари до март во 2018-2019 година. За целите на истражувањето, примерокот беше добиен по метод на случаен избор, согласно однапред утврдени инклузиони критериуми и тоа: активен доктор на стоматологија, вработен/ сопственик на стоматолошка ординација, сопственик на електронска адреса и спремност и желба за учество во истражувањето.Беше користен нестандардизиран анкетен прашалник со вкупно 59 прашања групирани во пет целини (4). Истиот беше објавен на социјалниот медиум - "Facebook" во затворени групи за доктори по стоматологија под назив "Стоматолози обединете се" и "Македонски стоматолози". Истиот беше аплициран со Google Forms услугата, а беше пополнуван преку интернет прегледник. Ризикот од пополнување на прашалникот повеќе од еднаш од страна на исто лице беше елиминиран со софтверско решение на платформата каде беше креиран прашалникот.

ЕТИЧКИ АСПЕКТИ

Податоците беа собирани со загарантирана анонимност и гаранција за нивно исклучиво користење за научни цели. Истражувањето беше одобрено од Конзорциумот за докторски студии по јавно здравје при Медицинскиот факултет, УКИМ, во Скопје.

СТАТИСТИЧКА АНАЛИЗА

Анализата беше направена во SPSS 22.0). За дескриптивната анализата на нумеричките серии користени беа мерките на централна тенденција (просек, медијана, минимални и максимални вредности и интерактивни рангови), како и мерки на дисперзија (стандардна девијација). Pearson Chi square test, Fisher Freeman Halton exact test и Fisher exact test беа користен за утврдување на асоцијација меѓу одредени атрибутивни дихотомни белези во групите на испитаници. За споредба на просечните вредности на нумеричките серии беше користен Mann Whitney U тест. За утврдување на статистичка значајност беше користено ниво на сигнификантност од $p<0.05$.

Резултати

Во истражувањето беа опфатени вкупно 232 доктори на дентална медицина (стоматолози) од кои 123 (53,02%) од машки, и 109 (46,98%) од женски пол со однос помеѓу половите од 1:1,13. Процентуалната разлика помеѓу застапеноста на половите, за $p>0,05$, не беше сигнификантна (Difference test: Difference 6,04% [(-3,04-14,98) 95% CI]; Chi-square=1,689; df=1 p=0,1937). Анализа според националност укажа на 200 (86,2%) Македонци, 20 (8,6%) Албанци и 12 (5,2%) други националности. Просечната возраст изнесуваше 38,4±8,2 години со минимална односно максимална возраст од 24 vs. 61 година, и 50% испитаници постари од 37 година за Median (IQR)=37 (31,5-44). Третина од анкетираните стоматолози или 75 (32,3%) беа специјалисти/ специјализанти во одредена област на денталната медицина. Кај најголемиот дел од испитаниците 81 (37,3%) искуството во лекување странци изнесуваше 0-5 години, следено со 61 (28,1%) кај кои тоа изнесуваше помеѓу 6-10 години и 43 (19,8%) со искуство од 11-15 години.

Најголемиот број од денталните туристи беа од западните европски земји и тоа 198 (85,3%) следено со прекуокеанските земји 115 (49,6%). Грција како земја на потекло на пациентите од странство била назначена од 76 (32,8%) од анкетираните стоматолози следено со Косово и Албанија застапени со консеквентно 38 (16,4%) и 37 (15,9%). Од посочените соседни држави најмалку дентални туристи сме имале од Бугарија 18 (7,8%) и Србија 27 (11,6%).

Анализата помеѓу специјалистичкиот статус и добиените одговори за бројот на денталните услуги на пациентите од странство, просечното траење на третманот, појавата на компликации и договор за текот на третманот, за $p>0,05$, не укажа на сигнификантна асоцијација (Табела 1). Досие/картон за пациентите од странство воделе 172 (79,6%) од анкетираните стоматолози, и тоа 34 (97,1%) од поликлиниките, 28 (87,5%) од специјалистичките ординации и 110 (73,8%) од општите ординации. Утврдивме сигнификантна асоцијација на водењето на досие/ картон, за $p<0,05$, (Fisher Freeman Halton exact test: p=0,0042) во прилог на сигнификантно почесто негово водење во поликлиниките и специјалистичките ординаци споредено со ординациите за општа стоматологија. Кај сите типови на стоматолошки ординации, денталниот туризам имал слично влијание на обемот на работа, приходите, вработувањата и развојот на ординацијата

(Табела 2). За p<0,05, утврдивме дека денталниот туризам резултирал со сигнификантно поголем број на вработувања во поликлиниките споредено со општите и специјалистичките стоматолошки ординации.

Табела 1. Анализа на селектирани прашања за дентални услуги на пациентите од странство според специјалистички статус

Параметар	Стручна подготовка						p
	Општ стоматолог		Специјалист		Вкупно		
	N	%	N	%	N	%	
Просечен број на посети по пациент од странство							
1	10	6,90%	3	4,23%	13	6,02%	Fisher Freeman Halton exact test: p=0,7627
2	34	23,45%	15	21,13%	49	22,69%	
3-5	70	48,28%	39	54,93%	109	50,46%	
≥6	31	21,38%	14	19,72%	45	20,83%	
Просечно траење на престојот на пациенти од странство (денови)							
1	13	8,97%	5	7,04%	18	8,33%	Fisher Freeman Halton exact test: p=0,2756
2	2	1,38%	2	2,82%	4	1,85%	
3-5	31	21,38%	23	32,39%	54	25%	
≥6	99	68,28%	41	57,75%	140	64,81%	
Процент на непредвидени компликации при третман на пациенти од странство							
1-2%	121	83,45%	56	78,87%	177	81,94%	Fisher exact test: p=0,3327
3-5%	19	13,10%	14	19,72%	33	15,28%	
≥6%	5	3,45%	1	1,41%	6	2,78%	
Договор за текот на третманот							
Пред третман	118	81,38%	51	71,83%	169	78,24%	Pearson Chi-square: 2,55; df=1; p=0,1101
При третманот	27	18,62%	20	28,17%	47	21,76%	
* сигнификантно за p<0,05							

Табела 2. Анализа на обем на работа, приходи, вработувања и развој според тип на стоматолошка ординација

Параметар	Тип на стоматолошка ординација								p
	општа		поликлиника		специјалистичка		вкупно		
	N	%	N	%	N	%	N	%	
Дали лекувањето пациенти од странство го зголемило обемот на работа и приходите?									
да	90	90%	9	90%	17	80,95%	116	88,55%	Fisher Freeman Halton exact test: p=0,4907
не	10	10%	1	10%	4	19,05%	15	11,45%	
Дали лекувањето пациенти од странство резултирало со дополнителни вработувања?									
да	20	20%	6	60%	8	38,10%	34	25,95%	Fisher Freeman Halton exact test: p=0,0087*
не	80	80%	4	40%	13	61,90%	97	74,05%	
Поврзани со други стоматолошки ординации/клиники заради привлекување пациенти од странство?									
да	20	20%	2	20%	4	19,05%	26	19,85%	Fisher Freeman Halton exact test: p=0,9949
не	80	80%	8	80%	17	80,95%	105	80,15%	
Влијание на пациентите од странство за развој на ординацијата?									
неважно	35	35%	2	20%	7	33,33%	44	33,59%	Fisher Freeman Halton exact test: p=0,9949
важно	48	48%	7	70%	13	61,90%	68	51,91%	
многу важно	17	17%	1	10%	1	4,76%	19	14,50%	
* сигнификантно за p<0,05									

Во рамките на истражувањето направена беше анализа во однос на активностите кои странските пациенти ги комбинираат заедно со стоматолошките интервенции. Согледавме дека најголемиот дел од анкетираните стоматолози и тоа 120 (51,7%) изјавиле дека нивните пациенти од странство доаѓаат само за лекување. Според стоматолозите, стоматолошките услуги ги комбинираат со одмор 66 (28,4%) од пациентите од странство, а најмал број или 30 (12,9%) го комбинираат лекувањето со посета на роднини. Анализата укажа дека најголемиот дел од ординациите кои третирале пациенти од странство и тоа 154 (71,3%) не им нуделе помош за реализација на дополнителни туристички услуги. Ваква иницијатива остварувале само 21 (9,7%) од ординациите. Помош при организација на превоз нуделе 21 (9,7%) од стоматолошките ординации, 49 (22,7%) нуделе помош при организација на сместување, а 21 (9,7%) нуделе помош при организација на додадтни туристички активности.

ДИСКУСИЈА

За територијата на Република Северна Македонија, проблемот на денталните услуги за пациентите од странство или генерално прашањето на денталниот туризам е само инцидентно обработувано. Резултатите од нашето истражување укажуваат дека најголемиот дел докторите по општа стоматологија односно специјалистите по некоја од стоматолошките гранки имаат искуство со давањето на дентални услуги на пациенти од странство. Кај дел од нив ваквото искуство изнесуваше 10 и повеќе години, што укажува на традиција за денталниот туризам во нашата земја. Слични истражувања се направени меѓу стоматолозите во Унгарија (10), Хонг Конг(18) и Хрватска (4).

Најголемиот дел од денталните туристи во нашата земја доаѓаат од развиените западни и прекуокенски земји, следено со пациенти од Грција и Бугарија. Според истражувањата во Хрватска, емитивни земји за нејзиниот дентален туризам се Германија, Словенија и Италија (4). Во Унгарија, странските пациенти кои бараат дентални услуги најчесто доаѓаат од Германија, Австрија, Велика Британија и Швајцарија (10). Истражување спроведено во Хонг Конг укажува дека најголемиот дел од денталните туристи доаѓаат од Кина (18).

Во нашето истражување согледавме дека најголем дел од општите стоматолози и специјалисти, третманот на странските пациенти го изведуваат во 3-5 посети. Повеќето испитаници одговорија дека престојот на странските туристи заради добивање стоматолошки третман траел повеќе од шест дена. Ова укажува дека во најголем дел биле спроведувани комплексни или мултипли дентални третмани. Истражувањето во Хрватска покажало слични резултати по ова прашање. На хрватските стоматолози им биле потребни најмногу 3-5 посети на странскиот пациент, со просечен престој од 3-5 дена (4). Во Хонг Конг, повеќето испитаници ги завршувале третманите на денталните туристи во рок од неколку седмици и за тоа им биле потребни 3-5 посети на пациентот (18).

Според стоматолозите во нашето истражување, процентот на компликации при третманот на странските пациенти изнесувал 1-2%. Ова е во согласност со согледувањата добиени од хрватските стоматолози (4). Процентот на компликации во нашето и хрватското истражување е помал од европскиот статистички просек како и од тој на унгарските стоматолози, кој изнесува 5%. Дури 72,1% од стоматолозите во епропските земји изјавиле дека обезбедуваат соодветна грижа и следење по третманот (aftercare) за странските пациенти, со отворање прекугранични канцеларии за консултација (10).

Повеќето стоматолози практикуваат текот на третманот, да го договараат пред да дојдат странските пациенти во нивната ординација. Во Хонг Конг, само 1% од испитаниците имале претходна консултација со денталниот турист, пред неговата првична посета(18). Во Хрватска, пак, поголемиот број стоматолози никогаш или речиси никогаш не го договараат текот на лекувањето пред посетата на странскиот пациент (4). План на третман пред првичната посета на странскиот турист прават 23,3% од унгарските стоматолози (10).

Практикувањето на денталниот туризам има свои импликации на типот на здравствената установа каде работат испитаниците. Лекувањето странски пациенти го зголемило обемот на работа и приходите на 90% од општите стоматолошки ординации, на 90% од поликлиниките и на 80,95% од специјалистичките ординации. Сепак, денталниот туризам само кај 20% од општите стоматолошки ординации, кај 60% од поликлиниките и кај 38,10% од специјалистичките ординации резултирал со дополнителни вработувања. За $p<0,05$ постои значајна разлика меѓу општите стоматолошки ординации наспроти поликлиниките и специјалистичките кои дополнително вработиле персонал. Ваков сличен расчекор бележи и

истражувањето во Хрватска, каде зголемувањето на обемот на работа и приходите од дентален туризам, исто така не резултирало со пропорционално дополнително вработување на персонал во ординацијата (4). Во Хонг Конг, кај повеќето испитаници, приходот од дентален туризам се зголемил за помалку од 10% (18). Повеќето од општите и специјалистичките ординации, како и поликлиниките не се поврзуваат и не соработуваат со други ординации заради придобивање повеќе странски пациенти. Повеќето и од хрватските стоматолози не се поврзани со други ординации поради унапредување на дентален туризам (4). Во студиите проведени во Хонг Конг, повеќето испитаници го препознаваат денталниот туризам како потенцијал за развој на нивната стоматолошка пракса. Таму, специјалистите биле повеќе заинтересирани за унапредување на денталниот туризам од неспецијалистите. Тамошното истражување покажало дека нема сигнификантна асоцијација меѓу полот, возраста, местото на дипломирање, времето на работа или животот во странство со подготвеноста за унапредување на денталниот туризам (18).

ЗАКЛУЧОК

Ова истражување покажува дека денталниот туризам има важно влијание за развојот на повеќето општи стоматолошки ординации, поликлиники и специјалистички ординации, и дека кај повеќето од нив, го зголемил обемот на работа и приходите на ординацијата. И покрај тоа, денталниот туризам не резултирал пропорционално со нови вработувања, што може да асоцира на нееднакви развојни можности и услови на помалите во однос на поголемите ординации и поликлиники. Согледавме дека голем дел од докторите по стоматологија имаат искуство во давањето на дентални услуги на пациенти од странство, што укажува на неоспорна традиција за постоење на дентален туризам во нашата земја. Неопходно е поопсежно научно докуметирање на оваа дејност во нашата земја со што ќе се овозможи промоција во пошироки рамки како и поттик за подобра организациона структира и соодветна законска регулатива за развој и меѓународна етаблираност.

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Profesional paper

DIAGNOSTIKIMI DHE TRAJTIMI I HERSHËM I DEPRESIONIT PARA DHE PAS LINDJES

Slavica Arsova[1], Kadri Haxhihamza[1], Stojan Bajraktarov[1], Nensi Manusheva[1]

[1]Klinika Universitare e Psikiatrisë – Shkup

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ABSTRAKT

Sfondi: Statistikat tregojnë një rritje të depresionit në të gjithë botën, dhe shifrat janë dy herë më të larta tek gratë, veçanërisht në periudhat e rrezikut siç janë shtatzënia, periudha pas lindjes dhe menopauza. Konsiderohet se çrregullimi depresiv më së shpeshti fillon në periudhën riprodhuese, rreth moshës 20 vjeç, dhe kështu 1 nga 20 vajza në këtë periudhë vuan nga depresioni, e nga ana tjetër, vetëm 1 nga 3 prej tyre do të trajtohet me terapi adekuate farmakologjike .

Parathënie: Sipas treguesve statistikorë të Shoqatës Psikiatrike Amerikane (APA) të marra nga ekspertët e shëndetit mendor perinatal, vetëm gjysma e nënave me depresion perinatal janë duke u diagnostikuar dhe trajtuar.

Autorët britanikë mendojnë se depresioni tek nënat e reja është dukshëm më i lartë sot sesa më herët ose në krahasim me gjeneratat e nënave të tyre. Me shumë mundësi shkaqet e rritjes së depresionit tek të rinjtë janë: stresi kronik, privimi i gjumit, ushqimi i dobët i nënës, mënyra sedentare e jetesës, presioni ndaj nënave për t'u rikthyer në punët e tyre sa më shpejt të jetë e mundur pas lindjes, duke u përballur me vështirësitë në menaxhimin e numrin e shumtë të roleve: të qenurit nënë, grua, punëtore e zellshme dhe në të njëjtën kohë të kesh një jetë shoqërore. Rreziku më i madh për nënën e re në depresion është vetëvrasja, e cila po konsiderohet shkaku i dytë i vdekjes tek të rinjtë gjatë viteve të riprodhimit. Fatkeqësisht, kjo ndodh zakonisht në fund të shtatëzanisë ose gjatë vitit të parë pas lindjes.

Materjalet dhe metodat: Studimi përfshinte 69 pacientë në moshë midis 18 dhe 44 vjeç, me diagnozën e vendosur F32 gjatë shtatëzanisë ose F32.01 ose F32.02, që është depresion pas lindjes. Pacientët u diagnostikuan sipas kritereve të KNS 10 dhe u trajtuan gjatë shtatzënisë dhe periudhës pas lindjes në Departamentin për trajtimin e grave shtatzëna ose grave pas lindjes. Pacientët me instrumente psikodiagnostike u monitoruan gjatë gjithë procesit, dhe matjet me HAM-A dhe HAM-D paraqiten në fillim të trajtimit dhe pas tre muajsh.

Rezultatet: Rezultati mesatar e shkallës HAM-A në muajin e parë ishte 30.8 ± 2.4, në diapazon nga 26 deri në 38 dhe tregoi një ankth të fortë. Pas tre muajve me terapi, rezultati mesatar i HAM-A u ul në 21 dhe demonstroi një ankth të moderuar. Sipas testit Wilcoxon Matched Pair, diferenca ishte statistikisht e rëndësishme për $p < 0.05$. Rezultati mesatar e shkallës HAM-D në muajin e parë ishte 30.3 ± 2.7, në diapazon nga 26 deri në 36, dhe demonstroi një depresion të rëndë. Pas tre muajve me terapi, rezultati mesatar i HAM-D u ul në 3.4, dhe demonstroi një depresion të moderuar. Sipas palëve të përputhura Wilcoxon, diferenca ishte statistikisht e rëndësishme për $p < 0.05$.

Diskutim: Rezultatet kanë treguar prani statistikisht të rëndësishme të faktorëve të rrezikut te pacientet me depresion prenatal ose postnatal. Numri më i madh i pacienteve përjetuan episodet e mëparshme depresive, ngjarje traumatike, shtatzëni të paplanifikuar ose dhunë familjare.

Përfundim: Njohja e hershme e faktorëve të rrezikut për zhvillimin e depresionit para lindjes çon drejt parandalimit të shfaqjes së depresionit antenatal ose postnatal. Trajtimi i hershëm që përbëhet nga një trajtim të kombinuar (me ndërhyrje psikologjike dhe antidepresantë SSRI) që sjellë uljen e ankthit dhe depresionit dhe forcimin e mekanizmëve mbrojtëse psikologjike të nënës dhe gjithashtu zvogëlon rrezikun e lindjes së parakohshme, lindjes cezariane dhe kujdes më të mirë si për nënën ashtu edhe për fëmijën , në periudhën para lindjes dhe pas lindjes.

Fjalët kyçe: depresioni, shtatzënia, faktorë të rrezikut, SSRI, psikoterapia postnatale.

HYRJE

Statistikat tregojnë një rritje të depresionit në të gjithë botën, ndërsa shifrat janë dy herë më të larta tek gratë, veçanërisht në periudhat e rrezikut siç janë shtatzënia, periudha pas lindjes dhe menopauza. Konsiderohet se çrregullimi depresiv më së shpeshti fillon në periudhën riprodhuese, rreth moshës 20 vjeç, ashtu që 1 nga 20 vajza në këtë periudhë vuan nga depresioni, dhe nga ana tjetër, vetëm 1 nga 3 prej tyre trajtohet me terapi adekuate farmakologjike. Treguesit thonë se te 54% të vajzave të reja që kanë vuajtur nga ndonjë çrregullim depresiv, rreziku i shfaqjes së depresionit gjatë shtatëzanisë është afërsisht 50% më i lartë në krahasim me ato që nuk kishin episode depresive. Nëse kemi parasysh faktin se në një numër të madh të vajzave në depresion shtatzënitë janë të paplanifikuara (të paqëllimta), atëherë situata është edhe më delikate për shkak të mos njohjes së depresionit ose për shkak të ndërprerjes së trajtimit ose trajtimit jo adekuat dhe sjelljes së rrezikshme (pirja e duhanit, konsumi i alkoolit, ilaçet, kontrollet e parregullta, kujdesi i dobët shëndetësor) (2, 13).

Sipas treguesve statistikorë të Shoqatës Psikiatrike Amerikane (APA) të marra nga ekspertët e shëndetit mendor perinatal, vetëm gjysma e nënave me depresion perinatal janë diagnostikuar dhe trajtuar (1).

Autorët britanikë, bazuar në rezultatet e tyre të botuar në JAMA në 2018, mendojnë se depresioni tek nënat e reja është dukshëm më i lartë sot sesa më herët ose në krahasim me gjeneratat e nënave të tyre. Me shumë mundësi shkaqet e rritjes së depresionit tek të rinjtë janë: stresi kronik, privimi nga gjumi, ushqimi i dobët i nënës, mënyra sedentare e jetesës, presioni ndaj nënave për t'u rikthyer në punët e tyre sa më shpejt të jetë e mundur pas lindjes, duke u përballur kështu me vështirësitë në menaxhimin e numrit të shumtë të roleve: të qenurit nënë, grua, punëtore e zellshme dhe në të njëjtën kohë të jesh aktive në jetën shoqërore (7).

Rreziku më i madh për nënën e re në depresion është vetëvrasja, e cila konsiderohet shkaku i dytë i vdekjes tek të rinjtë gjatë viteve të riprodhimit. Fatkeqësisht, kjo ndodh zakonisht në fund të shtatëzanisë ose gjatë vitit të parë pas lindjes.

Numri më i madh i këtyre grave kryejnë vetëvrasje të dhunshme duke u varur ose duke kërcyer nga lartësia, që është një alarm për njohjen dhe trajtimin e hershëm e depresionit para lindjes dhe pas lindjes (10, 16).

Supozohet se tek 80% të nënave të reja gjatë ditëve ose muajve të parë pas lindjes ka ndryshime që përkojnë me çregullim të humorit, por jo të gjitha këto ndryshime kanë të bëjnë me depresionin pas lindjes. Pikëllimi (trishtimi) pas lindjes është i pritur dhe manifestohet me nervozizëm, marramendje, ankth të moderuar, por të gjitha këto nuk ndërhyjnë në aftësinë e nënës për të funksionuar dhe për t'u kujdesur për fëmijën e saj. Përkundër kësaj, depresioni pas lindjes që shpesh i shtohet gjendjes depresive gjatë shtatëzënësisë manifestohet me trishtim të veçantë, ankth ekstrem, ndjenjën e irracionalitetit / absurditetit ose dëshpërimit, çregullim të gjumit, ngurrim, mosgatishmëri, mendime destruktive për veten ose foshnjën që mund të çojë në vetëvrasje ose vrasje të foshnjës (10,13).

Faktorët më të zakonshëm të rrezikut për zhvillimin e depresionit para lindjes ose pas lindjes përfshijnë historinë e gjendjes depresive të mëparshme, faktorët e dobët psikosocial (mbështetje të dobët familjare, prindërit beqarë, sjellja e dhunshme nga partneri intim, shtatzënia e paplanifikuar / e paqëllimshme), ndryshimet hormonale e tj. (3, 4, 15)

Ndikimi i depresionit në zhvillimin e foshnjës është i madh. Përkeqësimi i marrëdhënies midis nënës dhe foshnjës, prania e mendimeve negative për mëmësinë duke e refuzuar ate ose sjellje ndërhyrëse, shprehje (grimasa) negative të fytyrës, ndërprerja e ushqyerjes me gji (mëntjes), çojnë në probleme të ndryshme emocionale tek fëmija, i cili përjeton vështirësi në të ngrënë, gjumë, plasje (vërshime) zemërimi, tërbimi, hiperreaktiviteti, vonesat në zhvillimin konjitiv dhe çrregullimet e sjelljeve shoqërore, me një rrezik të shtuar të kequshqyerjes ose mbipeshes.

QËLLIMET E STUDIMIT

- Përcaktimi i pranisë së faktorëve të rrezikut për zhvillimin e depresionit antenatal (para lindjes) ose postnatal (pas lindjes),

- Përcaktimi i efikasitetit të procesit terapeutik tek nënat që trajtohen me një trajtim të kombinuar

- Përcaktimi i dallimeve sociodemografike te pacientet me depresion antenatal (para lindjes) ose postnatal (pas lindjes).

MATERIALI DHE METODAT

Kërkimi përfshinte 69 paciente në moshë midis 18 dhe 44 vjeç, me diagnozën e vendosur F32 gjatë shtatëzanisë

ose F32.01 ose F32.02, që është depresion pas lindjes. Pacientet u diagnostikuan sipas kritereve të KNS 10 dhe u trajtuan gjatë shtatzënisë dhe periudhës pas lindjes në Departamentin për trajtimin e grave shtatzëna ose grave në periudhën pas lindjes. Ata u trajtuan si paciente ambulatore ose në spital. Pacientet u analizuan duke përdorur një intervistë psikiatrike të strukturuar diagnostikuese, një pyetësor të strukturuar jo-standard të sociodemografisë (mosha, arsimi, statusi martesor, numri i shtatëzënive, prania e faktorëve të rrezikut - episodet depresive të mëparshme, dhuna familjare, ndërprerja e terapisë, ngjarjet e traumës), duke përdorur instrumente psikodiagnostike për vlerësimin e ankthit dhe depresionit, shkallës së vlerësimit të ankthit Hamilton (HAM-A) dhe shkallës së vlerësimit të depresionit Hamilton (HAM-D). Depresioni dhe ankthi u vlerësuan në fillim të trajtimit dhe pas tre muaj trajtimi. Pacientet u trajtuan me ndërhyrje psikologjike dhe trajtim farmakologjik, terapi antidepresive SSRI ose SNRI, gjatë shtatëzanisë ose periudhës pas lindjes. Trajtimi antidepresiv gjatë shtatëzanisë përfshiu doza terapeutike që ishin efektive, me ulje graduale. Në periudhën pas lindjes pacientet u këshilluan të zgjasin ushqyerjen me gji të foshnjeve të tyre, me qëllim sigurimin e një bashkëveprimi cilësor nënë-foshnjë. Pacientet dhe familjet e tyre u informuan në detaje në lidhje me trajtimin antidepresiv dhe raportin përfitim-rrezik. U arit një marrëveshje terapeutike me pacientet në lidhje me kontrollet e tyre të rregullta (të paktën një herë në dy javë), monitorim e vazhdueshëm të shëndetit të tyre trupor me vizita të rregullta të kryera tek gjinekologu familjar dhe pediatri, në mënyrë që të kemi një pamje të qartë të gjendjes në periudhën antenatale (para lindjes) dhe postnatale (pas lindjes). Gjatë procesit terapeutik, u përfshinë edhe partnerët intimë të pacienteve, dhe nëse ishte e nevojshme, anëtarët e tjerë të ngushtë të familjes për marrjen e mbështetjes adekuate. Procesi terapeutik përfshinte ndërhyrje intenzive psikiatrike dhe psikologjike te pacientet që synonin të jepnin njohuri për gjendjen e tyre dhe forcimin e gjendjes së tyre psikologjike në sjelljen e vendimeve të pavarura lidhur me shtatzëninë dhe trajtimin e gjendjes depresive në periudhën para lindjes dhe pas lindjes, si dhe në marrjen e vendimeve për mënyrat e ushqimit të fëmijëve të tyre. Gjatë periudhës pas lindjes shpesh këshillohej monitorimi i gjendjes së pacientes (së bashku me regjistrimin e telefonit celular të partnerit) lidhur me procedurat rutinore në lidhje me prindërinë. Kjo ishte e rëndësishme për të forcuar vetëbesimin dhe rolin e nënës, dhe nga ana tjetër, për të forcuar marrëdhëniet e partnerit dhe pjesëmarrjen e tyre të ndërsjellë në prindëri. Pacientet me instrumente psikodiagnostike u monitoruan gjatë gjithë procesit, dhe matjet me HAM-A dhe HAM-D paraqiten në fillim të trajtimit dhe pas tre muajsh.

REZULTATET

Ky ishte studim i kryer në periudhë 3-mujore dhe përfshinte 69 pacientë, nga të cilët 71.0% ishin më të vjetër se 30 vjeç, ndërsa 29.0% më të rinj se 30 vjeç. Përqindje më e lartë (49.3%) e pacienteve kishin mbaruar shkollën e mesme, 37.7% kishin diplomë universitare dhe 13.0% kishin mbaruar shkollën fillore. Nga numri i pacienteve të testuara 75.4% ishin të përkatësisë së krishterë dhe 24.6% ishin muslimanë.

Nga numri i përgjitshëm i pacienteve 81.5% morën antidepresantë (sertalinë, escitalopram dhe venlafaksinë), 24.6% kishin pranuar antipsikotikë (olanzapinë, risperidone) dhe anksiolitikë (alprazolam, diazepam), si monoterapi ose në kombinim me barërat tjera.

Numri i shtatëzënive në pacientë shkonte nga një në tre, mesatarisht 1.5 ± 0.7; 65.2% e pacientëve kishin vetëm një shtatëzani. Nuk ka asnjë lidhje midis numrit të shtatëzënive dhe moshës së pacientëve (Pearson Chi-shesh: 2.65137, f = .265621).

Nga numri i përgjitshëm I pacienteve 91.3% e pacientëve kishin një shtatëzani normale, 17.4% kishin lindje normale, dhe 6.7% kishin lindje cezariane (Tabela 1).

Tabela 1. Karakteristikat e pacienteve

Mosha	Numri	Përqindja
>30	49	71.0
< 30	20	29.0
Niveli i arsimimit		
Universitet	26	37.7
Shkolla e lartë	34	49.3
Shkolla fillore	9	13.0
Religjioni (feja)		
Krishten	52	75.4
Musliman	17	24.6
Trajtimi mjekësor		
Paciente të jashtme	53	76.8
Paciente në spital	12	17.4
I kombinuar	4	5.8
Terapia		
Pa terapi	3	4.3

Antidepresant		38	55.1
Anksiolitik		3	4.3
Antipsikotik		4	5.8
Antidepresant, Anksiolitik		8	11.6
Antidepresant, Antipsikotik		7	10.1
Anksiolitik, Antipsikotik		3	4.3
Antidepresant, Anksiolitik, Antipsikotik		3	4.3
Numri i shtatzanive			
1		45	65.2
2		14	20.3
3		10	14.5
Average	Minimum	Maximum	Std.dev.
1.5	1.0	3.0	0.740095
Shtatzania dhe lindja			
Normale		63	91.3
E rezikshme		6	8.7
Lindje normale		12	17.4
Lindje e parakohshme, seksion Cezarian		6	8.7

Faktorët e rrezikut nuk janë regjistruar te 5 paciente (7.2%). Nuk ka të dhëna për faktorët e rrezikut për 4 paciente (5.8%). Në 87.0% të pacienteve janë regjistruar faktorë rreziku. Në numrin më të madh të pacienteve, 29 (42.0%), episodet e mëparshme janë regjistruar vetëm ose në kombinim me faktorët e tjera të rrezikut. Gjendja e stresit postraumatik ishte faktori tjetër i rrezikut i regjistruar në 40.6% (28) të pacienteve, shtatzënia e paplanifikuar në 18.8% (13) dhe dhuna familjare në 17.4% (12) (Tabela 2).

Tabela 2.Shpërndarja e pacienteve sipas faktorëve të regjistruar të rrezikut

Faktorët e regjistruar të rrezikut	Numri	Përqindja
Asnjë	5	7.2
Dhuna në familje	6	8.7
Gjendja e stresit postraumatik	17	24.6
Shtatzënia e paplanifikuar	3	4.3
Episodet e mëparshme	15	21.7
Dhuna në familje, gjendja e stresit postraumatik	3	4.3
Dhuna në familje, Episodet e mëparshme	2	2.9
Gjendja e stresit postraumatik, Shtatzënia e paplanifikuar	1	1.4
Gjendja e stresit postraumatik, Episodet e mëparshme	4	5.8
Shtatzënia e paplanifikuar, Episodet e mëparshme	6	8.7
Dhuna në familje, Gjendja e stresit postraumatik, Shtatzënia e paplanifikuar	1	1.4
Gjendja e stresit postraumatik, Shtatzënia e paplanifikuar, Episodet e mëparshme	2	2.9
Nuk ka të dhëna relevante	4	5.8

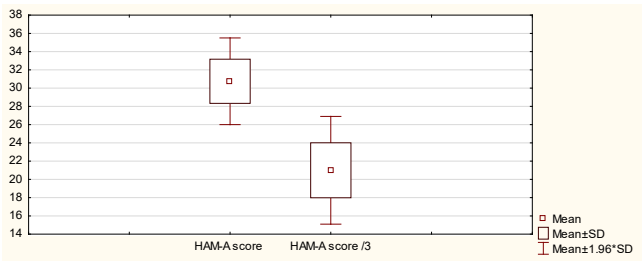
Rezultati mesatar e shkallës HAM-A në muajin e parë ishte 30.8 ± 2.4, në diapazon nga 26 deri në 38 dhe tregoi një ankth të fortë. Pas tre muajve me terapi, rezultati mesatar i HAM-A u ul në 21.0 dhe demonstroi një ankth të moderuar. Sipas testit Wilcoxon Matched Pair, diferenca ishte statistikisht e rëndësishme për $p < 0.05$ (Tabela 3 dhe Figura 3a).

Tabela 3. Rezultati mesatar i shkallës së vlerësimit të ankthit të Hamilton-it (HAM-A) dhe Shkalla e Vlerësimit të Depresionit të Hamilton-it (HAM-D)

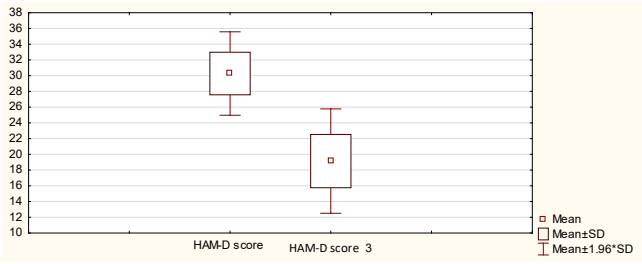
	N	mesatare	minimum	maksimum	Std.dev.	T	Z	p-vlera
HAM-A score	69	30.8	26.0	36.0	2.421751	0.00	7.219578	0.000000
HAM-A score/3m	69	21.0	14.0	30.0	3.009788			
HAM-D score	69	30.3	26.0	38.0	2.705572	0.00	7.219578	0.000000
HAM-D score/ 3m	69	19.1	10.0	28.0	3.383678			

Figura 3. Rezultati mesatar i shkallës së e vlerësimit të ankthit të Hamilton-it (HAM-A) dhe Shkallës së vlerësimit të depresionit të Hamilton-it (HAM-D)

A.



B.



Rezultati mesatar e shkallës HAM-D në muajin e parë ishte 30.3 ± 2.7, në diapazon nga 26 deri në 36, dhe demonstroi një depresion të rëndë. Pas tre muajve me terapi, rezultati mesatar i HAM-D u ul në 3.4, dhe demonstroi një depresion të moderuar. Sipas palëve të përputhura Wilcoxon, diferenca ishte statistikisht e rëndësishme për p <0.05 (Tabela 3 dhe Figura 3b).

Rezultati mesatar e shkallës HAM-A te pacientet me faktorë rreziku në muajin e parë ishte 2.4 ± 31.0 dhe tregoi një ankth të fortë. Rezultati mesatar e HAM-A te pacientet pa faktorë rreziku në muajin e parë ishte 29.6 ± 1.7, dhe demonstroi një ankth të rëndë. Sipas testit Kolmogorov-Smirnov, rëndësia statistikore nuk ishte domethënëse, për p> 0.05 (Tabela 4).

Tabela 4. Rezultati mesatar i shkallës së vlerësimit të ankthit të Hamilton-it (HAM-A) dhe Shkallës së vlerësimit të depresionit të Hamilton-it (HAM-D) në lidhje me praninë e faktorëve të rrezikut tek pacientët dhe testin Kolmogorov-Smirnov

	Maksimum diferencë negative.	Maksimum diferencë pozitive	p	Mestare - po	Mestare - jo	Std.Dev. - po	Std.Dev. - jo	Nr.– po	Nr - jo
HAM-A score	-0.05	0.25	p > .10	31.0	29.6	2.393494	1.673320	60	5
HAM-A score/3m	-0.05	0.25	p > .10	21.3	19.6	3.042588	1.673320	60	5
HAM-D score	0.0	0.8	p < .005	30.7	27.2	2.578212	1.095445	60	5
HAM-D score/ 3m	-0.03	0.9	p < .005	19.7	15.6	3.164912	0.894427	60	5

Pas tre muajve me terapi, rezultati mesatar i HAM-A u zvogëlua në 21.3 ± 3.0, dhe demonstroi një ankth të moderuar. Rezultati mesatar i HAM-A pas muajit të tretë në pacientet pa faktorë rreziku ishte 19.6 ± 1.7, dhe demonstroi një ankth të moderuar. Sipas testit Kolmogorov-Smirnov ndryshimi ishte statistikisht i rëndësishëm për p> 0.05 (Tabela 5).

Rezultati mesatar e HAM-D në pacientet me faktorë rreziku në muajin e parë ishte 30.7 ± 7 2.6, dhe demonstroi një depresion të rëndë. Rezultati mesatar e HAM-A në pacientet pa faktorë rreziku në muajin e parë ishte 27.2 ± 1.1, dhe demonstroi një depresion të rëndë. Sipas Kolmogorov-Smirnov ndryshimi ishte statistikisht i rëndësishëm për p <0.05 (Tabela 5).

Pas tre muajve me terapi, rezultati mesatar i HAM-D u zvogëlua në 19.7 ± 3.2, dhe demonstroi një depresion të moderuar. Rezultati mesatar i HAM-D pas muajit të tretë në pacientet pa faktorë rreziku ishte 0.9 ± 15.6 and, dhe demonstroi një depresion të moderuar. Sipas testit Kolmogorov-Smirnov ndryshimi ishte statistikisht i rëndësishëm për p <0.05 (Tabela 5).

Gjatë hulumtimit nuk kishte korelacion ndërmjet përkatësisë fetare, moshës, arsimit dhe numrit të shtatzënisë dhe faktorëve të regjistruar të rezikut (Pearson Chi-square, f> 0.05).

DISKUTIMI

Rezultatet kanë treguar prani statistikisht të rëndësishme të faktorëve të rrezikut te pacientet me depresion antenatal ose postnatal. Numri më i madh i pacienteve përjetuan episodet e mëparshme depresive, ngjarje traumatike, shtatzëni të paplanifikuar ose dhunë familjare. Në një grup pacientesh, është vërejtur ekzistenca e disa faktorëve të rrezikut, përfshirë episodet e mëparshme, dhunën në familje dhe ngjarjet traumatike në të kaluarën.

Në numrin më të madh të këtyre pacienteve, ekzistonte dhuna në familje, që është një fakt shumë shqetësues pasi që kjo dhunë u zbulua kryesisht në familjen themelore (bërthamë) dhe ndonjëherë vazhdoi në familjen aktuale. Gjithashtu, në numrin më të madh të pacienteve janë parë disa faktorë rreziku në të njëjtën kohë. Në 50% të pacienteve janë zbuluar episodet e mëparshme depresive dhe ato ishin ose të diagnostikuara dhe të patrajtuara ose u përkeqësuan gjatë shtatëzanisë pas ndërprerjes së ilaçeve antidepresive nga vetë gratë shtatzëna ose me një rekomandim.

Këto rezultate janë në lidhje me hulumtimet që tregojnë rolin e rëndësishëm të faktorëve të rrezikut, të cilat përveç dobësisë biologjike, përfshijnë histori familjare ose individuale të së kaluarës, ndryshime hormonale, por edhe faktorë psikosocialë – mungesën e mbështetjes sociale, dhunë familjare, ngjarje traumatike (si humbja financiare e çdo lloji), vdekja e një anëtari të familjes, ngjarje të tjera të pakëndshme me një rrezik shumë të lartë tek gratë e reja - viktima të dhunës aktuale të familjes ose të dhunës të mëparshme familjare ose ato me episodet e mëparshme depresive (1, 4, 8, 10, 14).

Kjo është mbështetur nga hulumtimet që sugjerojnë se afërsisht 50% e vajzave, të cilat kishin episode depresive të çfarëdo lloji në të kaluarën, ishin në rrezik të zhvillimit të depresionit antenatal. Nëse kemi parasysh se numri më i madh i tyre nuk janë njohur dhe nuk janë trajtuar, atëherë kjo është me të vërtetë një çështje shqetësuese / problematike (1, 15).

Kërkimi ynë përfshinte paciente, të cilët në numrin më të madh ishin me shtatëzëninë e parë; ishin mbi 30 vjeç; depresioni nuk u ndërlidh ndjeshëm me nivelin e arsimimit, megjithëse shumica e tyre ishin me shkollë të mesme ose fakultet. Numri më i madh i pacienteve ishte i përkatësisë krishtere dhe një numër i vogël myslimane, që mund të tregojë një shqetësim të shtuar për gjendjen mendore individuale ose kërkimin e ndihmës profesionale si rezultat i dallimeve kulturore.

Depresioni pas lindjes është i ndryshëm nga i ashtuquajturi trishtim pas lindjes, i cili zakonisht shfaqet menjëherë pas lindjes në dy javët e para dhe manifestohet me ankth të shtuar, nervozizëm, episode dramatike të qarjes, por në kundërshtim me depresionin pas lindjes nuk ndërhyn në aftësinë e nënës të kujdeset për fëmijën e saj. Nga ana tjetër, depresioni pas lindjes që është i regjistruar në 15% të numrit të përgjithshëm të nënave manifestohet me çregullim të humorit, apati ose shqetësim të prolonguar, pagjumësi, ide deluzive që lidhen me pamundësinë e nënës për të vepruar si nënë ose për gjendjen e foshnjës dhe rrezik të lartë të vetëvrasjeve ose vrasjes së foshnjave (10, 14, 16).

Rezultatet e marra në studimin tonë kanë treguar një ulje të ndjeshme të ankthit dhe depresionit pas aplikimit të terapisë me SSRI dhe ndërhyrjeve psikologjike individuale dhe grupore duke fuqizuar nënën që të kujdeset për veten dhe fëmijën e saj. Rezultatet kanë treguar gjithashtu se trajtimi me SSRI nuk ishte rrezik për vetë shtatzëninë: përkundrazi, depresioni para lindjes ishte rrezik i lindjes së parakohshme, lindjes së foshnjeve me peshë të ulët ose lindjes cezariane. Disa paciente të paraqitur me përkeqësim të shenjave të depresionit përfshirë ide delirante, mendime vetëvrasëse, të gjitha ishin një tregues për trajtimin spitalor. Vetëvrasja gjatë shtatëzanisë është më e larta në javët e fundit të gjestacionit ose menjëherë pas lindjes së fëmijëve, dhe paraqet indikacion absolut për trajtimin në spital (1, 10, 16).

Rezultatet nuk treguan ndonjë dallim statistikor në lidhje me statusin martesor. Numri më i madh i pacienteve kishte arsim të lartë. Disa studime kanë indikuar një nivel dukshëm më të lartë të depresionit tek nënat me gradë universitare, e cila mund të jetë për shkak të vetëdijes së tyre më të lartë për shëndetin e tyre somatik dhe mendor, ose / dhe për nevojën e tyre të kërkojnë ndihmë në kujdesin shëndetësor terciar (7).

Kërkimet sugjerojnë që depresioni pas lindjes jo vetëm që shkakton probleme tek nëna por gjithashtu ka ndikim negativ në zhvillimin e ardhshëm psikologjik të fëmijës. Nënat në depresion shfaqin sjellje më negative dhe të shkëputura ndaj foshnjeve të tyre; kanë vështirësi në krijimin e marrëdhënies nënë-fëmijë; tregojnë mënyrë depressive ose me më pak dashuri në komunikimin vokal ose vizual; ndërprerja e ushqyerjes me gji (mëntjes). Të gjitha këto janë parakushte për zhvillimin e dëmtuar psikologjik të fëmijës (10, 12).

Kjo ngrehë alarmin për rritjen e vetëdijes, njohjen e hershme dhe trajtimin e depresionit antenatal dhe pas lindjes në fillimin e shtatzënisë.

Rekomandimet për njohjen dhe trajtimin janë si vijon:

qasje e kujdesshme ndaj grave të reja që kanë vuajtur ose aktualisht vuajnë nga ndonjë ankth ose çrregullim depresiv;

diskutim rreth kontracepsionit;

diskutime rreth shtatzanisë që do të ndikonin në gjendjen

psikike të nënës;

diskutim mbi ndikimin e gjendjes psikike tek nëna ose fetusi;

trajtimi eventual;

mbështetje për nënën, partnerin e saj intim dhe tërë familjen;

përfshirja e nënës në marrjen e vendimeve për shtatzëninë e saj, ndërprerjen e saj ose trajtimin në të ardhmen, me përfshirjen e mundshme (të dëshirueshme) të partnerit;

kujdes i koordinuar me mjekun e familjes, gjinekologun, psikiatërin, pediatrin gjatë gjithë shtatëzanisë dhe pas lindjes, vëzhgimin / monitorimin e shëndetit psikik dhe fizik të nënës;

monitorimin e konsumit / abuzimit të alkoolit dhe ilaçeve;

qëndrimet i nënës ndaj shtatzënisë;

bashkëveprimi nënë-fëmijë;

trajtimi i mëparshëm;

izolim social;

historia familjare;

dhuna në shtëpi;

aftësia për t›u kujdesur për fëmijët e tjerë.

Ndërhyrje specifike në çrregullimet depresive - ndërhyrje psikologjike intensive (terapia konjitive bihejviorale ose të tjera)-SSRI si barëra të linjës së parë (përveç paroxetinës për shkak të rritjes së rrezikut të keqformimeve kardiake), doza optimale deri në 8 javët e fundit gestacionale kur doza është ulur ose ndoshta ndërpritet; shmangia e përdorimit të anksiolitikëve në tremujorin e pare- SNRI si barëra të linjës së dytë (4, 5, 6, 11, 15).

Rezultatet e marra në studimin tonë kanë treguar se pothuajse të gjithë pacientet janë trajtuar me terapi antidepresive SSRI, përveç paroxetine. Në mbi 90% të tyre është vërejtur shtatzënia normale dhe lindja, dhe vetëm në një përqindje të vogël ka ndodhur lindja e parakohshme ose cezariane.

Hulumtimi ka demonstruar rrezik më të vogël tek nënat e trajtuara me SSRI gjatë shtatëzanisë sesa tek ato që nuk trajtohen duke rezultuar në një rrezik më të vogël të lindjes së parakohshme, lindjes cezariane ose lindjes së bebeve me peshë të ulët (5, 9, 12).

Një studim tjetër zbuloi se një nivel i lartë depresioni tek nënat e patrajtuara rezultoi me zhvillim të vonuar të funksioneve ekzekutive të fëmijëve të tyre, të cilat u matën në moshën 3 vjeçare, dhe kjo nuk ndodhte me fëmijët, nënat e të cilëve u trajtuan me SSRI (12).

Nënat me rrezik të theksuar ose nënat me episoda depresive të mëparshme zakonisht duhet të ndiqen / monitorohen dhe këshillohen. Nënave pa asnjë episodë depresive të mëparshme ose lloje të tjera ankthi duhet ti parashtrohen disa pyetje të thjeshta nga mjekët familjar ose gjinekologët e tyre, si p.sh.: Gjatë dy javëve të fundit a jeni ndier e trishtuar, e pasigurt, e frikësuar, e mjeruar? Nëse përgjigjet janë pozitive, atëherë kjo mund të tregojë zhvillimin e një gjendje depresive, e cila imponon nevojën e udhëzimit te psikiatri për kontroll të rregullt dhe trajtim (8, 15).

PËRFUNDIM

Siç ka thënë tashmë një nënë, e cila ka vuajtur nga depresioni para lindjes dhe pas lindjes, kujdesi për shëndetin mendor të nënës është kujdesi për të gjithë shoqërinë: për nënën e shëndetshme, fëmijët e shëndetshëm dhe shoqërinë e shëndetshme. Njohja e hershme e faktorëve të rrezikut për zhvillimin e depresionit para lindjes çon drejt parandalimit të shfaqjes së depresionit antenatal ose postnatal.

Trajtimi i hershëm që përbëhet nga një trajtim të kombinuar (me ndërhyrje psikologjike dhe antidepresantë SSRI) që sjellë uljen e ankthit dhe depresionit dhe forcimin e mekanizmëve mbrojtëse psikologjike të nënës dhe gjithashtu zvogëlon rrezikun e lindjes së parakohshme, lindjes cezariane dhe kujdes më të mirë si për nënën ashtu edhe për fëmijën, në periudhën para lindjes dhe pas lindjes.

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УЛОГАТА НА NGAL, CYSTATIN C И β2-MICROGLOBULIN КАКО РАНИ МАРКЕРИ ЗА ДИЈАБЕТИЧНА НЕФРОПАТИЈА КАЈ ПАЦИЕНТИ СО ДИЈАГНОСТИЦИРАН ДИЈАБЕТЕС МЕЛИТУС ТИП 2: РЕВИЈАЛЕН ТРУД

Argjent Muca[1], Gazmend Amzai[2], Besarta Jonuzi Ibrahimi[3], Muhamed Ibraimi[4], Tatjana Milenkovik[1]

[1]University Clinic for Endocrinology, Diabetes and metabolic diseases, Medical Faculty, University "Sts. Cyril and Methodius", Skopje, Republic of North Macedonia

[2]University Clinic for Hematology, Medical Faculty, University "Sts. Cyril and Methodius", Skopje, Republic of North Macedonia

[3]General Hospital 'Ferid Murad', Gostivar, Republic of North Macedonia

[4]Institut for Transfusion Medicine, Skopje, Republic of North Macedonia

Corresponding author: Argjent Muca, MD, University clinic for endocrinology, diabetes and metabolic diseases, Medical Faculty, University "Sts. Cyril and Methodius", Mother Teresa, No 17, 1000, Skopje, Republic of North Macedonia, e-mail: argjent_muca85@hotmail.com ; phone: +38970883305

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АПСТРАКТ

Дијабетичната нефропатија (ДН) е прогресивно бубрежно оштетување кое се карактеризира со нарушување на бубрежната архитектура и функција, и е една од водечките причини за трајно бубрежно оштетување. Во секојдневната пракса во Р. Северна Македонија за детекција на ДН се користат серумскиот креатинин, микроалбуминурија и гломеруларна филтрациона рата. Меѓутоа овие стандарни тестови не овозможуваат секогаш детекција на почетни оштетувања кај ДН. Има многу студии каде што се испитуваат различни маркери кои би откриле бубрежно оштетување пред да се покачат стандардните маркери за детекција на ДН. Меѓу тие маркери се и NGAL, Cystatin C и β2-microglobulin. NGAL, Cystatin C и β2-microglobulin, биомаркери на бубрежно оштетување, се во корелација со пад на бубрежната функција кај пациенти со ДМ тип2, што укажува на тоа дека тие може да се користат како дополнителни тестови на постоечките (креатинин и микроалбуминурија) со цел да се демаскира раната бубрежна дисфункција.

Клучни зборови: дијабетична нефропатија, NGAL, Cystatin C, β2-microglobulin, диајбетес тип 2

ВОВЕД

Дијабетес мелитус (ДМ) представува хронично метаболичко нарушување, која се карактеризира со хронична хипергликемија настаната поради наследен и / или стекнат недостаток во производството на инсулин од панкреасот, или од неефективноста на произведениот инсулин [1, 2]. Дијабетесот настанува поради интеракција на различни фактори, пред се генетски фактори, начинот на живот и фактори на надворешната средина.

Дијабетесот зазема пандемиски размери и претставува еден од поголемите здравствени проблеми во 21 век. Според ИДФ (Интернационалнта федерација за дијабетес) вкупниот број на лица со дијабетес во светот заклучно 2019 година изнесува 463 милиони, а се очекува ова бројка во 2045 година да биде 700 милиони [3].

Најчести типови на дијабетес се: дијабетес мелитус тип 1, тип 2 и гестациски дијабетес. Дијабетес тип 2 е почест и опфаќа околу 90-95% од сите видови на дијабетес, како глобално така и кај нас [1, 2, 4].

ДМ предизвикува акутни и хронични микро- и макро-

васкуларни компликации [5-7].

Во акутните компликации спаѓаат хипогликемија, дијабетична кетоацидоза и хиперосмоларна состојба [5]. Додека во хроничните микроваскуларни компликации спаѓаат: дијабетична ретинопатија, нефропатија и невропатија [6, 7].

Дали, и кога ќе се појават хроничните микроваскуларни компликации зависат од многу фактори, меѓу кои:

Времетраење на дијабетот

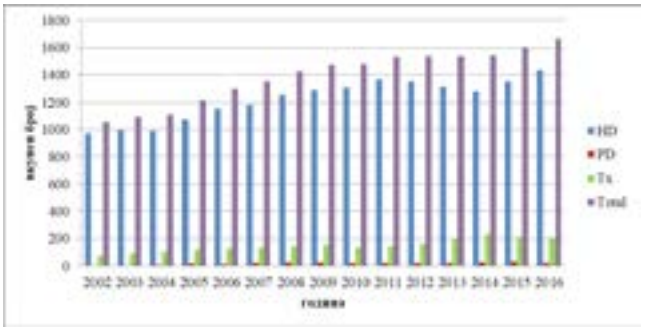
Диетата и физичката активност

Соодветната терапија

Контрола на гликемијата-вредностите на HbA1c, вредностите на гликемија на гладно и постпрандијалните гликемии

Дијабетичната нефропатија (ДН) е прогресивно бубрежно оштетување кое се карактеризира со нарушување на бубрежната архитектура и функција, и е една од водечките причини за трајно бубрежно оштетување [8, 9, 10]. Како резултат на тоа тие пациенти имаат потреба од ренална заместителна терапија (РЗТ)-хемодијализа (ХД) најчесто. Во последнтие години континуирано се зголемува бројот на болни со РЗТ, како во светот така и во Р. Северна Македонија. Така во 2002 година вкупниот број на болни со РЗТ е 1056 од кои 92% се на ХД, додека во 2016 година бројот на болни со РЗТ е 1665 од кои 86% се на ХД (табела 1) [11].

Табела. 1 Број на пациенти со потреба од ренална заместителна терапија-РЗТ во Р.Македонија за период од 2002 до 2016 година



*податоци од годишните регистри на ERA-EDTA,*интерни податоци за 2012-2013 година, *HD –хемодијализа,*PD –перитонеална дијализа, *Tx (трансплантација), *Total- Вкупно

Патофизиолошките промени кај ДН кои водат до намалување на реналната функција се поврзани со клеточни и екстрацелуларни нарушувања во гломеруларните и тубуло-интерстицијалните структури [10, 12, 13]. Гломеруларната и тубуларно-интерстициелната повреда на бубрезите игра улога во патогенезата на ДН [13]. Пациентите со ДН имаат висок морталитет, кој пред се се должи на кардиоваскуларните компликации.

Во секојдневната пракса во Р. Северна Македонија за детекција на ДН се користат серумски креатинин, албуминурија и калкулирање на гломеруларната филтрациона рата.

Микроалбуминуријата генерално се сметало за најран маркер за развој на дијабетична нефропатија, и често е поврзана со утврдено значително гломеруларно оштетување [14]. Сепак, неодамнешните студии покажаа дека МА не секогаш ги одразува присутните оштетувања на бубрезите. Покрај тоа, неколку линии на докази сугерираат дека раното оштетување на гломеруларните и тубуларните структури може да биде присутно кај нормоалбуминурични субјекти [13,15,16].

Неопходно е да се идентификуваат маркери кои ќе детектираат рано тубуларно оштетување независно од развојот на албуминурија кај пациенти со рана ДН и прогресија, бидејќи може да игра значајна улога во управувањето со случаи на ренална инсуфициенција кои се нормоалбуминурични [13, 15-17].

Се смета дека новите биомаркери како што се: NGAL (neutrophil gelatinase-associated lipocalin), Cystatin C и β2-microglobulin се посензитивни во однос на потребата од рана детекција на ДН.

NGAL- кој е познат и како lipocalin2, е составен од 178 аминокиселини, е 25 kDa протеин, за прв пат прочистен и идентификуван во 1993 година од Кјелдсен и сор, се чини дека е ветувачки биомаркер [13,17]. Главно се произведува во бубрежни тубули како одговор на структурна повреда на бубрезите, но исто така, во помал степен, во белите дробови, душникот, желудникот и дебелото црево, додека се излачува во урината [18, 19]. NGAL вредностите може да бидат под влијание на бубрежни заболувања, хипертензија, воспалителни состојби, хипоксија и малигнитети [18]. NGAL како бубрежен биомаркер за прв пат е опишан во 2003 година, преку предизвикување на експериментална бубрежна исхемија кај глушец [20].

За разлика од конвенционалните серумски маркери, како што е креатинин, NGAL се смета за маркер на бубрежно структурно оштетување, чии вредности во

плазмата и уринатa се зголемуваат како резултат на тубуларно бубрежно оштетување, и неговите вредности се покачуваат пред да се открие бубрежно оштетување со другите методи [18, 19, 21]. Освен кај акутно и хронично бубрежно оштетување, овој биомаркер има значење и во прогресијата на бубрежното оштетување.

Cystatin C е мал протеин кој се филтрира од телото преку гломерулите, кој има висока корелација со степенот на гломеруларна филтрациона рата (ГФР) [22]. Не е под влијание на воспалителни состојби, мускулна маса, пол, состав на тело и возраст (по возраст од 12 месеци) [23]. Супериорноста на CysC во однос на другите маркери на опаѓање на бубрежната функција лежи во неговата способност да остане неповрзан со протеините и слободно да се филтрира низ гломерулите. Кај здрави субјекти, CysC е скоро слободно филтриран од гломерулите и скоро целосно се реапсорбира во проксималните тубули, како и другите протеини со ниска молекуларна тежина, без или само со делумна тубуларна секреција.

При бубрежно оштетување, со намалување на ГФР, вредностите на овој биомаркер се покачуваат. Во повеќе студии е докажано кога ГФР и вредностите на креатинин се сеуште во граници на нормалата, Cystatin-C се покачува кога имаме почетно бубрежно оштетување [24, 25].

Високи вредности на CysC кај пациенти со дијагностициран дијабетес мелитус го покачуваат ризикот за кардиоваскуларен морбидитет и прогресија на атеросклерозата [26, 27].

β2-microglobulin Бета 2- (b2-m) е 11-kDa протеин препознаен како компонента на лесниот ланец на молекулата MHC-I. Се произведува од страна на нуклеарни клеточни мембрани и може да се детектира во серумските и другите телесни течности. [28] Вредностите на b2-m се покачен кај различни нарушувања и има прогностичка вредност кај лимфопролиферативните нарушувања како што се мултипниот миелом и акутната лимфоцитна леукемија. Освен кај овие болести вредностите на b2-m се покачуваат и кај оштетувања на бубрежната функција [29].

Направени се повеќе студии, меѓу кои и кај пациенти со дијагностициран дијабетес мелитус, во кои е докажано дека вредностите на b2-m се покачени кога имаме дијабетична нефропатија [28, 29]. Вредностите на овој биомаркер растеле пропорционално со бубрежното оштетување. Резултатите од некои студии покажале дека вредностите на овој биомаркер биле покачени кога сеуште вредностите на микроалбуминурија биле нормални, а после тоа со бубрежна биопсија било потврдено дека имало инципиентно бубрежно оштетување [28, 29].

Заклучок Дијагностицирањето на ДН (дијабетичната нефропатија) во почетниот стадиум е од особена важност, затоа што преземените терапевтски мерки во раните стадиуми на ДН овозможуваат спречување на прогресивниот тек на ДН, а со тоа и намалување на кардиоваскуларниот и севкупниот морталитет кај популацијата со дијабетес [9, 30].

Употребата на новите биомаркери (NGAL, Cystatin C и β2-microglobulin) како дополнителни тестови на постоечките (креатинин и микроалбуминурија) за рано дијагностицирање на ДН, ќе ги забрза ефикасните пристапи за управување и третман, кои се очајно потребни за да се минимизираат стапките на тешкиот кардиоренален морбидитет и морталитет кај пациенти со Т2Д. Затоа е потребно овие податоци да бидат потврдени со понатамошни големи лонгитудинални студии, пред да бидат интегрирани во проценката на ризик на ДН кај пациенти со Т2Д.

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ANTIPHOSPHOLIPID SYNDROM

Prim. Dr. Bekim Pocesta

University clinic of cardiology, Skopje

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ABSTRACT

Antiphospholipid syndrome (APS) is a multisystem autoimmune condition characterized by vascular thromboses and/or pregnancy loss associated ëith persistently positive antiphospholipid antibodies (aPL). Catastrophic APS (CAPS) is the most severe form of APS ëith multiple organ involvement developing over a short period of time, usually associated ëith microthrombosis. 'Definite' and 'probable' CAPS have been defined based on the preliminary classification criteria; hoëever, in a real-ëorld setting, aPL-positive patients ëith multiple organ thromboses and/or thrombotic microangiopathies exist ëho do not fulfill these criteria. Previous APS diagnosis and/or persistent clinically significant aPL positivity is of great importance for the CAPS diagnosis; hoëever, almost half of the patients ëho develop CAPS do not have a history of aPL positivity.

The purpose of this paper is to summarize the diagnostic challenges and the recently updated diagnostic algorithms for CAPS providing a 'step-by-step' approach for clinicians (and researchers) in the assessment of patients ëith multiple organ thromboses.

INTRODUCTION

Antiphospholipid syndrome (APS) is a multisystem autoimmune condition characterized by vascular thromboses and/or pregnancy loss associated with persistently positive antiphospholipid antibodies (aPL; measured with lupus anticoagulant [LA] test, anticardiolipin antibody [aCL] enzymelinked immunosorbent assay [ELISA], and/or anti-β2-glycoprotein-I antibody [aβ2GPI] ELISA).

Updated antiphospholipid syndrome classification criteria [Miyakis *et al.* 2006].

Clinical criteria

- vascular thrombosis

≥ 1 clinical episodes of arterial, venous, or small vessel thrombosis, in any tissue or organ

- Pregnancy morbidity:

≥ 1 unexplained deaths of a morphologically normal fetus at or beyond the 10th week of gestation, or

≥ 1 premature births of a morphologically normal neonate before the 34th week of gestation because of: eclampsia, severe preeclampsia, or recognized features of placental insufficiency, or

≥ 3 unexplained consecutive spontaneous abortions before the 10th week of gestation, with maternal anatomic or hormonal abnormalities and paternal and maternal chromosomal causes excluded

Laboratory criteria

- Lupus anticoagulant present in plasma, on ≥ 2 occasions at least 12 weeks apar

- Anticardiolipin antibody of IgG and/or IgM isotype, in medium or high titer (>40 GPL or MPL, or > the 99th percentile), on ≥ 2 occasions, at least 12 weeks apart

- Anti-β2-glycoprotein-I antibody of IgG and/or IgM

isotype, in medium or high titer (> the 99th percentile), on ≥ 2 occasions, at least 12 weeks apart.

Definite APS is present if at least one of the clinical criteria and one of the laboratory criteria are met.

In its most severe form, a minority of patients develop life-threatening multiple organ thromboses, usually associated with microthrombosis, recognized as catastrophic APS (CAPS)

Preliminary classification criteria for catastrophic antiphospholipid syndrome [Asherson et al. 2003].

- Evidence of involvement of three or more organs, systems and/or tissues

- Development of manifestations simultaneously or in less than a week

- Confirmation by histopathology of small-vessel occlusion*

- Laboratory confirmation of the presence of antiphospholipid antibodies†

Definite catastrophic antiphospholipid syndrome

- All four criteria present

Probable catastrophic antiphospholipid syndrome

- All four criteria, except only two organs, systems, and/or tissues involved

- All four criteria, except for the absence of laboratory confirmation of antiphospholipid antibodies

- Criteria 1, 2, and 4

- Criteria 1, 3, and 4, with the development of a third event more than 1 week but within 1 month of presentation, despite anticoagulation

CASE REPORT

Patient S. D.,woman, born in 1973, hospitalized in the Clinic for Rheumatology from 22.10.2013 to 29.10.2013 under the diagnosis of systemic sclerosis.

Diagnosed systemic sclerosis 18 years ago.

Treated with Methotrexate.

CVI 7 years ago,

At admission gives the impression of severely painful, contactable, in an orthopnoic position. On auscultation weakened to inaudible breathing right basal.

On admission TA 140/100, frequency 80 / min.

New chest pain with dyspnea appeared on October 25, 2013,.

On 28.10.2013, an echocardiogram was performed with a finding for present thrombi in the right ventricle and atrium, expressed pulmonary hypertension and suspension for pulmonary thromboembolism.

A CT of the lungs was performed with the finding of a massive acute pulmonary embolism with thromboembolism present in the right main pulmonary artery as well as the lobar branches for both inferior lobes.

On October 29, 2013, the patient was transferred to the Cardiology Clinic.

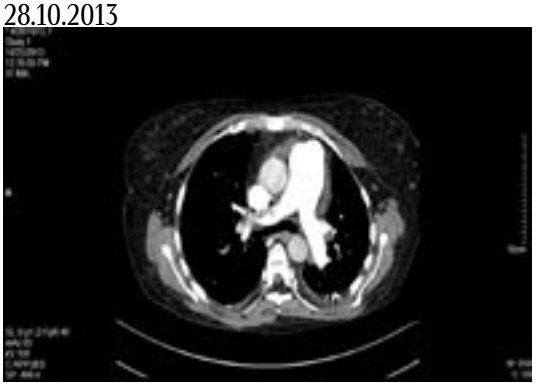
Laboratory:

Hgb – 177; Er- 6,2; Hct - 0,58; tr – 54, 103, Le – 23; glicemia 7,0; urea 3,0 kreat- 98; Na- 136; K – 3,8; CRP-109;RF – 9,3; anti-DNA – neg; ANA 1:80(+); anti-Scl- neg. D-dimeri >4500.

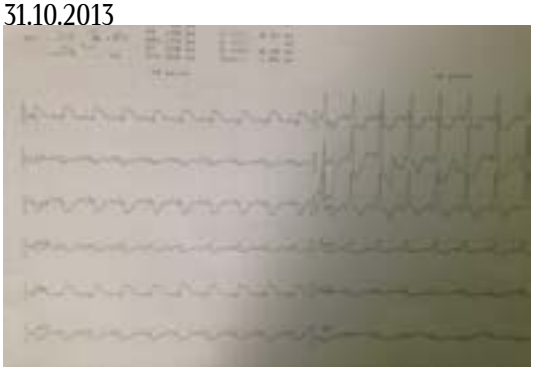
Patient was treated with Streptocinase according to the protocol for pulmonary embolism.

On October 31, 2013, she complained of tight chest pain. In the ECG with signs of lateral myocardial infarction. The patient immediately is taken to the coronary angiography room.

28.10.2013

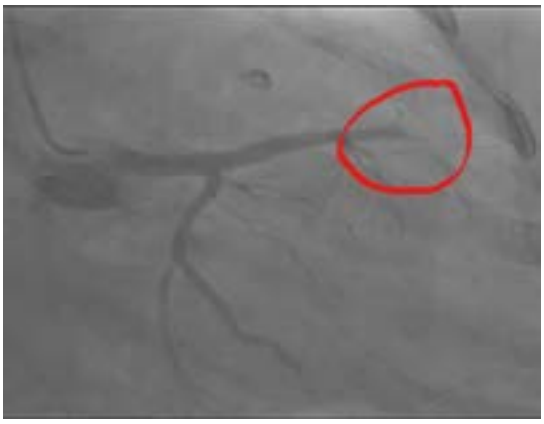


31.10.2013



In angiography cathlab it was performed thrombaspiration and ballon angioplastic of LAD, with poor flow results TIMI 0-1.

After the intervention the patient was constantly in cardiogenic shock. Exitus letalis on 1.11.2013.



DISCUSSION

In this cases raises the question if we have enough data to prove that we are dealing with antiphospholipid syndrome and a thrombotic storm.

Based on the criteria mentioned above, we lack positive laboratory results for aPL. Regarding the clinical criteria in the patient , we have two thrombotic events in two different organs within a week (as well as an earlier event - CVI a few years ago).

Based on Clinical characteristics of thrombotic storm (adapted from Kitchens et al. The American Journal of Medicine 124 (4): 290–6. [2011]).

Younger age (< than 50 years old) and ≥ 2 of the following:

-Acute, ≥ 2 arterial and/or venous thromboemboli, with or without thrombotic microangiopathy in 1–2 weeks, which may recur over years

-Unusual locations of thrombosis

-Progressive/recent unexplained recurrence

-Refractory to acute therapy or atypical response to therapy

-Exacerbation in setting of inadequate or interrupted therapy

(e.g. subtherapeutic anticoagulation).

APS, CASP, thrombotic storm ?!

CONCLUSION

APS is a systemic autoimmune disease with both thrombotic and nonthrombotic manifestations in which non-aPL thrombosis risk factors as well as the importance of the 'clinically significant' aPL profile should be kept in mind for diagnosis. CAPS is the most severe form of APS with multiple organ thromboses, usually accompanied by microthrombosis and hematologic manifestations. The clinical manifestations of CAPS may evolve gradually, commonly overlapping with other thrombotic microangiopathies, requiring a high index of clinical suspicion. Although the discussion about the treatment of CAPS is beyond the scope of this article, it is critical to initiate the treatment urgently if the diagnosis of CAPS is clinically suspected, even without the confirmatory aPL tests. I hope that our case report will help physicians better assess aPL positive patients with multiple organ thromboses, with the ultimate goal of preventing both 'underdiagnosis' and 'overdiagnosis' of this complex and highly fatal disease.


Guidelines on the investigation and management of antiphospholipid syndrome

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KWASHIORKOR FROM DIETARY RESTRICTION SECONDARY TO COW'S MILK ALLERGY

Kareva L, Mironska K, Stavrik K, Hasani A, Bojadzieva S

University Pediatric Hospital, Ss Cyril and Methodius of Skopje, Skopje, R .N. Macedonia

Address for correspondence
Dr.Lidija Kareva ,University Pediatric Hospital, Ss Cyril and Methodius of Skopje, Vodnjanska 17 Skopje, RN Macedonia, kvlidija@yahoo.com

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ABSTRACT

Kwashiorkor is a type of protein-calorie malnutrition seen in children with poor nutrition, especially in developing countries. The condition occurs when children suffer from insufficient protein intake in the presence of sufficient caloric intake. We report a case of a 13-month-old male child from Skopje, R.N. Macedonia who had diffuse edema, redness of the skin with desquamation and lethargy, consistent with kwashiorkor. At the age of 5 months breastfeeding was replaced with cow`s milk formula, and the child had an allergic reaction. Then he was placed on a severely restrictive diet, consisting of fruit juice, rice, potatoes, and bananas. When the child was 9 months old he developed skin rash which was several times observed by a dermatologist and treated as atopic eczema. At the age of 13 months, he had peripheral edema with a persistent rash, sepsis and he was admitted for hospital treatment. This case may represent the tip of the iceberg showing that malnutrition secondary to cow`s milk allergy (CMA) is under-diagnosed or misdiagnosed in our country. Physicians must consider this diagnosis, recognize potential risk factors and be able to accurately assess the overall nutritional status of the patients, as well as, to be familiar with feeding options for children with a CMA.

Keywords: kwashiorkor, malnutrition, cow milk allergy

BACKGROUND

The World Health Organization (WHO) (1) defines malnutrition as "the cellular imbalance between the supply of nutrients and energy and the body's demand for them to ensure growth, maintenance, and specific functions." The term protein-energy malnutrition (PEM) applies to a group of disorders that include marasmus, kwashiorkor, and intermediate states of marasmus-kwashiorkor. Marasmus represents an adaptive response to starvation, whereas kwashiorkor represents a maladaptive response to starvation. Children may present with a mixed picture of marasmus and kwashiorkor, and children may present with milder forms of malnutrition. In 2000, the WHO (2) estimated that malnourished children numbered 181.9 million (32%) in developing countries. The most affected regions in the world include Southeast Asia, Central America, Congo, Puerto Rico, Jamaica, South Africa, and Uganda. Prevalence can vary, but it is seen mostly during times of famine. Rural and farming communities are often affected the hardest. According to 2018 WHO data, 52 million children younger than 5 years are wasted (low weight-for-height), 17 million are severely wasted, and 155 million are stunted (low height-for-age)(3).

CASE PRESENTATION

We are presenting a case of a 13-month-old male child from Skopje, R.N. Macedonia who presented with diffuse edema, redness and desquamation of the skin and lethargy, consistent with kwashiorkor. At the age of 5 months breastfeeding was replaced with cow`s milk formula and the child had an allergic reaction with generalized hives. Then he was placed on a severely restrictive diet, consisting only of fruit juice, rice, potatoes and bananas. At the age of 9 months, the child started

to have skin rash which was several times observed by a dermatologist and treated as atopic eczema. By the age of 13 months, it showed peripheral edema with a persistent rash, hypovolemia and sepsis which was the reason for hospitalization. (Fig.1) At the admission, the child had skin redness with desquamation predominantly on the extremities, lower parts of the trunk and in the napkin area, bull-dog face, perioral rash, thin pale hair, edema of the hands and legs, enlarged liver, hypothermia. He had mild peripheral cyanosis and was lethargic with signs of hypovolemic shock. Laboratory findings showed profound disturbances in the internal environment. The child had deep hypochromic anemia with hemoglobin levels of 62 g / l and erythrocytes of 2.29 x 10 * 12 / l, elevated C reactive protein 80 mg / l, and leukocytosis of 15.85 x 10 * 9 / l which indicated an infection. There were significantly low values of total protein of 42 g / l and albumin of 18 g / l, slightly elevated liver enzymes indicating hepatic lesion AST 179 U / l and ALT 90 U / l, as well as low calcium levels. Initial blood culture was positive for Staphylococcus aureus methicillin- resistant (MRSA). Upon admission child received an intensive correction of hypovolemia with saline solutions and glucose, correction of hypoproteinemia with freshly frozen plasma and albumen. Anemia was corrected with blood transfusion. Staphylococcal sepsis (MRSA) was treated with antibiotics until two consecutive negative blood cultures were obtained. Skin changes were treated with antibiotics creams. The child was feed with complete protein hydrolyzate of milk. The hydrolyzate was well tolerated by the child without any allergic reaction or diarrhea. After the initial period of weight loss due to edema reduction, the weight began to increase gradually. There was also a change in his behavior from lethargy and disinterest, the child became active, moody, and communicative. The child was discharged home with a recommendation for proper nutrition with the inclusion of a complete protein hydrolyzate of milk and a protein-enriched diet, as well as multivitamins and minerals.

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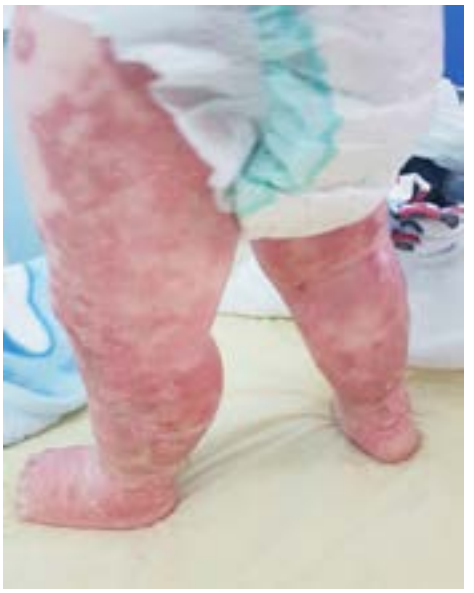

Figure 1.

DISCUSSION

Kwashiorkor is characterized by peripheral edema in a person suffering from starvation. Edema results from a loss of fluid balance between hydrostatic and oncotic pressures across capillary blood vessel walls. Albumin concentration contributes to the oncotic pressure, allowing the body to keep fluids within the vasculature. Children with kwashiorkor were found to have profoundly low levels of albumin and, as a result, became intravascularly depleted (4). Subsequently, the antidiuretic hormone increases in response to hypovolemia, resulting in edema. Plasma renin also responds, causing sodium retention (5.)These factors contribute to edema.

The clinical manifestations of kwashiorkor include peripheral edema, muscle atrophy, abdominal distension, round face, thin, dry, peeling skin with confluent areas of scaling and hyperpigmentation, dermatitis, dry, hypopigmented hair (6), hepatomegaly from fatty liver infiltrates, growth retardation, psychic changes like lethargy or irritability. Complications of kwashiorkor include cardiovascular system collapse/hypovolemic shock, urinary tract infections, atrophy of the pancreas with glucose intolerance, atrophy of the mucosa of the small intestine, lactase deficiency, bacterial overgrowth, which can lead to bacterial septicemia and death, septic shock and death, metabolic disturbances and hypothermia. Electrolyte abnormalities are common.

In the past, it was argued that hypoalbuminemia was not the cause of edema in kwashiorkor disease. Additional

analysis has revealed a big error in this conclusion, and indeed, profound hypoalbuminemia was proven to be linked to the development of co-existing edema in the hypovolemic child (7,8,9,4).

Because of the fear that giving a fluid volume to malnutrition children could lead to congestive heart failure (10), the recommendations of the WHO for treatment are that children present with malnutrition to be treated with a hypotonic solution with caution, followed by oral feeding. Those who are not shocked are likely to survive if they are treated according to WHO guidelines (11). However, it makes a vital difference when it comes to treating malnourished children who also have a shock. Treating this with intravenous albumin is life-saving (4). No distinction is made by the WHO between managing shock in marasmus and kwashiorkor, despite the fact that mortality is linked directly to the degree of edema (11).

Protein-energy malnutrition is a disease that still occurs in present days even in developed nations. (12, 13,14). Children solely fed on rice milk for various reasons like skin rashes or atopic dermatitis are at risk of developing the disease (15,16,17).

There are also reports of cases of misdiagnosis of atopic dermatitis in cases of malnutrition (18) because the lesions are similar in appearance and physicians do not pay sufficient attention to the nutritional history of their patients.

The prevalence of malnutrition in our country has not been investigated, as well as a prevalence of CMA. Some studies have been done in the study of sensitization of food allergens in children with atopic dermatitis (19) as well as neutrophil function in malnourished children (20).

Many cases of malnutrition remain undiagnosed. The reason for this is a lack of understanding of the disease by the general practitioners, pediatricians and dermatologists, inadequately taken history of a child's diet and knowledge of the possible implications of poor nutrition. CMA occurs early in infancy, after the introduction of cow`s milk formula into the diet. Two problems should be considered regarding the nutrition of children with a CMA. One is a problem caused by doctors who are not sufficiently informed about the nutritional options for those children with a CMA. The second problem are parents who considered hydrolysate formulas costly and either have no money or don't want to spend a lot of money on milk, following the advice of older people in the family that potatoes, rice, and sugary juices are good substitutes for milk. Physicians must consider this diagnosis, be familiar with feeding options for children with a CMA, recognize potential risk factors and be able to accurately assess the overall nutritional status of the patients. It is also very important for the doctor to talk to the parents about the importance of properly selected foods in a child with a CMA and what impact the correct nutrition will have on the child physical and mental development.

CONCLUSION

This case may represent tip of the iceberg showing that malnutrition secondary to cow`s milk allergy is under-diagnosed or misdiagnosed in our country. Primary care physicians some pediatricians and dermatologists are not well familiar with the diagnosis of malnutrition as well as feeding options for children with a CMA. The results, if unrecognized or untreated, may be devastating. Physicians must consider this diagnosis, be familiar with feeding options for children with a CMA, recognize potential risk factors and be able to accurately assess the overall nutritional status of the patients. Additional pressure should be placed on the healthcare system to compensate for the costs of the expensive hydrolyzed milk formulas for some groups of children with a CMA.

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ROLE OF FAMILY PHYSICIAN IN SMOKING CESSATION IN DAILY WORK USING A COMBINED METHOD: VERY BRIEF ADVICE AND PHARMACOTHERAPY - CASE REPORT

Dragan Gjorgjievski[1], Svetlana Kocheva[2], Katarina Stavrikj[2,3], Svetlana Stojkova[1], Natalija Saurek-Aleksandrovska[4], Bekim Ismaili[5]

[1]PZU Svetlana A. Stojkova - Skopje

[2]Pediatric Disease Clinic, Medical Faculty, Skopje

[3]Center for Family Medicine, Medical Faculty, Skopje

[4]PZU Femilihelt - Skopje

[5]PZU Dr Bekim-Tetovo

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ABSTRACT

Tobacco use is a leading cause of job loss and premature mortality in Europe. Each year more than 700,000 Europeans die from tobacco-related illnesses. North Macedonia has a long tradition in tobacco consumption, with the smoking rate increasing over the last few decades. In 2015, the prevalence of smoking in North Macedonia was 36% for men and 21% for women. Quitting smoking is one of the most pressing challenges a family doctor faces in his career. There are a number of smoking cessation tools in the world. Studies over the years have proven that the combination of counseling and medication is more effective than just medication or counseling alone. The family doctor schedules regular checkups to support the patient in quitting smoking and coping with abnormal symptoms. On this paper we report a thrty seven years old patient who was given very brief advice which contain the harmful effects of cigarettes and what are the benefits of quitting smoking. An important emphasis in successful smoking cessation is the support and advice of family physicians on quitting smoking and the simultaneous use of nicotine replacement therapy. Aim: The role of the family physician in supporting patients in the smoking cessation process by applying very brief advice and in combination with pharmacological therapy

Key words: Canceling, smoking, therapy, CO, family doctor

INTRODUCTION

Tobacco use is a leading cause of job loss and premature mortality in Europe. (1,2). Each year more than 700,000 Europeans die from tobacco related diseases (2).

Cigarette smoke affects not only smokers but also non-smokers. Passive smoking can cause respiratory conditions, cancer and heart disease (3).

North Macedonia has a long tradition in tobacco consumption, with the smoking rate increasing over the last few decades. (4) In 2015, the prevalence of smoking in North Macedonia was 36% for men and 21% for women. (5) Legislation for tobacco control in North Macedonia includes the introduction of plain packaging, a ban on advertising and a ban on smoking in public places.(5)

Quitting smoking is one of the most pressing challenges a family doctor faces in his career. Smokers find it very difficult to quit smoking and need constant reminders from family physicians about the harmful effects of smoking as well as the benefits that can be achieved by quitting smoking. There are a number of smoking cessation tools in the world. Studies over the years

have proven that the combination of counseling and medication is more effective than just medication or counseling alone. Therefore, whenever possible and appropriate, counseling and medication should be provided to patients attempting to quit smoking or to find alternative ways of giving up such as microspirometry, carbon monoxide determination, forced expiratory volume determination, and so on(6). Two international projects have already been implemented in the Republic of North Macedonia to quit smoking. Both are funded by the Global Bridges project. The first involves doctors of secondary and tertiary health (7) and the latter of primary level physicians and this second project is led by the Center for Family Medicine at the University "Ss Cyril and Methodius" in Skopje, Republic of North Macedonia (CFM).(8) Doctors in this project recognized the need to improve their smoking cessation skills and were trained in methods of supporting smokers who quit smoking based on the recommendations of the National Center for Smoking Cessation in the UK (9). There is also a strong association between the number of behavior support visits when combined with medication and the likelihood of successful smoking abstinence. Therefore, in addition to medications, family physicians should provide more brief behavior support visits for their patients trying to quit smoking (6).

CASE REPORT

A thirty-seven years old patient from Skopje, a graduate electrical engineer employed in a private company. He smokes 25 cigarettes on a daily basis. Gives information that he has been smoking since he was eighteen, which means that he has been smoking for nineteen years. On the Fager strom Scale the score is 5 points indicating a moderate degree of dependency. The patient consults his family doctor for a cough. He gives information that has difficulty of breathing and cough for a long time early in the morning. After anamnesis , examination is performed and on auscultation have vesicular breathing without accompanying tones. Laboratory tests were performed with CRP and chest x-ray was scheduled. The laboratory analysis shows an orderly finding as well as an orderly radiography. Taking into account the analysis, the patient is advised to stop smoking because the cigarettes are harmful to his lungs and the cough that appears to him in the morning is due to the nicotine which is a constituent of the cigarette. He was given very brief advice which contain the harmful effects of cigarettes and what are the benefits of quitting smoking. Exhaled carbon monoxide was measured to show that his lungs had a higher concentration of carbon monoxide than oxygen, disrupting their normal functioning. The measurement result is 20 ppm. The doctor explained the value of the measured carbon monoxide and emphasized that by quitting smoking for 24 hours the lungs would get rid of carbon monoxide. During the visit, the patient said he was aware of all the harmful effects of cigarettes but was also concerned about the value of carbon monoxide for which he agreed to try to quit smoking. The doctor congratulates the courageous decision and told the patient that he should choose a date when he will stop smoking. In agreement with the patient, a date of two days from the date of the intervention was chosen for the patient to stop smoking, which would be considered his smoking cessation date. It has been suggested to the patient to quit smoking, he must remove all ashtrays, all lighters and cigarettes from his residence and car, notify his close friends and friends that he has stopped smoking and begs in his presence more not to smoke. The family doctor also advises him on how to deal with abstinence if it appears during his smoking cessation. The doctor told the patient that there are also nicotine replacement therapies such as chewing gum, pills and many other smoking cessation drugs that would help him quit smoking. The patient agrees that the doctor's advice is very useful but that engaging with the therapy can make it easier to persevere. He is prescribed Varenicline tablets and a one-week scheduled visit.

After a week, the patient informed the doctor that he is not smoking anymore. The patient feels better and the cough that tortured him early in the morning decreases but said that he occasionally barely manages not to light a cigarette and to start smoking again. The result this time is 4 ppm which is a normal result. The doctor reiterates that it is very important for his health to endure smoking cessation and that the doctor is available whenever he feels the need. A one week visit has been arranged. At the next visit, the patient informed that the cough has completely disappeared and he is feeling better. He was once again expelled carbon monoxide and now the value is zero. The doctor again told that with the pills he gives and the advice he will succeed in quitting smoking and stresses that he is at his disposal whenever needed. A family doctor scheduled regular checkups to give visitors a guide to quit smoking and to control it with free symptoms. 6 month control and logs and doctors who may be satisfied with the outcome when they are determined

not to appear and whether they can be organized by force or select the "demon" and all users that may appear.

DISCUSSION

The motive for presenting this case from practice is due to the growing number of chronically ill patients, and many of them are smokers. At the same time, patients are poorly informed about the ways and the pharmacological means available to them to stop smoking.

In our case there is a patient who consulted a family doctor for a prolonged cough. After the necessary analysis has been done it is established that the patient has no diseases and that the cough is a consequence of cigarettes. The patient is fully aware that quitting smoking is necessary but is afraid that he cannot quit smoking only with advice and regular visits, and therefore requires his family doctor to introduce nicotine replacement therapy. The physician decides to introduce Varenicline tablets that the patient should use regularly. At the same time, the literature advises that the combination of counseling and medication is more effective than just medication or counseling alone (6). There is some evidence that it is more effective to offer quitting help to any smoker, regardless of his willingness to quit smoking, than to offer health advice in an effort to increase smoking cessation efforts. (10). Very brif advice can have a major impact on public health because of the large number of smokers who consult with physicians each year (10). The effectiveness of the brief (3-5 minutes) advice given by a physician or other health professional leads to an increased degree of long-term smoking abstinence(10).It is recommended practice to provide assistance to all tobacco users in quitting. Literature advises that in addition to nicotine replacement therapy, alternative methods of withdrawal such as the determination of expired carbon monoxide, the determination of forced expiratory volume in the first second, the determination of age of the lungs, etc., should be introduced. Carbon monoxide in the exhaled air is the most easily monitored biomarker. The half-life of carbon monoxide is approximately 2-6 hours. (11) The level of CO in the exhaled air of a smoker can reach 10-20 ppm. (11). There is some correlation between the number of cigarettes smoked per day and the results of CO measurements; however, significant individual variations should be expected. (11) Physical exertion also affects CO. Carbon monoxide reaches normal values 24 hours after smoking abstinence. Under normal conditions, the concentration of CO in a non-smoker does not exceed 4 ppm(12). The recommended limit value that separates smokers from non-smokers is 9 ppm (12). Alternative nicotine replacement therapies are available in the form of transdermal patches, oral preparations (chewing gums, lozenges, sublingual tablets, inhalers) and in some countries also in the form of nasal spray. nicotine substitutes to increase the dose of nicotine, to achieve a nicotine level approximately similar to the nicotine level achieved by smoking.(12) Recent research has shown that nicotine replacement therapy in addition to counseling and other methods has a great effect on quitting smoking.

A meta-analysis by Wu et al, including 70 articles reporting the results of placebo-controlled studies, indicated superiority of varenicline over bupropion, nicotine replacement therapy and placebo over a period of one year.(13) Niedes et al. observed abstinence rates of 48% for 4 weeks in the group taking 2 mg of varreniline and 37% in the group taking 1 mg versus 17% in those taking placebo.(13) In the longer follow-up, such as the one performed by Onken et al., An 18% reduction in efficacy was expected, but even so 22.4% of patients in this study taking 1 mg varenicline were abstinent, versus 18, 5% taking 0.5 mg and 3.9% taking placebo.(13)

In both cases, patients clearly reported a significant decrease in their desire for smoking compared to other attempts. Despite the short period of abstinence (8 and 7 months, respectively), the result of these reports promises to encourage physicians and patients to consider this treatment as a truly effective treatment for many patients (13).

Primary care physicians are among the most important groups of key influentials that have not yet been brought into the tobacco control effort in an effective way (14). This is in large part because their tobacco prevention role has been defined around cessation and not more broadly as crucial societal leaders in the "denormalization" of tobacco use (14).

CONCLUSION

The motive for presenting this case from practice is due to the growing number of chronically ill patients, and many of them are smokers. At the same time, patients are poorly informed about the ways and the pharmacological means available to them to stop smoking. Behavioral interventions can reduce the likelihood of smoking initiation in nonsmoking youth and young adults. Research is needed to identify effective behavioral

interventions for youth who smoke or who have used cigarettes or other tobacco products and to understand the effectiveness of pharmacotherapy (14). An important emphasis in successful smoking cessation is the support and advice of family physicians on quitting smoking and the simultaneous use of nicotine replacement therapy. Family doctors are a key link in the chain, which should provide adequate support to quit smoking.

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CARDIAC AND LIPID MARKERS AS PREDICTORS FOR CORONARY ARTERY DISEASE IN PREDIBET PATIENTS

Dr. Vera Penshovska Nikolova

Diabetes Center, Skopje, PHI Health Center, Skopje

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ABSTRACT

Introduction: Coronary artery disease (COPD) is the leading cause of mortality and morbidity in patients with type 2 diabetes mellitus (DMt2). One of the diagnostic methods for assessing CAD is laboratory blood tests that include: lipid status and cardiac markers. N-terminal pro-B-type natriuretic peptide (NT-proBNP) is a cardiac biomarker whose predictive power for cardiovascular events in patients with DMT2 and prediabetes is the target of this case study. Apolipoproteins A and B are lipid biomarkers that correlate with atherosclerosis and are factors for cardiovascular events.

Materials and Methods: This is a case study of a 38-year-old patient followed over a 12-month period. The respondent was called for laboratory tests every 3 months in the first year. The change in the levels of cardiac and lipid markers NT-proBNP and apolipoprotein A and B was monitored. Results: The case study examines the correlation between the increased values of NT-proBNP and Apolipoprotein A and B with the predictability for CAD at the beginning and during follow-up in a patient with prediabetes. In patients with prediabetes, the increased value of cardiac and lipid biomarkers is expected to be a predictor of coronary events. Antilipemic and antiaggregation therapy is also expected to have a protective effect on cardiovascular events.

Conclusion: Determining the association of elevated cardiac and lipid marker values in the occurrence of CAB in patients with prediabetes and timely use of antiliepemic and antiaggregation therapy may prevent unwanted cardiovascular events in diabetic patients.

Keywords: Coronary artery disease; Diabetes mellitus; NT-proBNP natriuretic peptide; apolipoproteins.

INTRODUCTION

Coronary artery disease (CAD) is the leading cause of mortality by up to 30% and morbidity in developed countries in the world. Between the ages of 35 and 55, male mortality is higher. Because CAD occurs most often in the working period of life, it is not only a medical but also a social problem. Diabetes is one of the risk factors for CAB.

Impaired glucose tolerance (IGT) is a pre-diabetic condition of hyperglycaemia associated with insulin-independent diabetes and an increased risk of cardiovascular disease.

According to the criteria of the World Health Organization and the American Diabetes Association, 10 to 15 percent of adults in the USA have (IGT) and could be defined as:

• Glucose levels of 140–199 mg per dl (7.8–11.0 mmol / l) two hours after a 75 g oral glucose tolerance test. The patient is said to have IGT when there is an intermediate increase in glucose levels after 2 hours, but less than the level that would qualify for type 2 diabetes.(9;10)

Atherosclerotic changes in the coronary arteries in patients with Diabetes are more pronounced, diffusely distributed in small blood vessels, and unsuitable for dilatation.

Clinically CAB in patients with Diabetes is manifested by:

-dispnea (equivalent to Angina)

- «silent ischemia" is a consequence of autonomic

heart denervation caused by a disturbance of the normal connection between the afferent and efferent pathways of the autonomic nervous system.

- «silent infarction» of the myocardium

One of the diagnostic methods for assessing CAB is laboratory analysis of blood, which includes: lipid status, biochemical markers of necrosis and inflammation, and natriuretic peptides.

The lipid profile is extremely important as it is used for patient risk stratification (Systematic Coronary Risk Evaluation SCORE) for future adverse events. (1; 2; 3 and 4)

The natriuretic peptide is specific in controlling cardiovascular system function. The following natriuretic peptides have been described: atrial natriuretic peptide (ANP), B-type natriuretic peptide (BNP), and C-type natriuretic peptide (CNP). (5;6)

Pro BNP contains 108 amino acids. It is mainly secreted by the ventricle and converted to physiologically active BNP (77–108). The subject of this case study is the N-terminal fragment NT-proBNP (1-76), which is a cardiac biomarker whose predicting power for cardiovascular events in patients with DM T2 is the target of this study. Apolipoproteins A and B are lipid biomarkers that correlate with atherosclerosis and are factors in cardiovascular events. The case examines the correlation between elevated values of NT-proBNP and Apolipoprotein A and B with the predictability to CAD in a patient with prediabetes. (7; 8)

CASE STUDY

Patient M.A. on 08 10 2018 god, 38 years old. does consult us for the first time in the Center for Diabetes, Skopje due to frequent evening hypoglycemias that appear after a normal dinner with a frequency of 5 times in the last year. Subjectively it feels like cooling, tachycardia and sweating in a dream. They are accompanied by shortness of breath, fatigue, and chest pain with intracapsular propagation. The patient denies other comorbidities. He works as a coach of a basketball junior team. Confirms diseases of interest. Namely, his mother suffers from DM T 2 and is on OAD and his father suffers from DM t2 but without any diabetic therapy.

At the first examination, the following laboratory findings were identified: FPG gl 6.81; hol 6.65, tr 2.05; gl 4.8 venous blood. A recommendation for laboratory tests-Ogtt (Oral glucose tolerance test) is given; Hba1c; insulin, lipid status, cardiac markers, degradation products, and immune status.

During the re-examination on 15.10.2018. in the Center for Diabetes, the following results were obtained; Hba1c 5.5; a1cwb 11.71; Lp (a) 112.97 (reference values up to 30); LDL 4.8, apolipioprotein B 1.57 (reference values 1.57); hol 5.8; apolipoprotein A1 1.34 (reference values 1 do 2,25), lipase 22,14; tr 2.0; insulin 6.88; urine crystals, probnpnt 135, acidum uricum 450, CK 180, CK mb 15, ASO 320. OGTT is positive in addition to impaired glucose tolerance (IGT); first portion (0 hours) 6.2 mmol / l, after two hours second portion - 8.6 mmol / l. He has been advised about a hygienic diet. He was referred to echocardiography and KST (coronary stress test);

During the second examination after 3 months on January 4, 2019, laboratory findings; Ck 117 (reference values 26 -308); ldh 204 reference values (100 -190); Troponin 0.006 (reference values 0.78); Ck Mb 0.65 reference values (15 do 25); ProBNPnt 125, Tr 2,3, uric acid 485.

The findings of Echo and Kst from the Philip II Special Hospital are within normal limits. The patient still complains of night sweats, tachycardia, and pain in intra scapular region. MCKT coronary angiography was indicated.

MSKT coronary angiography report - finding of muscle bridging in the middle segment of the LAD towards the distal with an insufficient display without other signs of coronary heart disease.

Ordinary therapy-tbl Kardiopirin 100mg 1x1 (because he does not tolerate Aspirin 100mg and has dysphagia) and tbl Rosuvastatine 5 mg once daily. A laboratory with thyroid status and ASO was indicated. Due to dysphagia, he was referred to Gastroenteropatology Clinic for suspected diaphragmatic hernia.

During the control examination on 11.01.2019 laboratory findings: hol 6.1; ldl 4.2; apolipoprotein 1.48; apolipoprotein B 1,83; lpa 125.41; lipase 72.05; thiroid status bo; Aso 319; salts crystals in urine.UT echo is indicated; nasal and throat swab with antibiogram.

Third Review-April 18, 2019. Referred to the laboratory.

Control Review-23.04.2019: RBC 5.07 10 ^ 12 / L (4.20-5.50); HGB 152 g / L (120-180); HCT 0.45 (rv 0.37-0.54); MCV 90.5 (82.0-98.0); MCH 30.1 pg (27.0-33.0); MCHC 33.2 g / dL (32.0-36.0); RDW-SD (37.0-54.0); RDW-CV 12.1% (11.0-16.0); WBC 5.9 10 ^ 9 / L (4.00-9.00); LYMPH 45.4% (15-50); NEUT 47.6%

(35-80); LYMPH_N 2.7 10 ^ 9 / L (0.5-5.0); MXD_N 0.4 10 ^ 9 / L (0.1-1.5), NEUT_N 2.8 10 ^ 9 / L (1.2-8.0;) PLT 201 10 ^ 9 / L (150-450); PDW fL (9.0-17.0); MPV 8.6 (fL 9.0-13.0); P-LCR% (13.0-43.0); MONO% (0.0-14.0); BASO% (0.0-1.0); EO% (0.0-6.0); HEART MARKERS: Troponin T (up to 34.2 males to 15.6 females) 6.09 ng /; LIPID STATUS: Lp (a) 97.5 nmol / L to 75; Apolipoprotein B 1.80 g / (0.7-1.3); Apolipoprotein A1 1.61 g / L (1.0-2.25); LDL cholesterol 4.7 mmol / L (2.2-3.7); HDL cholesterol 1.3 mmol / L (0.9-2.0); Total cholesterol 6.8 mmol / L to 5.5; Triglycerides 1.8 mmol / L (up to 2); Lipase 28.24 U / L (10-73); IMMUNOLOGICAL STATUS: ASO 239 U / ml (up to 200); ENZYMIC STATUS: Aminotransferase (AST) 27 U / L (10-34) ; Alanine aminotransferase (ALT) 38 U / L (10-45); CK-MB 16 U / L (up to 25) ; Lactate dehydrogenase (LDH) 168 U / L (up to 248); Gamma glutamyl transpeptidase (GGT) 28 U / L (9-64); Creatine kinase (CK) 157 U / L (24-173); DEGRADATION PRODUCTS: Serum creatinine 90 umol / L (45-109); Urea in serum 6.8 mmol / L (2.7-7.8); GLUCID STATUS: A1cWB 44 mM / mol (29-42); Glycosylated hemoglobin (HbA1C) 6.2% (4.4-5.9); Serum glucose 6.0 mmol / (3.5-5.6). ac uric 478.5 (r v do r450); N Terminal proBNP 38.46 pg / ml (pp. B. 0-125).

Fourth Review 30.09.2019 Find from the laboratory - elevated values of Lpa, Ck, cholesterol, Ldl, echo report on the abdomen and consultation with a cardiologist. Hyperlipidaemia. Ordinary therapy - tbl Atoris 10 mg 1x1, tbl Asa 100 mg 1x1.HEMATOLOGICAL STATUS: RBC 5.01 10 ^ 12 / L (4.20-5.50); HGB 157 g / L (120-180); HCT 0.441 rv (0.37-0.54); MCV 88.0 ref v (82.0-98.0); MCH 31.4 pg (27.0-33.0); MCHC 35.6 g / dL (32.0-36.0); RDW-SD rv (37.0-54.0); RDW-CV 12.2% (11.0-16.0); WBC 5.7 10 ^ 9 / L (4.00-9.00); LYMPH 39.8% (15-50); MXD 8.0% (2-15); NEUT 52.2% (35-80); LYMPH_N 2.2 10 ^ 9 / L (0.5-5.0); MXD_N 0.6 10 ^ 9 / L (0.1-1); NEUT_N 2.9 10 ^ 9 / L (1,2-8,0); PLT 197 10 ^ 9 / L (150-450) PDW rv (9,0-17,00); MPV 8.4rv (9.0-13.0); P-LCR% (13.0-43.0); BASO% (0.0-1.0); EO% (0.0-6.0); MONO% (0.0-14.0); URINARY STATUS with sediment: URINARY STATUS with sediment: Cut. Color YELLO W worth. / Clear CLEAR value. / Glucose quality. NEGAT IVE neg. / Bilirubin NEGAT IVE neg. / Acetone NEGAT IVE neg. / Spec. heavy. 1,020 value. (1.01-1.025) Blood NEGAT IVE neg. / pH 7.0 value (4.6-6.4.) Protein quality. NEGATIVE . / Urobilin 0.2 ng. / Leukocytes NEGAT IVE con. 3-10 Erythrocytes. 0-2 Cylinders - granular neg. / Epithelial cells + / Amorphous salts and crystals + / Bacteria NEGAT IVE neg. / Additional box 1 unit. / Additional field 2 con. / Diuresis dU-L 0.8-1.5 Osmolality mOsm / L> 500 Cylinders - hyaline con. 0-1 HEART MARKERS: Troponin I up to 34.2 males to 15.6 females 0.94 ng / L 756571 LIPID STATUS: Triglycerides 2.0 mmol / L (up to 2); Total cholesterol 6.7 mmol / L (up to 5.5); LDL cholesterol 4.7 mmol / L (2.2-3.7); HDL cholesterol 1.1 mmol / L (0.9-2.0); Apolipoprotein B 1.79 g / L (0.7-1.3) Lp (a) 119.3 nmol / L (up to 75); Lipase 25.09 U / L (10-73); Apolipoprotein A1 1.48 g / L (1.0-2.25); ENZYMIC STATUS: Lactate dehydrogenase (LDH) 198 U / L to 248 EXP CK-MB 16 U / L (up to 25); Creatine kinase (CK) 235 U / L (24-173) HIGH Alanine aminotransferase (ALT) 35 U / L (10-45); Aminotransferase (AST) (10-34) HI GH 35 U / L; ELECTRICAL STATUS - serum: Iron (11-28) men (7-26) women 20.1 umol / L; DEGRADATION PRODUCTS: Serum uric acid 420 umol / L (150-450); Serum creatinine 89 umol / L (45-109) EXP; Urea in serum 5.1 mmol / L (2.7-7.8); GLUCID STATUS: A1cWB 44 mM / mol (29-42); ASO 225. Glycosylated hemoglobin (HbA1C) 6.2% (4.4-5.9) Serum glucose 5.72 mmol / L (3.5-6.1); pro Bnpnt 0.94.

Echo report from UT 11.09.2019: In the middle group of the left kidney, a suspected 7 mm diameter calculus that interferes with urodynamic, the kidney is with initial stagnant changes. Right kidney with initial stagnant changes. The liver, gallbladder, biliary trunk, pancreas, spleen are in order. The paraaortic region is neat. There is no free fluid in the abdomen. Bladder full, no filling defects. The patient is referred to nephrology.

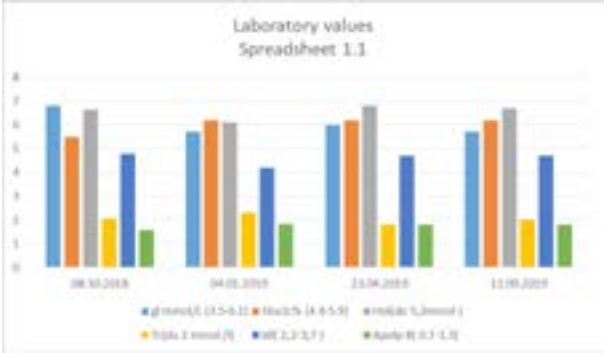
1. Analysis of the laboratory values of biomarkers followed every 3 months for one year

Data of examination	08 10 2018	04 01 2019	23 04 2019	30.09 2019
gl mmol/L (3.5-6.1)	6,81	5,72	6,0	5,72
hba1c% (4.4-5.9)	5,5	6,2	6,2	6,2
Insulin	6,88			
ogtt	6,2/8,6			
Hol (up to 5,2mmol)	6,65	6,1	6,8	6,7
Tr (up to 2 mmol /l)	2,05	2,3	1,8	2,0
Hdl (0,9-2,0) mmol /l			1,3	1,1
Ldl (2,2-3,7) mmol /l	4,8	4,2	4,7	4,7
Apolp A1 (Rv from 1 do 2,25)g/l	1,34	1,48	1,61	1,48
Apolp B (0.7-1.3)g/l	1,57	1,83	1,80	1,79
Lpa nmol/l (Rv do 30do 75)	112,97	125,41	97,5	119,3
ast U/ml (до 35)			27	35
alt U/L (10-45)			38	35
Lipaza U/L (10-73)	22,14	72,05	28,24	25,09
(GGT) U/L(9-64)			28	
Creatinin umol/L(45-109)			90	89
Fe8-28umol/l				20.1 umol/L

Ac uric umol/L(150-450)	450	485	478,	420
Urea mmol/L (2.7-7.8)			6,8	5,1
Urine (aceton ; gl; prot)	Crystal	Crystal	Her	Her
Ck U/L (24-173)U/L	180	117	157	235
Ck mb (0-25)U/L	15	0,65	16	16
TroponinT ng/L(do 15z do 34m)ng/l	6 . 0 9 ng/L		6,09	
Troponin I (0,78)ng/L male up to 34,2 , female up to 15,6 ng/L		0,006		0,94
Ldh U/L до 248		204	168	198
ASO U/ml (до 200)	320	319	239	225
Thyroid status		Normal values		
proBNPnt pg/ml (R V 0-125)	135	125	38,46	0,94

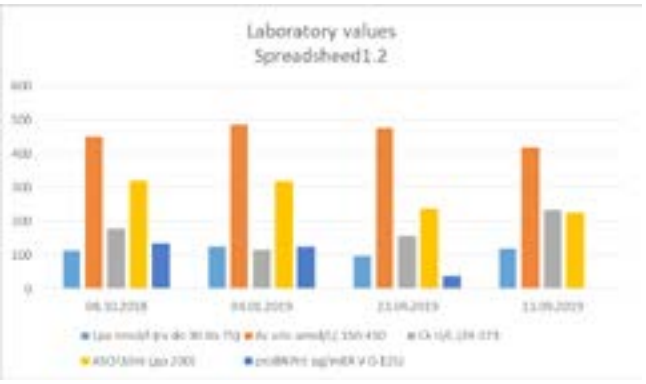
1.1 Analysis of the elevated and reduced values of laboratory parameters (biomarkers) monitored every 3 months during a year

Date of examination	08 10 2018	04 01 2019	23 04 2019	11.09 2019
gl mmol/L (3.5-6.1)	6,81	5,72	6,0	5,72
hba1c% (4.4-5.9)	5,5	6,2	6,2	6,2
Hol (up to 5,2mmol)	6,65	6,1	6,8	6,7
Tr (up to 2 mmol /l)	2,05	2,3	1,8	2,0
Ldl (2,2-3,7)	4,8	4,2	4,7	4,7
Apolp B(0.7-1.3)	1,57	1,83	1,80	1,79



1.2.Analysis of the elevated and reduced values of laboratory parameters (biomarkers) monitored every 3 months during a year

Date of examination	08 10 2018	04 01 2019	23 04 2019	11.09 2019
Lpa nmol/l (Rv do 30do 75)	112,97	125,41	97,5	119,3
Ac uric umol/L (150-450	450	485	478	420
Urine (aceton ; gl; prot)	Crystal	Crystal	Negative	Negative
Ck U/L (24-173	180	117	157	235
ASO U/ml (up to 200)	320	319	239	225
proBNPnt pg/ml (R V 0-125)	135	125	38,46	0.94



DISCUSSION

During the one-year follow-up and laboratory analysis of the biomarkers in the patient, a decrease and increase of certain values of the same is visible:

Glycemia has seen a slight drop in value on second examination.

A significant drop in Lpa was recorded during the third examination.

An evident decrease in the elevated three values of acid uricum to normal values during the fourth examination.

Reduction of ASO exponentially to the fourth examination.

Reduction of proBNPnt exponentially to the fourth examination to normal values.

Hba1c values were raised and remained approximately the same during all 4 examinations.

The value of cholesterol, triglycerides and LDL was high in all 4 examinations. The patient provided data for non-use of antiliepemic therapy and ant lipid diet.

Apolipoprotein B has increased significantly after the second examination. The elevated values were maintained until the fourth examination.

Significantly enormous increase in CK values in the fourth examination.

The exponential decline in acid uricum and ASO during the one-year follow-up of patients with prediabetes remains unclear. Perhaps there is a correlation and association between the reduced values of these markers and the statins and antiaggregation therapy used.

CONCLUSION

Decreased glycemia was due to the hygienic regime and diet performed after the first examination.

A significant drop in Lpa and proBnpnt is thought to be due to the hygienic regimen administered and therapy with acetylsalicylic acid more pronounced by Cardiopyrin than by Aspirin (no effect).

Elevated CK values and the symptomatology of less common angina and fatigue have indicated the need for KST and possible coronary angiography.

The link between stagnant renal changes of the first degree and elevated values of uric acid and crystalluria is also clear.

Elevated LPa and proBPnt values have been shown to be a true predictor of possible coronary events in patients with prediabetes. In the future, their predictive value could be used to include them in protocols for macrovascular complications, namely coronary artery disease in patients with type 2 diabetes mellitus.

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RECONSTRUCTION OF THE URINE BLADDER WALL WITH SURROUNDING TISSUE FLAP AFTER EXCISION OF POST TRAUMATIC VESICOCUTANOUS FISTULA

Ivchev J[1,2], Izairi A[1], Minev I[1], Markovski D[1], Ivcheva N[3], Ivchev Lj[1]

[1]Department of Urology, General City Hospital ,,8th September", Skopje, R of North Macedonia
[2]Facullty of Medical Sciences, University ,,Goce Delcev", R of North Macedonia
[3]Department of Psychiatry, General City Hospital ,,8th September", Skopje, R of North Macedonia

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ABSTRACT

Introduction: The vesicocutaneous fistula is a rare but very complex urology surgical condition due to the cause of constant presence of urinary infection, discomfort and exhaustion of the affected patient. The most commonly described causes of vesicocutaneous fistula in practice so far are listed: pelvic trauma with pelvic fractures, pelvic infections, bladder calculosis, malignant infiltration of the bladder, diverticulum perforation, iatrogenic bladder perforation due to transurethral resections or after prostatectomy, post radiation therapy or as a consequence of pelvic phlegmona (gangrene Fournier). The treatment of the vesicocutaneous fistulas varies according to the etiology, extension of the fistula and the general condition of the patient, from conservative to various variants of surgical care.

Objective: To analyze rare surgical cases with vesicocutaneous fistulas, their etiology, diagnostic methods, operative and postoperative treatment in the current available literature. To compare the surgical method of the reconstruction of the urine bladder wall after the excision of the vesicocutanous fistula used in our patient, with the methods described so far and to confirm its effectiveness.

Case report: Patient 53 (male), transferred from Traumatology Clinic in severe general condition, immobile due to multi fragmental "open book" pelvic fracture, with local postoperative finding of a large vesicocutaneous fistula in the suprapubic region, collocutaneous fistula localized over the right spina iliaca anterior superior, and symptoms of overdose with basic neuroleptics, anxyolitics and opioid pain medications. 18 months prior, the patient was admitted at the Traumatology Clinic because of mutlitrauma with "open book" fracture of the pelvis caused by severe fall on the scales. Osteosynthesis of the bilateral symphysis pubica was performed with an osteosynthetic plate. 10 months later the osteosynthetic material was removed with second surgical treatment due to development of osteomyelitis with pelvic phlegmona and external fixation of the pelvis was performed in order to stabilize the pelvis and verticalize the patient. The external fixator was removed after 7 days, again, due to severe pelvic phlegmona with signs of sepsis. Vesicocutaneous and collocutanous fistula occurred 8 days after the last surgery and existed for the next 6 months independently of catheterization and intensive antibiotic therapy.

After the necessary preoperative preparations fistulectomy and reconstruction of the front vesical wall with a flap of the surrounding tissue (piece of the lower abdominal aponeurosis together with the left pyramid muscle flap with preserved vascularity) was performed.

Cystostoma with 12 Fr Foley catheter and 22 Fr Foley urethral catheter was install at the end of the surgical procedure. The cystostoma was removed the 7th postoperative day, and the urethral catheter remained for 3 weeks. The patient was released from the hospital the 12th postoperative day. Complete closure of the fistula was achieved after the surgery itself.

Conclusion: The vesicocutaneous fistula in our case occurred due to a postoperative infection of the pelvis (osteomyelitis and phlegmona of the front abdominal wall). The period of 6 months with conservative therapy (dual antibiotic therapy and urethral catheter), was too long to expect spontaneous healing of the fistula. Immobile patients such as ours are often exposed to mixed urinary infections which prevent spontaneous closure of the

vesicocutaneous fistula. According to our experience we should not wait more than 1.5 months with conservative treatment in order to expect spontaneous closure of the vesicocutaneous fistulas. Spontaneous closer of the vesicocutaneous fistula should be expected in cases without persistent urinary infection and infection of the surrounding tissue. The method of reconstruction of the urine bladder depends on the condition of the bladder wall itself. The closure of the defect with flap made of the aponeurosis of the lower abdominal wall and the left pyramidal muscle in our case proved to be a good permanent surgical solution.

Key words: urine bladder fistula, pelvis fracture, urine bladder reconstruction, vesicocutaneous fistula, phlegmona pelvis

INTRODUCTION

The vesicocutaneous fistula is a rare but very complex urology surgical condition due to the cause of constant presence of urinary infection, discomfort and exhaustion of the affected patient. The most commonly described causes of vesicocutaneous fistula in practice so far are listed: pelvic trauma with pelvic fractures, pelvic infections, bladder calculosis, malignant infiltration of the bladder, diverticulum perforation, iatrogenic bladder perforation due to transurethral resections or after prostatectomy, post radiation therapy or as a consequence of pelvic phlegmona (gangrene Fournier). According to the current urology practice the treatment of the vesicocutaneous fistulas (VCF) caused by trauma, infection, iatrogenic perforation and especially after radiotherapy, should begin conservatively with catheterization combined with antibiotic therapy for approximately one month or using so called vacuum-assisted closure therapy. This method enables rapid creation of granulation tissue and closure of the fistula and surgical wound, thus avoiding surgical treatment (1,2). However, in most cases described so far, various variations of surgical resection of vesicocutaneous fistulas and reconstruction of the bladder wall have been used as a permanent solution such as: reconstruction with buccal mucosa graft (3,4), reconstruction with omental flap interposition (5), reconstruction with the surrounding tissue and various types of direct closure of the bladder wall (6).

Objective: To analyze rare surgical cases with vesicocutaneous fistulas, their etiology, diagnostic methods, operative and postoperative treatment in the current available literature. To compare the surgical method of the reconstruction of the urine bladder wall after the excision of the vesicocutanous fistula used in our patient, with the methods described so far and to confirm its effectiveness.

Case report: Patient 53 (male), transferred from Traumatology Clinic in severe general condition, immobile due to multi fragmental "open book" pelvic fracture, with local postoperative finding of a large vesicocutaneous fistula in the suprapubic region, collocutaneous fistula localized over the right spina iliaca anterior superior, and symptoms of overdose with basic neuroleptics, anxyolitics and opioid pain medications. 18 months prior, the patient was admitted at the Traumatology Clinic because of mutlitrauma with "open book" fracture of the pelvis caused by severe fall on the scales. Osteosynthesis of the bilateral symphysis pubica was performed with an osteosynthetic plate. 10 months later the osteosynthetic material was removed with second surgical treatment due to development of osteomyelitis with pelvic phlegmona and external fixation of the pelvis was performed in order to stabilize the pelvis and verticalize the patient. The external fixator was removed after 7 days, again, due to severe pelvic phlegmona with signs of sepsis. Vesicocutaneous and collocutanous fistula occurred 8 days after the last surgery and existed for the next 6 months independently of catheterization and intensive antibiotic therapy.

At our Urology Department additional laboratory analyses, microbiological swabs, ultrasound, CT urography, MR of the pelvis and urethrocystography were performed in order to get a better picture of the patient (figure 1,2,3).

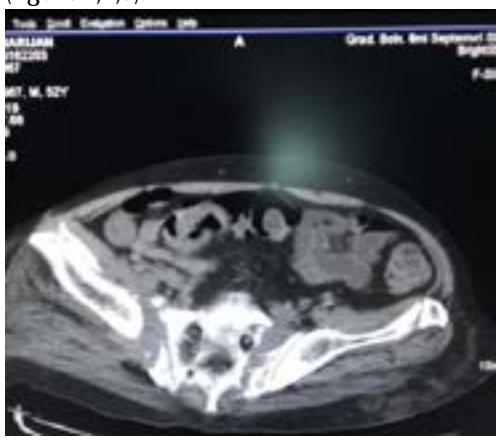

Figure 1. "Open book" fracture of the pelvis

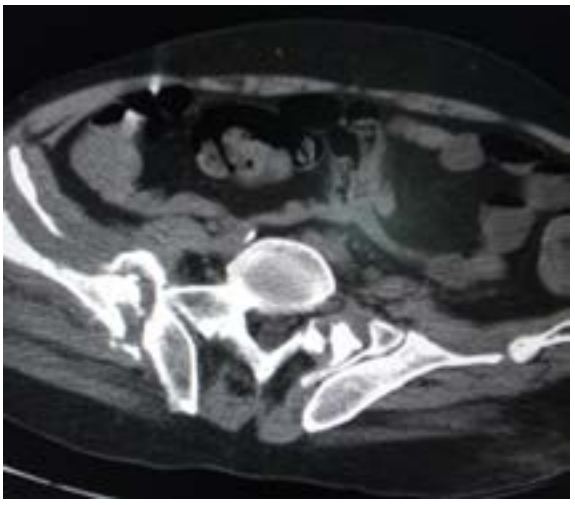

Figure 2. Multifragmented pelvic fracture

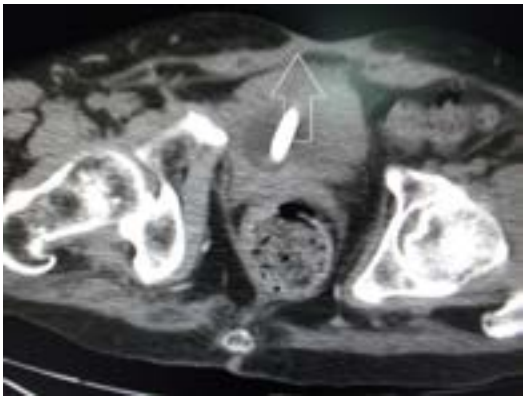

Figure 3. Vesicocutaneous fistula

After stabilizing the general condition and improving the patient with the appropriate treatment given by the psychiatrist, we performed surgical treatment consisted of fistulectomy and reconstruction of the missing front vesical wall with a flap of the surrounding tissue (piece of the lower abdominal aponeurosis together with the left pyramid muscle flap with preserved vascularity (Figure 1,2,3,4).

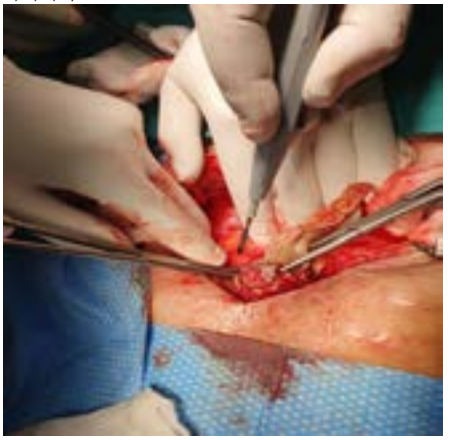

Figure 1. Excision of the VC fistula

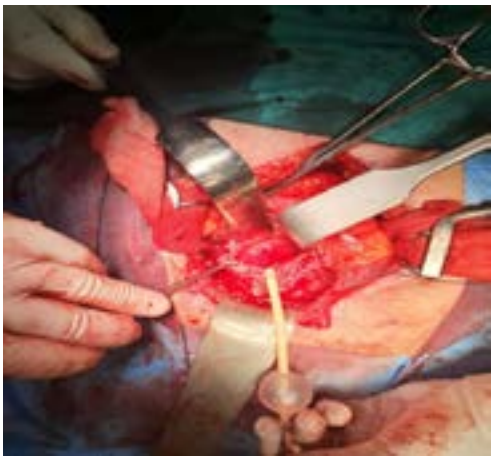

Figure 2. Post excision defect of the front wall

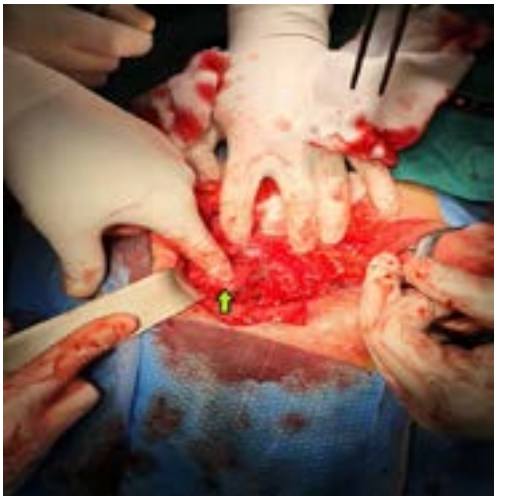

Figure 3. Closure of the front wall with flap of the surrounding tissue

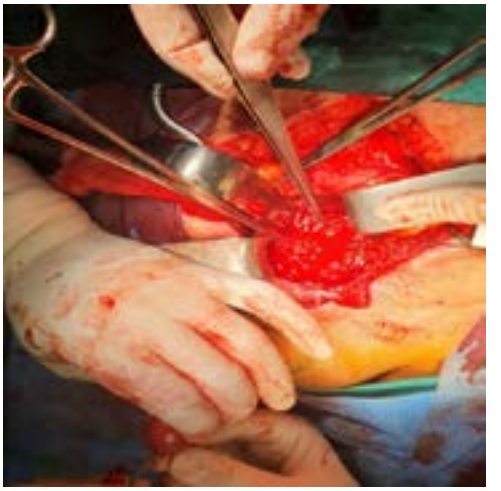

Figure 4. Reconstructed vesical wall flap of the surrounding tissue

During the excision of the fistulous canal and removal of the devitalized parts of the bladder wall, we extracted

4 bone fragments that were impacted in the front wall (figure 5,6).

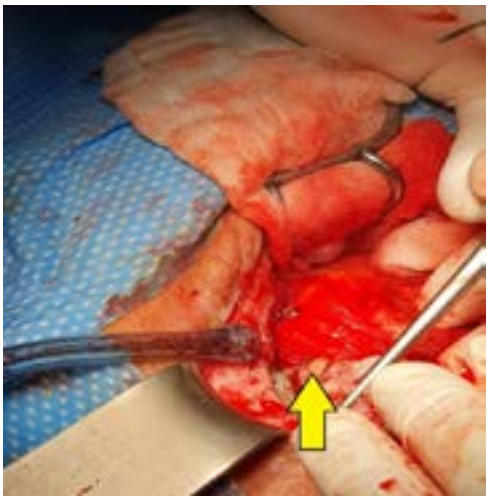

Figure 5. Bone fragment in the front wall

Figure 6. Devitalized part of the front wall

Cystostoma with 12 Fr Foley catheter and 22 Fr Foley urethral catheter was install at the end of the surgical procedure. The cystostoma was removed the 7th postoperative day, and the urethral catheter remained for 3 weeks. The patient was released from the hospital the 12th postoperative day. Complete closure of the fistula was achieved after the surgery itself (figure 7).

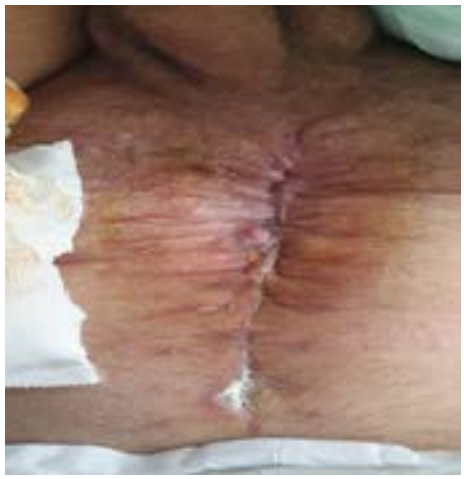

Figure 7. Complete closure of the extensive vesicocutaneous fistula

The thin collocutaneous fistula closed spontaneously after the conservative treatment with regular dressings, dual antibiotic infusion therapy and diet regime, about 1.5 months after the admission to our hospital.

The multifragmented pelvic fracture was treated conservatively in combination with physical therapy in the course of further treatment, with verticalization and mobility achieved after three months from our surgical treatment. The patient's mental state was completely normalized by the clinical psychiatrist's treatment.

CONCLUSION

The vesicocutaneous fistula in our case occurred due to a postoperative infection of the pelvis (osteomyelitis and phlegmona of the front abdominal wall). The period of 6 months with conservative therapy (dual antibiotic therapy and urethral catheter), was too long to expect spontaneous healing of the fistula. Immobile patients such as ours are often exposed to mixed urinary infections which prevent spontaneous closure of the vesicocutaneous fistula. According to our experience we should not wait more than 1.5 months with conservative treatment in order to expect spontaneous closure of the vesicocutaneous fistulas. Spontaneous closer of the vesicocutaneous fistula should be expected in cases without persistent urinary infection and infection of the surrounding tissue. The method of reconstruction of the urine bladder depends on the condition of the bladder wall itself. The closure of the defect with flap made of the aponeurosis of the lower abdominal wall and the left pyramidal muscle in our case proved to be a good permanent surgical solution. The postoperative follow-up of the patient should consist of regular microbiological urine analysis and ultrasound

examination of the urinary tract every 3 months during the first year in order to prevent possible recurrence of the vesicocutaneous fistula.

Key words: urine bladder fistula, pelvis fracture, urine bladder reconstruction, vesicocutaneous fistula, phlegmona pelvis

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TRANSVERSUS ABDOMINIS RELEASE: A CASE REPORT

D-r Aleksandar Mitevski[1,2], D-r Ilija Milev[3], D-r Tahir Shenol[4], D-r Nikola Trokovski[3], D-r Petar Markov[2], D-r Katerina Nikoloska[5]

[1]Department of digestive surgery at General Hospital RE-MEDIKA

[2]GoceDelcev University, Stip, Macedonia

[3]Departmen of general surgery, Clinical hospital – Stip, Macedonia

[4]Department of digestive surgery, University clinic of surgical diseases St. Naum Ohridski, Skopje, Macedonia

[5]University clinic of gynecology and obsetrics, Skopje, Republic of North Macedonia

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ABSTRACT

Introduction: Patients with large abdominal wall defects experience significant deformity, pain and decreased energy due to a loss of normal abdominal wall mechanics, severely impacting their quality of life.Reconstructive techniques for complex ventral hernia repair are numerous but most of them are unable to achieve the goals of hernioplasty. Posterior component separation with transverses abdominis muscle release (TAR) is a novel approach that offers a solution for complex ventral hernias.

Case: A 59 year old patient was admitted to our hospital for treatment of clinically and radiologically verified incisional hernia with 20% loss of domain characteristics, acquired after cesarean section and hysterectomy.

Discussion/Conclusion: Typical reconstructive techniques may struggle to reestablish abdominal domain and to create a lasting repair. Posterior component separation with transversus abdominis release is a novel technique that offers a durable solution to a variety of complex ventral hernias.The lack of sufficient tissue requires the insertion of prosthetic material or transposition of autologous material to bridge the fascial gap.Retromuscular or sublay hernia repair with mesh has proven to be a durable technique for ventral hernia defects, and completely avoids subcutaneous flap elevation.

TAR allows for significant posterior rectus fascia advancement, wide lateral dissection, preservation of the neurovascular supply, avoids subcutaneous tissue undermining and provides a large space for mesh sublay which allowsfor bilaminarin growth of the mesh.

Keywords: Complex hernia, incisional hernia, abdominal hernia repair, transverse abdominal muscle release, TAR.

INTRODUCTION

Patients with large abdominal wall defects often experience significant deformity, pain and decreased energy due to the loss of normal abdominal wall mechanics, severely impacting their quality of life(Figure 1). Thus it is important to remember that abdominal wall reconstruction should almost always be performed as an elective procedure and as one with potential burden for significant morbidity.[1]

Because herniorrhaphy failure and complication rates appear proportional to the number of previous repairs, multiply recurrent hernias represent a formidable challenge.[2]

Many surgeons are discouraged in abdominal wall reconstruction procedures because of the technical difficulties, the high morbidity and the relatively high recurrence rate associated with these procedures. However, many patients with large hernias have infirmity complaints such as bulging of the abdominal wall, chronic wounds, immobility and back pain, necessitating surgical treatment. [3]

Reconstructive techniques for complex ventral hernia

repair are numerous but most of them are unable to achieve the goals of hernioplasty. Posterior component separation especiallytransverses abdominis muscle release (TAR) is a novel approach that offers a solution for complex ventral hernias. [4]

CASE

A 59 year old patient was admitted to our hospital for treatment of clinically and radiologically verified incisional hernia with 20% loss of domain characteristics, acquired after cesarean section and hysterectomy. (Figure 2) The patient is operated under general anesthesia.

Median laparotomy incision with the scar excision was performed. Sharp dissection of the subcutaneous tissue is made to the point of identification of the hernia sac which is then opened. The abdominal cavity is visualized and full adhesiolysis of the viscera from the abdominal wall is conducted.

At the level of the medial border of the rectus is entered in the retromuscular plane. Using combined sharp and blunt dissection, the posterior layer of the rectus abdominis muscle is released laterally to the level of the posterior vagina of m. rectus abdominis and m. transversus abdominis.

At this level, the aponeurosis is incised and the dissection is brought to the posterior axillary line. The same procedure is done on the other side after which an additional 7-10 cm of tissue is obtained. (Figure 3)

The peritoneum is then closed using absorbable suture (Figure 4) and a 30x30 cm polypropylene mesh was diagonally placed (diamond shaped). The mesh is fixed to the Cooper ligament and the pubic crest with simple non absorbable sutures. Due to the magnitude of the defect, additional 15x15 cm polypropylene mesh is placed fixed with sutures just beneath the xiphoid processus and the superior edges of the previously diagonally placed mesh.

A drain is applied in this sub muscular plane. The retracted rectus muscles are than reaproximatedwith single sutures on the medial anterior rectus sheet, recreating the lineaalba.Another drain is added in the subcutaneous tissue. The skin incision is closed with staples. Postoperative recovery was uneventful; abdominal binder was applied from day one, preperitoneal drain was extracted on the third postoperative day and the subcutaneous drain was extracted on fourth postoperative day, the same day the patient was discharged.

DISCUSSION/CONCLUSION

Ventral hernia formation is a frequent and increasingly difficult problem. Nonmidline hernias, parastomal hernias, hernias near bony landmarks, and recurrent ventral hernias (especially after anterior component separation) present particular challenges. Typical reconstructive techniques may struggle to reestablish abdominal domain, reconstruct abdominal wall function and to create a lasting repair. Posterior component separation with transversus abdominis release is a novel technique that offers a durable solution to a variety of complex ventral hernias. [5]

The lack of sufficient tissue requires the insertion of prosthetic material, transposition of autologous material or both to bridge the fascial gap.

Retromuscular or sublay hernia repair with mesh has proven to be a durable technique for ventral hernia defects and completely avoids subcutaneous flap elevation. Technically, the retromuscular technique requires developing the space dorsal to the rectus abdominis muscles up to the edge of the rectus sheath. In the average patient, this translates into a 6–8 cm lateral space on each side of the midline. Repair of large hernia defects with diameters greater than 15 cm may require a larger mesh overlap than can be afforded by dissection limited to the confines of the rectus sheath. By incising the posterior rectus sheath and creating the plane between the internal oblique and transversus abdominis muscles (“classic” posterior CST), there is a space virtually unlimited in size in which to place large meshes for hernia repair. [6]

The component separation technique (CST) was introduced to abdominal wall reconstruction to treat large, complex hernias. It is very difficult to compare the published findings because of the vast number of technical modifications to CST as well as the heterogeneity of the patient population operated on with this technique. [7]

Novitsky and Rosen developed a novel technique of posterior component separation using transversus abdominis muscle release (TAR). This modification allows for significant posterior rectus fascia advancement, wide lateral dissection, preservation of the neurovascular supply, avoids subcutaneous tissue undermining and provides a large space for mesh sublay [8].

Transversus abdominis release (TAR), as a type of posterior component separation is a new myofascial release technique in complex ventral hernia repair. TAR creates an immense retromuscular plane and allows bilaminar ingrowth of the mesh. [9]

This novel technique for posterior component separation is associated with low perioperative morbidity and a low recurrence rate. Overall, transversus abdominis muscle release may be an important addition to the armamentarium of surgeons undertaking major abdominal wall reconstructions. [10]

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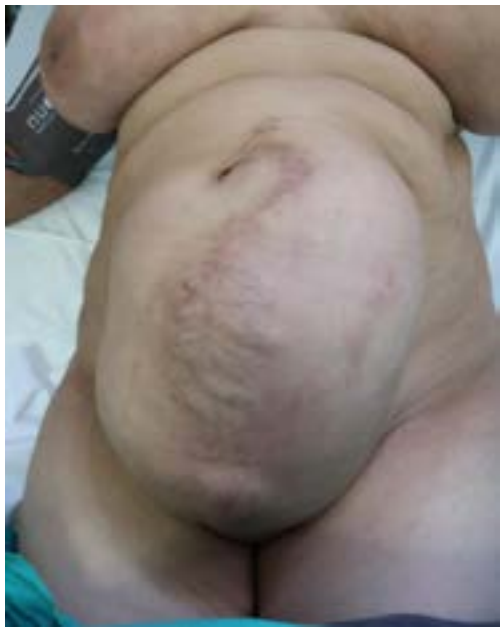


Figure 1. Hernia before pre operation

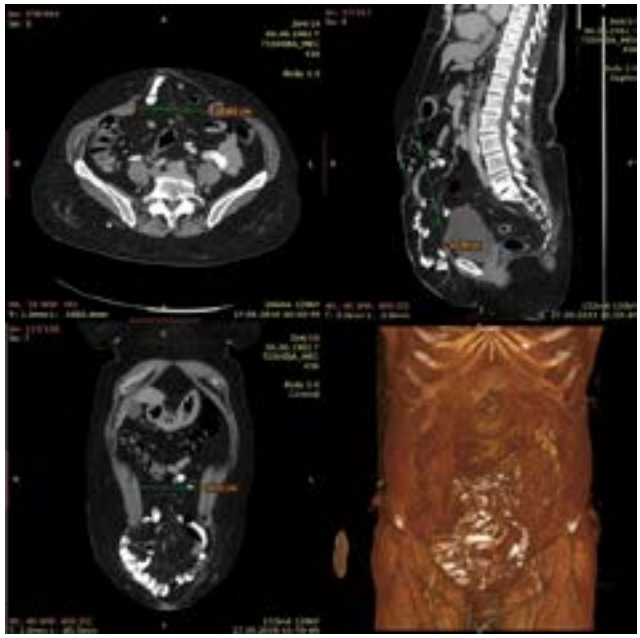


Figure 2. Abdominal defect

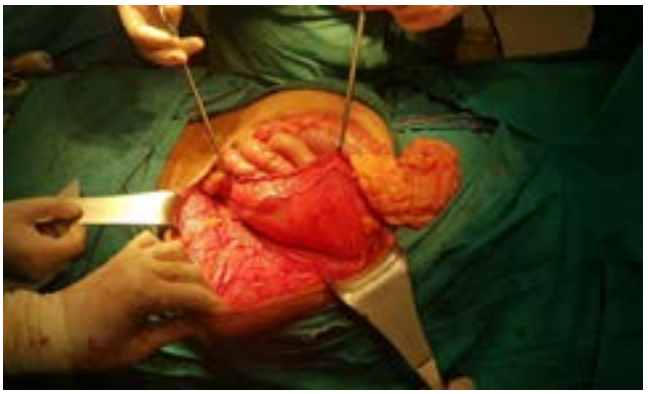


Figure 3. Flap after releasing transversus abdominis muscle

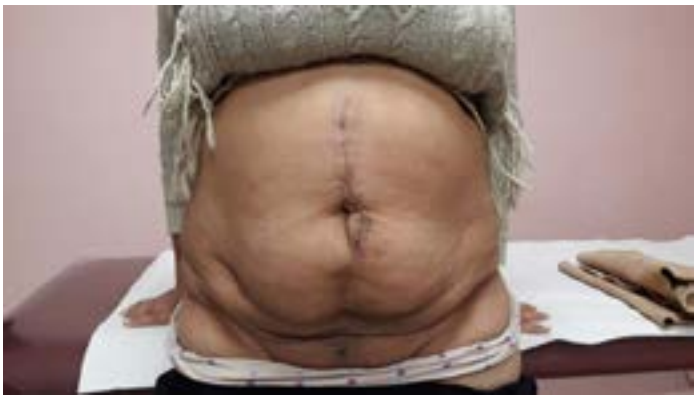


Figure 6. One month after surgery

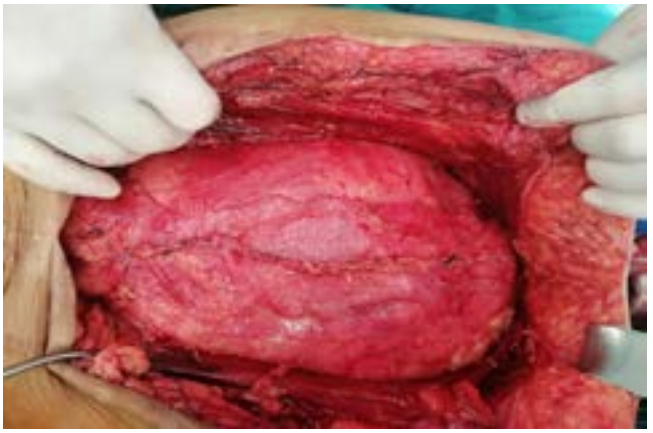


Figure 4. Closed peritoneum

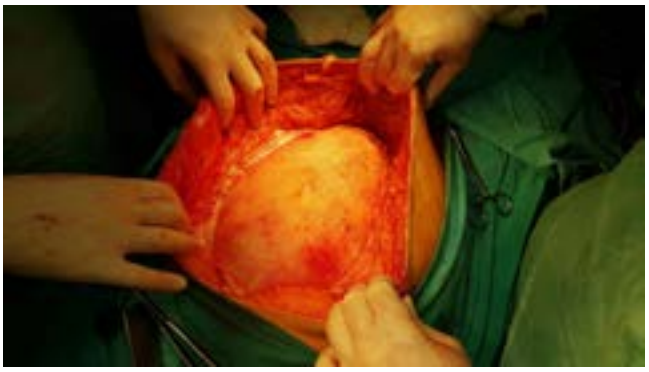


Figure 5. Applied mesh

Case report

TRAJTIMI I KANINIT TË RETINUAR (RAPORTIM RASTI)

Msc. Iris Çaçani; Prof. Vergjini Mulo

Klinikë Dentare Private "Çaçani", Tiranë

Medicus 2020, Vol. 25 (2): 272-276

ABSTRAKT

Rezultatet maksimale të trajtimit të kaninit të retinuar janë të lidhura ngushtë me diagnostikimin e saktë dhe sa më të shpejtë, me përdorimin e aparaturave ndihmëse (radiografitë), dhe me një bashkëpunim të ngushtë me mjekun kirurg apo periodontistin. Në disa raste, zgjidhja do të ishte ekstraksioni i kaninit të retinuar, por ne do të sjellim rastin klinik të një pacienteje 14 vjeçare me dy kaninë maksilarë të retinuar, i trajtuar me ndihmën e bashkëpunimit ortodont- kirurg.

FJALË KYÇE: kanini maksilar i retinuar, ekstraksioni, menaxhimi i kaninit të retinuar.

HYRJE

Menaxhimi efektiv i kaninit maksilar të retinuar është ende një sfidë në fushën e dentistrisë. Zgjidhja sa më e mirë e rasteve me kaninë të retinuar do të kishte domosdoshmëri bashkëpunimin e ngushtë të ortodontit, radiografitë dhe mjekut kirurg oral. Diagnoza e kaninit të retinuar ka të bëjë me interpretimin radiologjik të rastit, si dhe me palpimin apo analizat biometrike.

Sipas Bishara ka disa shenja që tregojnë kur një kanin është i retinuar: vonesa në daljen e kaninit të përhershëm, prania e kaninit të qumështit (pas moshës 14 vjeç), mungesa në palpim e të fryrës bukale, ndërsa palatinal preket me dorë e fryra.

Diagnoza e saktë arrihet nëpërmjet mjeteve të ndryshme radiografike (panorameksi, grafitë intraorale, grafitë tredimensionale dhe Dental Scan).

QËLLIMI

I këtij punimi është të tregojë një rast klinik të një pacienteje me dy kaninë maksilarë të retinuar, dhe menaxhimin ortodontiko- kirurgjikal të këtij rasti.

Ka disa mënyra të trajtimit të kaninit të retinuar:

Reimplantimi, e cila është një metodë që kërkon kohë më të shkurtër, por nevojitet hapësira e nevojshme ku të reimplantohet kanini.

Ekstraksioni i kaninit të retinuar dhe zëvendësimi i dhëmbit me impiant apo mënyra protetike.

Ekspozimi kirurgjikal i kaninit dhe vendosja në hark me anë të aparateve ortodontike fikse. Kjo është metoda më e mirë por kërkon kohëzgjatje më të madhe.

Indikacionet për ektsraksion të kaninit të retinuar, sipas Bishara janë:

Ankilozimi i kaninit të retinuar;

Retinimi i vështirë (i vendosur midis rrënjëve të lateralit dhe centralit);

Premolari i parë është i vendosur në vend të kaninit dhe kafshimi është në klasin e parë të Anglit;

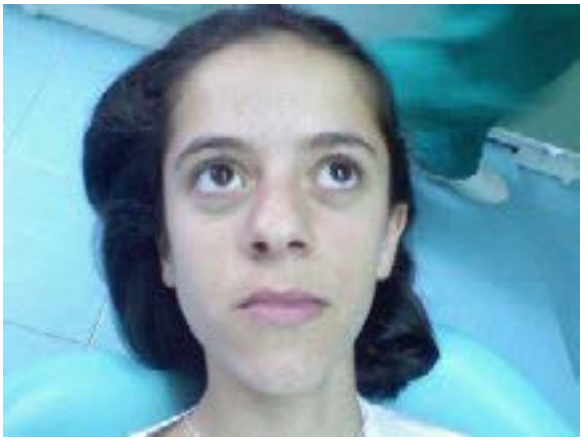
Procese patologjike rreth dhëmbit të retinuar, p.sh. ciste;

Kur pacienti nuk dëshiron të vendosë aparatet ortodontike.

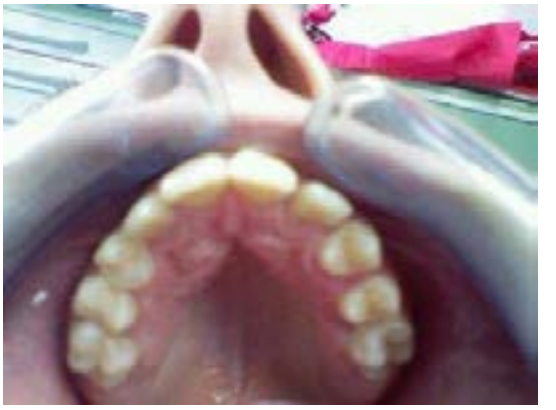
Ka shumë raste komplikimesh të lidhura me ekstraksionin e kaninit të retinuar: defekt i madh kockor, dëmtim i dhëmbëve pranë (luksimi, dëmtim i periodontit, frakturë e rrënjëve), dëmtimi i sinusit maksilar, neuropatitë. Për këto arsye, heqja e kaninit maksilar të retinuar është zgjedhja e fundit.

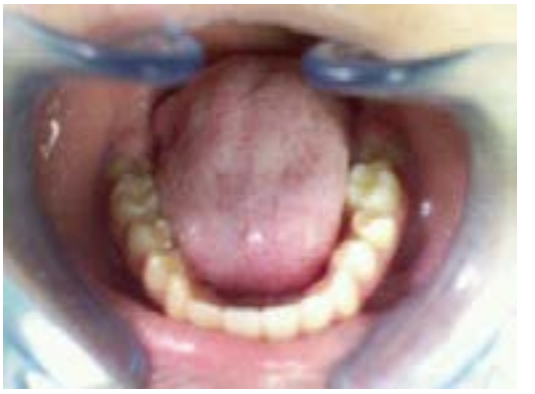
RAST KLINIK

E. K. 14 vjeç, u paraqit në klinikë me malokluzion të klasës së IIItë të Anglit dhe me maksilë të pazhvilluar. Në ekzaminimin klinik u vu re mungesa e kaninëve maksilarë, si dhe mungesa e hapësirës për to, për shkak të zhvillimit të pakët të maksilës. Në ekzaminimin radiologjik vumë re praninë e kaninëve në pozicion ektopik dhe të retinuar. Trajtimin ortodontik e nisëm me një RPE (zgjerues palatinal të shpejtë). Pas katër muajve vendosëm aparatet ortodontike fikse (braketa) dhe u procedua me hapjen e hapësirave për kaninët e retinuar. Pasi u krijua hapësira e nevojshme, kryem, në bashkëpunim me kirurgun oral, ndërhyrjen kirurgjikale për ekspozimin me lembo të kaninëve të retinuar. Metoda e përdorur ishte ajo e tunelimit. Mbi kaninët e retinuar vendosëm braketa me zinxhir të inkorporuar dhe filluam tërheqjen e kaninëve. Dalja e tyre kërkoi rreth 7 muaj kohë. Ndërkohë, vendosëm dhe aparatin fiks në nofullën e poshtme, dhe punuam edhe për rregullimin e kafshimit në klasë të Irë të Anglit. Trajtimi ortodontiko - kirurgjikal zgjati rreth dy vjet e gjysëm, kohë e përshtatshme dhe e pranueshme për raste të tilla. Pacientja rifitoi një buzëqeshje të bukur dhe të plotë.

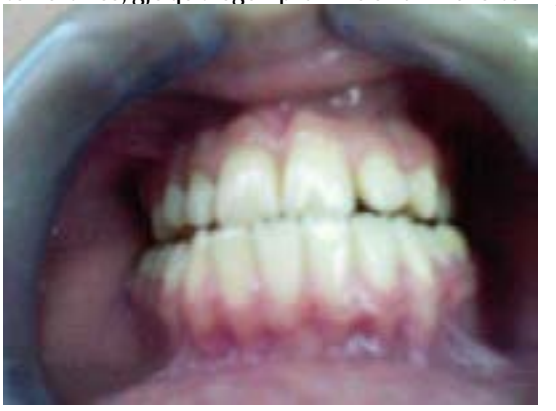


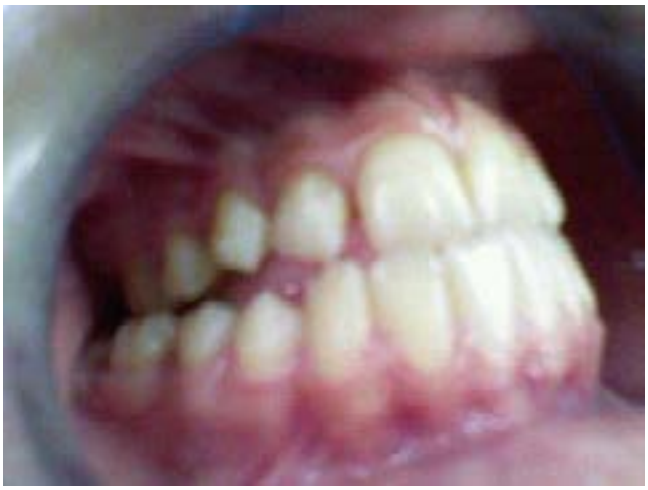
Pacientja E.K. 14 vjec, me fytyre hiperdivergjente dhe profil te protuduar ne pjesen mandibulare. Bie ne sy hypozhvillimi i maksiles dhe kendi nasolabial i gjere. Ne ekzaminimin ekstraoral pacientja duket e shtypur ne regjionin e kanineve, kjo per shkak te mungeses se rrenjeve te kanineve ne pozicionin e tyre normal.

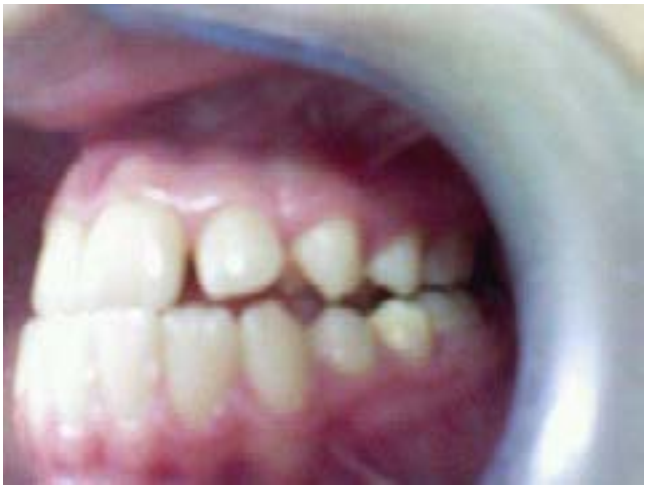




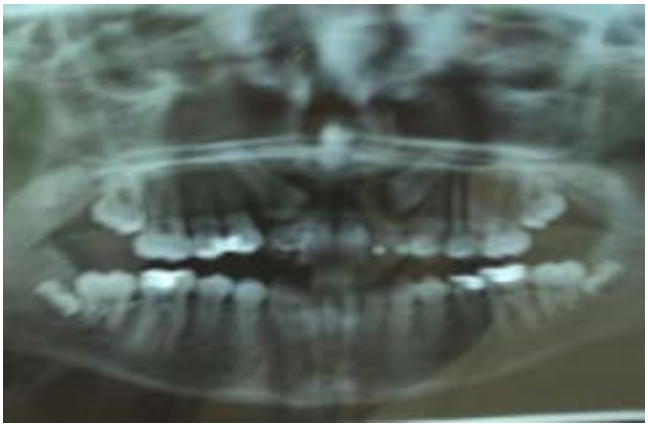
Ne ekzaminimin intraoral vihet re nje mandibul e zhvilluar mire dhe dhembe te drejte, ndersa ne nofullen e siperme vihet re nje maksile e pazhvilluar, mungesa e te dy kanineve, dhe prania e dy te fryrave ne anen palatinale te nofulles, gje qe tregon pranine e kanineve te impaktuar

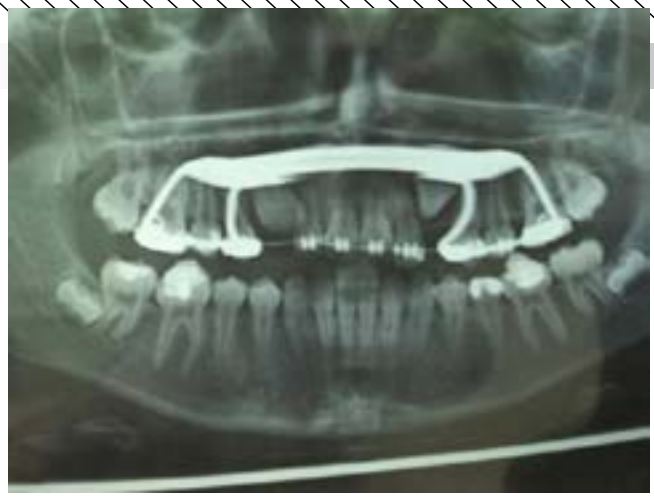




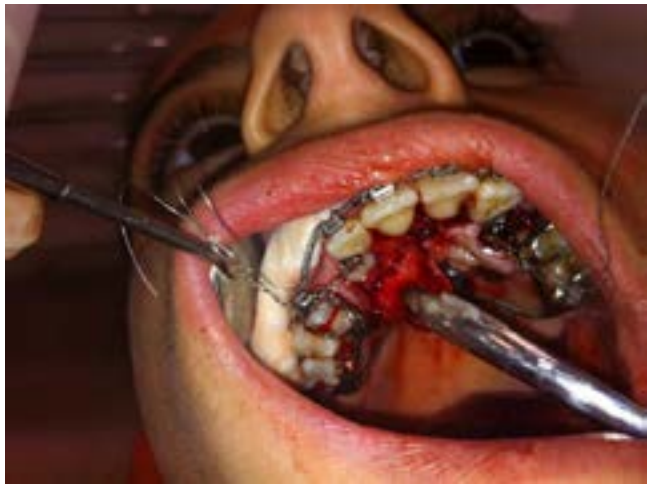


Pacientja paraqitet me maloklusion te klases se trete, kafshim maje me maje, me overjet dhe overbite zero. Kafshimi eshte i hapur lateralisht dhe gjate gelltitjes pacientja interferon me gjuhen midis harqeve dentare.

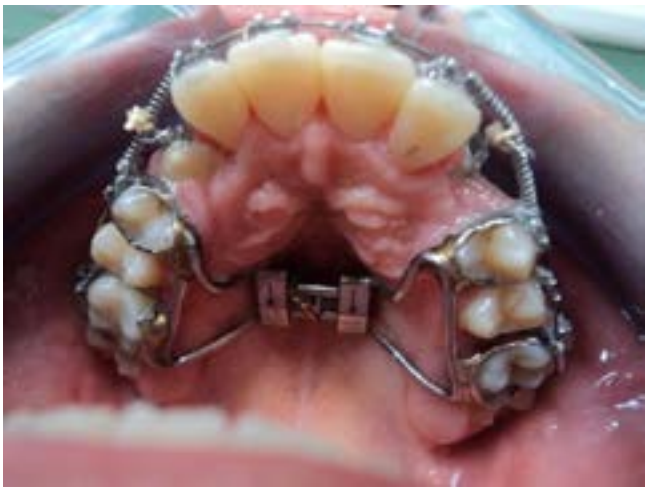


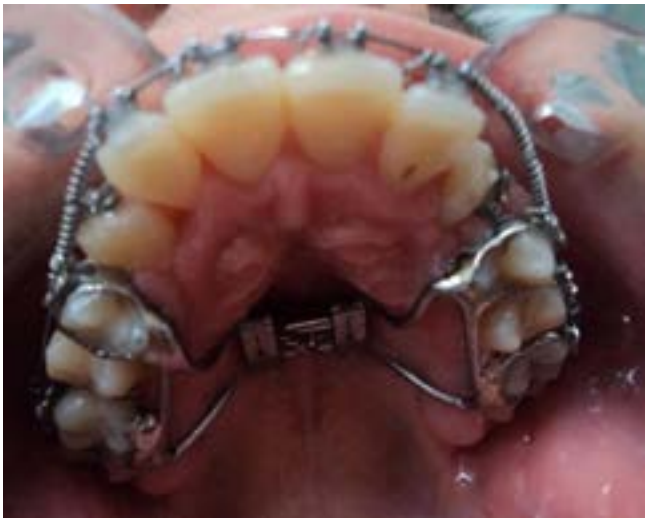


Ne grafine panoramike vihet re pozicioni palatinal i kanineve dhe pozicioni ektopik e i impaktuar i tyre. Ne fazen e pare te trajtimit vendosem nje zgjerues te shpejte, gje qe pati si pasoje permiresimin e dimensioneve te nofulles se siperme. U arrit zgjerimi i dimensoneve transversale e sagitale te maksiles, dhe pervec kesaj , nga ky zgjerim u perftua nje ripozicionim i kanineve ne nje pozicion me te favorshem.. Me pas, vendosem braketat e aparatit fiks dhe drejtuam hapjen e hapesirave ne regjionin e kanineve te impaktuar.

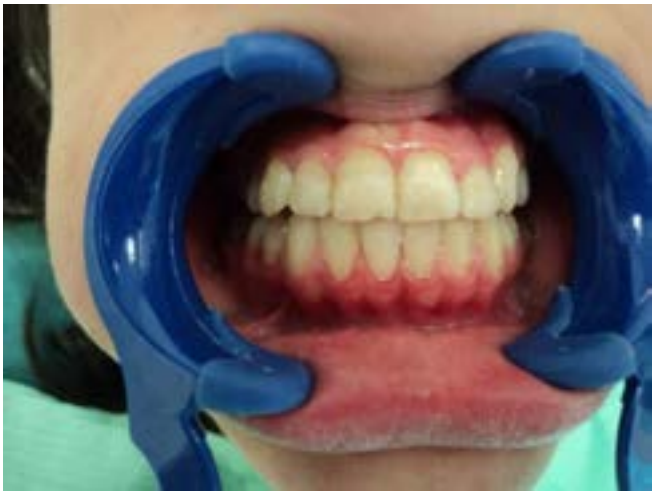


Ne momentin kur ne harkun dentar te nofulles se siperme kishim krijuar hapesirat e mjaftueshme per daljen e kanineve, ne vendosem te kryenim nderhyrjen kirurgjikale me ndihmen e kirurgut oro maksilo facial. Nderhyrja konsistoi ne hapjen e nje lemboje te gjere ne anen palatinale, e cila na lejon zbulimin e te dy kanineve te impaktuar. Mbi kaninet e ekspozuar vendosem nga nje brakete mbi te cilat eshte inkorporuar nje zinxhir metalik me hallka i cili do te na ndihmoje per terheqjet elastike qe do te ushtrojme mbi dhembe. Me pas lemboja qepet ne pozicionin fillestar dhe ne fund te nderhyrjes kirurgjikale ne shohim zinxhirat metalike qe dalin nga submukoza.

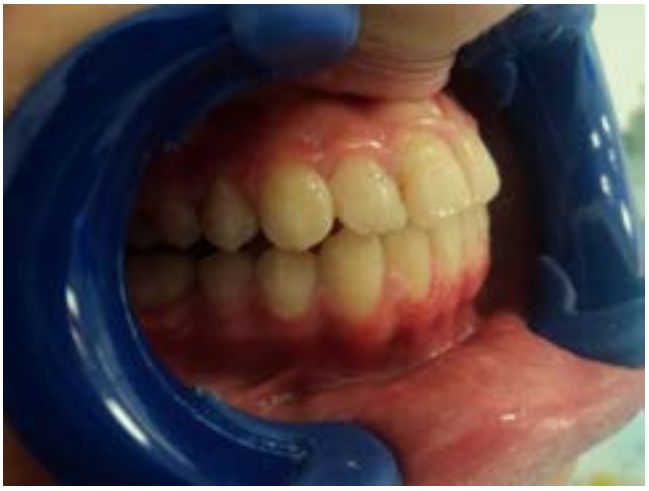


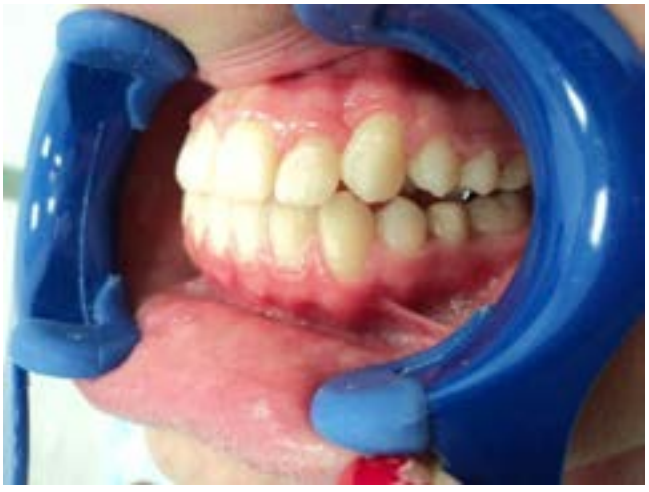


Per te nxjerre dhembet e impaktuar ne kryejme terheqje elastike periodike e te vazhdueshme, deri sa te kemi daljen e dhembeve nga mukoza, e me pas spostojme dhembet ne pozicionin e tyre ne harkun dentar. Ne keto foto kemi momente te ndryshme gjate daljes se dhembeve e gjate spostimit te tyre drejt poziionit perfundimtar ne harkate.



Trajtimi ortodontiko kirurgjikal zgjati dy vjet e gjysem. Ne fund te trajtimit u arrit nxjerrja e te dy kanineve te impaktuar dhe vendosja e tyre ne pozicionin e pershtashem ne harkun dentar. Me ane te trajtimit ortodontik u arrit gjithashtu edhe rregullimi i maloklusionit, duke cuar ne perfundim te trajtimit ne arritjen e kafshimit te klases se pare te Anglit. Overjet dhe overbiti u cuan ne vlerat e tyre mesatare.





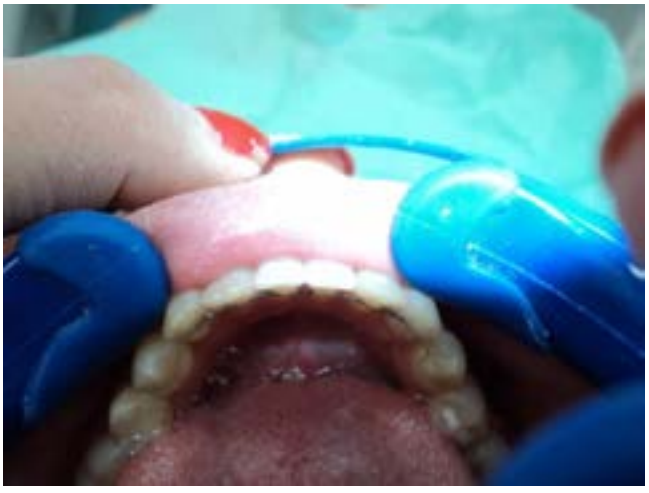


Foto te rastit te trajtuar pas heqjes se aparateve.Ne nofullen e poshtme shihet vendosja e retainerit metalik, ndersa ne nofullen e siperme kemi bere nje aparat te levizshem te cilin

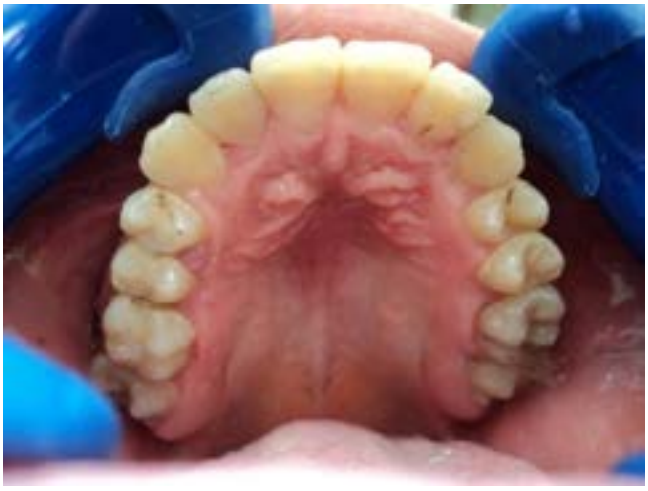


Foto perfundimtare e pacientes diten qe ka hequr aparatin.Shihet qarte ndryshimi i buzeqeshjes se pacientes per shkak te zgjerimit te nofulles se siperme dhe pranise se kanineve, dhembeve aq te rendesishem ne estetiken e buzeqeshjes.

KONKLUZIONE

Trajtimi ortodontiko kirurgjikal i kaninit të retinuar është metoda më e mirë e manaxhimit të këtyre rasteve për arsye se në harkun dentar kemi dhëmbët natyralë të vendosur në vendin e tyre. Bashkëpunimi me mjekun radiolog dhe kirurg oral është thelbësor për suksesin e trajtimit.

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WEGENER GRANULOMATOSIS PRESENTED WITH EPISTAXIS, HEMOPTYSIS AND POLYARTHRALGIA: A CASE REPORT

Buklioska Ilievska D[12]

[1]City General Hospital ,,8mi Septemvri", Department of Pulmonology and Allergology; Hospital address: ,,Pariska bb", Skopje, Macedonia

[2]Medical Faculty, University "St. Cyril and Methodius" Skopje, Macedonia

*Author and contact: Daniela Buklioska Ilievska MD, MSc, PhD candidate,
Ass. Prof. of Internal Medicine, specialist of internal medicine
Adress: "Nikola Parapunov" 31/1-3 Skopje, Macedonia
Phone: 00389 70304066
e-mail: dbuklioska@yahoo.com

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ABSTRACT

Wegener granulomatosis (WG) is a rare, multisystem, autoimmune disease with necrotizing granulomatous inflammation, tissue necrosis, vasculitis in small and medium-sized blood-vessels. The classic clinical pattern is a triad involving upper airways, lungs and kidneys. A 33-year-old woman was admitted to hospital because of dry cough, shortness of breath, polyarthralgia, intermittent fever, epistaxis, hemoptysis. Chest X-ray presented multiple, small infiltrates bilaterally. Laboratory results: Hgb 90g/L, hematocrit 30%, erythrocytes 3,6×1012/L, leucocytes 13,8×109/L, platelet 4,45×109/L, CRP 110mg/L, sedimentation 70mm/h. Urine sediment: erythrocytes(16-18), proteins(+), epithelial cells(++), 24hour-proteinuria 0,5g/L. ECG: sinus tachycardia 120 beats/min. Gas analyses: partial respiratory failure, hypoxemia 7,5kPa, hypocapnia 3,6kPa, saturation 91%. Lung-CT revealed multiple bilateral infiltrates. Chest-ultrasound with bilateral, subpleural, hypoechogenic changes with central necrosis. Because of intermittent fever, polyarthralgia, chest X-ray changes, elevated sedimentation, rheumatologist was consulted and tests for autoimmune disease were performed (positive c-ANCA 95U/ml, RF 158IU/ml, ASO 88U/ml). Ophthalmologist revealed punctiform conjunctival bleeding. Bronchoscopy: intranasal coagulum without changes of nasal mucosa, transoral intubation presented diffuse erythema and edema of the vulnerable tracheobronchial mucosa without ulcerous lesions or infiltrative changes. Bronchial alveolar lavage detected small increase of neutrophils (total cell counts 320/αL, neutrophils 19,2%, macrophages 85,0%, lymphocytes 7,4%, eosinophils 0,0%), no growth of bacterial culture, negative Gene X-pert. Transbronchial biopsy was performed, histologic analysis detected necrotic granulomas with multinucleated giant cells accompanied by inflammatory cells. According to all investigations, the diagnosis was WG. The patient was successfully treated multidisciplinary with high-dose steroids and cyclophosphamide. Recognition of multisystem disease involving joints, kidney, eye and lung is critical for diagnosis.

Key words: Polyangiitis, Autoimmune disease, Necrotizing granulomatous vasculitis, Granulomatosis.

INTRODUCTION

Wegener granulomatosis (WG) is a rare, multisystem, autoimmune disease with necrotizing granulomatous inflammation, tissue necrosis, vasculitis in small and medium-sized blood-vessels, first described by German pathologist Friedrich Wegener in 1936 (1,2). The classical clinical triad consists of upper airway involvement (sinusitis, otitis, nasal mucosa ulcers, bone deformities, subglottic stenosis), lower respiratory tract involvement (cough, chest pain, hemoptysis, dyspnea, fever) and glomerulonephritis (in 80%). It is believed that the disease begins as a localized respiratory tract granulomatosis,

which then generalizes into a vasculitis that affects small and medium-sized vessels (1,3). WG most commonly occurs in whites and affects men and women equally. The mean age at diagnosis is 40 years, but the disease can develop at any age (2). Patient presentation varies and depends on the organ system affected. Some patients present with chronic nasal obstruction, which may be misdiagnosed as chronic sinusitis, others may present with acute renal or respiratory failure. Patients with pulmonary involvement, mononeuritis multiplex or unexplained multisystem disease (1,3). Elevation of serum c-antineutrophil antibodies against protease 3 in cytoplasmic granules (c-ANCA) titers frequently occurs in patients with WG and can be used to assess disease activity. The reference standard for diagnosis is biopsy. Renal biopsy, the most common approach, usually shows a nonspecific glomerulonephritis. Lung biopsy may show a granulomatous small-vessel necrotizing vasculitis (2,4). Some infectious diseases, such as bacterial endocarditis may sometimes show high titers of ANCA, mimicking vasculitis (5). Lung nodules are the most common manifestation of WG on chest X-ray and occur in approximately 40–70% of patients (6,7). Treatment includes immunosuppressant therapy, most commonly systemic steroids and cyclophosphamide. Remission rates are approximately 90%, but relapses may occur (6). Before the routine use of glucocorticoids and cyclophosphamide, the one year mortality was 82% (1).

CASE PRESENTATION

A 33-year-old woman was admitted to our hospital with a history of progressively worsening dry cough, shortness of breath, polyarthralgia, fever, epistaxis, general fatigue and hemoptysis. Three months before admission, she had episodes of nasal bleeding, dry cough, intermittent fever not more than 38.2γC. Her primary physician did not detect any abnormal findings in the chest radiogram performed at that time. After three months, she consulted the doctor again due to symptom worsening. The second chest X-ray was with multiple small infiltrates in both lungs (Figure 1). Because of the chest radiogram and laboratory result with high sedimentation rate, the patient was immediately admitted to hospital. She had a smoking history of 10 pack-year, mother of one 10year-old child, without any problems during pregnancy and delivery, no allergies reported, no regular therapy used, one operation of left-sided inguinal hernia twenty years ago. She reported family illness, diabetes mellitus type 2 (by her mother's side).

Physical examination on admission, blood pressure was 120/80mmHg, the pulse 120 beats per minute, temperature 38γC, oxygen saturation 91%, weight 61kg. Her skin was pale, without any rashes, normal lung auscultation, heart rate rhythmic, tachycardic, without murmurs. Abdomen without pain or tenderness on palpation. Mild, bilateral, ankle edema, but other joints were without swelling or any other changes on inspection or palpation. Eyes with emphasized conjunctival, vascular pattern. Small clots in the nose.

Laboratory results revealed anemia with Hgb 90g/L, hematocrit 30%, erythrocytes 3,6×1012/L, leucocytes 13,8×109/L (85,9% neutrophils, 10,8% lymphocytes), platelet count 4,45×109/L, C-reactive protein (CRP) 110mg/L (normal values less than 3,03 mg/L), sedimentation rate (SR) 70mm/h per first hour (normal values 0-20 mm per hour). Renal, liver function tests, hemostasis were within normal limits. D-dimer 4000ng/ml. Urine sediment – erythrocytes 16-18, proteins +, epithelial cells ++. 24hour proteinuria 0,5g/L (upper limit 0,2g/L). ECG with sinus tachycardia of 120 beats/min. Gas analyses in partial respiratory failure with hypoxemia 7,5kPa and hypocapnia 3,6kPa, oxygen saturation 91%. Chest radiography and lung computed tomography (CT) showed multiple bilateral infiltrates (Figure 2). Chest ultrasound with bilateral, subpleural, hypoechogenic changes with zones of central necrosis, maximal diameter 26x18,9mm (Figure 3). Because of persistent fever, chest X ray and lung CT scan, significantly elevated SR, rheumatologist was consulted and tests for autoimmune disease were performed. Rheumatoid antibodies: positive c-ANCA 95U/ml (normal up to 30U/ml), RF 158IU/ml, ASO 88U/ml. Because of the significant 24hour proteinuria and hematuria, an examination by nephrologist was asked. Renal ultrasound revealed no pathological changes, and nephrologist's opinion was that there was no need of renal biopsy in that stage, because of preserved renal function. Ophthalmologist examination detected punctiform conjunctival bleeding. Bronchoscopy finding of intranasal coagulum without changes of nasal mucosa. Transoral intubation revealed diffuse erythema and edema of the vulnerable tracheobronchial mucosa without any ulcerous lesions or infiltrative changes (Figure 4 a, b). Bronchial alveolar lavage (BAL) was performed. Cytology report showed small increase of neutrophils (total cell counts 320/γL, neutrophils 19,2%, macrophages 85,0%, lymphocytes 7,4%, eosinophils: 0,0%). BAL gram stain

and culture showed no growth. BAL sample for Gene X-pert PCR was negative. Transbronchial biopsy was performed and histologic analysis revealed necrotic granulomas with multinucleated giant cells accompanied by inflammatory cells in the bronchial and parenchymal lesions using hematoxylin and eosin stains. According to the pathology result the diagnosis was granulomatosis with polyangiitis, Wegener's granulomatosis.

During the hospital stay until diagnosis, the patient was treated with broad spectrum antibiotics, antifever drugs, fluids, systemic corticosteroids, low-molecular weight heparin, gastro-protective therapy, oxygen, supportive therapy. The treatment continued multidisciplinary after confirmed diagnosis WG, with high-dose of systemic steroids (prednisolone, with gradual decreasing of the dose) and cyclophosphamide. The symptoms, chest X-ray results and c-ANCA level, were significantly reduced after two months follow-up.

DISCUSSION

Granulomatosis with polyangiitis (GPA), formerly known as Wegener's granulomatosis (WG), belongs to the group of ANCA-associated necrotizing vasculitides (8, 9). The clinical manifestations are diverse, and this is reflected in the manner of their presentation (4). It is a rare disease, during the past 15 years, the epidemiology of Wegener's granulomatosis (WG) has become better understood. Descriptive epidemiological studies carried out primarily in European countries estimate a prevalence of WG ranging from 24 to 157 per million and annual incidence rates from 3 to 14 per million, depending on geographic location (10). Chest radiographic findings are often the first to suggest the diagnosis, but CT has superior sensitivity and specificity for evaluation. Common pulmonary radiologic findings include waxing and waning nodules, masses, ground-glass opacities, and consolidation. Airway involvement is usually characterized by circumferential tracheobronchial thickening, which can be smooth or nodular. Pleural effusions are the most common manifestation of pleural disease and can result from primary involvement or be secondary to renal failure (11).

This is a case report of granulomatosis with polyangiitis (Wegener's granulomatosis) in a younger patient than the average onset of WG, 33 years old, where the diagnosis was identified by transbronchial biopsy which identified granuloma with giant cells. These findings led to a diagnosis of WG. Clinical course, positive c-ANCA, negative RF, chest imaging results, urine analysis were considered diagnostic for WG. Flexible bronchoscopy and transbronchial biopsy were very helpful procedures in this case. Usually, renal involvement is severe and the leading cause of mortality, but our patient's renal function was preserved. The significant proteinuria was also suggestive of WG-associated glomerulonephritis (4). Differential diagnosis included systemic lupus erythematosus, Churg-Strauss Syndrome, rheumatoid arthritis.

According to the medical intervention in WG, the immune system has been the major target of therapy with immunosuppressive drugs such as prednisolone, cyclophosphamide, azathioprine, and more recently, methotrexate and mofetil mycophenolate. Also, it is proposed treatment with the antibiotic trimethoprim-sulfamethoxazole (co-trimoxazole) for reducing the incidence of disease relapses in WG (12). Open-label clinical studies suggest a beneficial effect of infliximab or rituximab in addition to standard therapy in refractory Wegener's granulomatosis (13). Plasma exchange is the best complement to immunosuppressants in advanced renal disease at present (14).

Conclusion

Despite recent progress, the prevention of relapses and treatment of refractory cases remain the greatest challenge in the treatment of Wegener's granulomatosis (12, 15). Long-term treatment and disease-related morbidity are major threats, there is a need for safer and more effective medications. Early diagnosis and multi-specialty collaboration among physicians is necessary to adequately manage the disease and the potential complications that may result from drugs used in the treatment of the disease (15).

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ADDITIONS

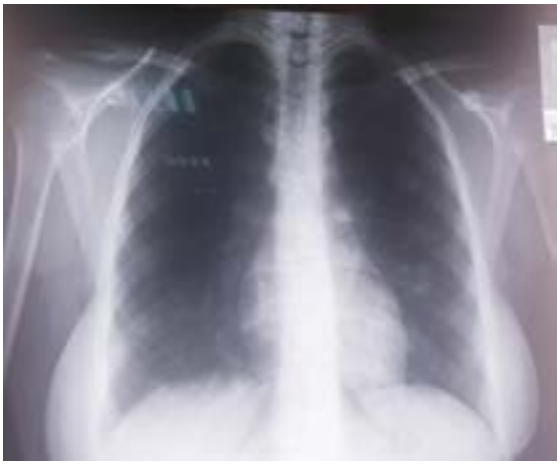


Figure 1. Chest radiography showing small, multiple, bilateral lung infiltrates.

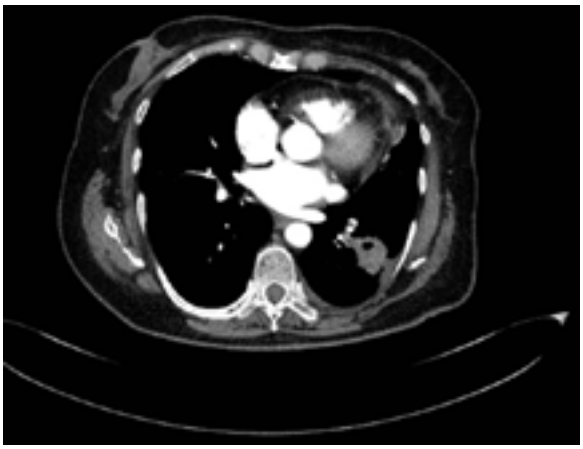


Figure 2. High resolution CT image showing nodule in lung parenchyma with spiculate margins and central necrosis.

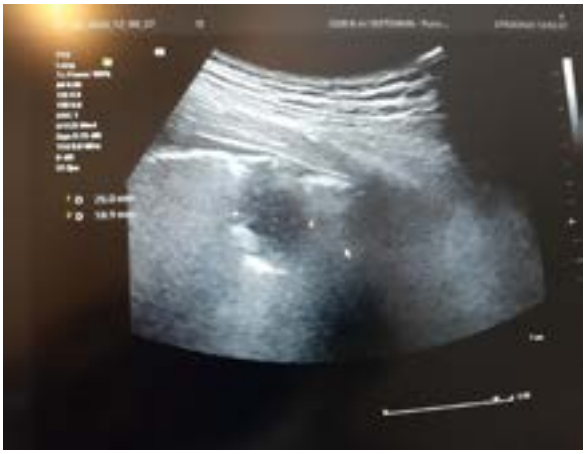
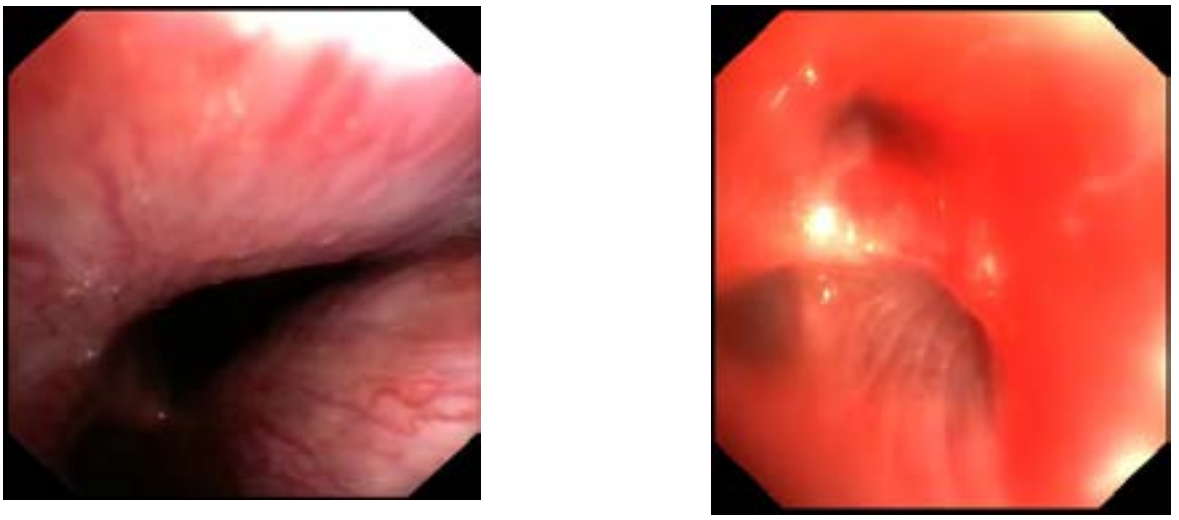


Figure 3. Chest ultrasound presenting subpleural, hypoechogenic change with central necrosis.



(a) (b)

Figure 4. Bronchoscopy findings of edematous mucosa and prominent capillary vessels, beginning from distal trachea (a), diffuse erythema and edema of the vulnerable tracheobronchial mucosa in right upper bronchus, with contact bleeding (b).

RADIOLOGICAL EVALUATION OF RENAL CELL CARCINOMA,CASE REPORT

Katerina Kitanovska[1], Dragana Mogilevska Gruevska[2], Argjend Imeri[3]

[1]JZU Zeleznicar-Skopje,
[2]JZU Opsta Bolnica so prosirena dejnost –Kocani
[3],JZU Klinicka bolnica-Tetovo

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ABSTRACT

Renal cell carcinoma is the most common malignant renal tumor, account for 85-90% of all renal malignant neoplasm in adults,with male predilection 2:1. It can be symptomatic flank pain, macroscopic hematuria, palpable flank mass) and asymptomatic, diagnosed incidentally, or can be presented with paraneoplastic syndrome (hypercalcemia,hypertension, polycythemia). Radiology imaging methods(ultrasound, computed tomography and magnetic resonance) are primary in diagnosing this neoplasm and their differential diagnosis, so the main goal in this paper is to introduce the sensitivity and specificity of this methods in early diagnosis of patients with renal cell carcinoma. We present a case of 72years old female, with occasional macroscopic hematuria for one month and history of hypertension. Patient was radiologically investigated with ultrasound, computed tomography and magnetic resonance, the diagnose of malignant neoplasm of kidney was established, which was histopathological confirmed.

Key words: renal cell neoplasm, ultrasound, computed tomography, magnetic resonance

INTRODUCTION

Renal cell carcinomas are malignant adenocarcinomas, which origin from tubular epithelium and encompasses a number distinct histological varieties: clear cell renal carcinoma:70-80%, papillary renal cell carcinoma 13-20%, cromophobe renal cell carcinoma 5%, collecting duct renal carcinoma<1%, renal medullary carcinoma: rare. According to the classification of the tumor, researchers made an effort to identify the tissue of genesis for renal carcinoma. The pathogenesis of renal epithelial tumors was debated for decades, by several researchers, initiated by Paul Grawitz, who concluded that papillary tumors arise from renal tissue, than Paul Sudeck published description of renal tumors, in which he equated atypical features within renal tubules and gradation of this features with near malignant tumors,and Otto Lubasch who supportedpriviestheory, gave the term hypernephroied tumor which was supplement by Felix Victor Birch Hirschfelf to hypernephroma, Macroscopically RCC are variable in appearance, from solid and homogenous to heterogeneous with areas of hemorrhage, necrosis and cystic change, this changes give main characteristics in radiological appearances in imaging. Risk factors are presented in 50% of all cases and include: obesity , smoking andhypertension. Classical clinical picture is very rare, and includes trias of symptoms: macroscopic hematuria, flank pain and palpable flank mass, in the practice almost half of all renal carcinomas are incidentally found on images for other purposes. Paraneoplastic syndrome is also associated with RCC, presented with different symptoms, due to cancers present in the body and substances that circulate in the blood stream. Treatment is surgical, partial or radical nephrectomy is performed, although the management of this neoplasm depends on the stage of diseases, type of renal cell carcinoma, co- morbidities and age of the patient. Renal cell carcinoma is metastatic, the most common sites of metastasis are: the lungs, the

bones, lymph nodes, the liver, adrenals and the brain. Prognosis can be variable depending both on histological subtype and stage. In this case we introduce adult female patient, symptomatic with macroscopic hematuria, radiologically presented with heterogeneous solid mass of right kidney, surgically treated with total nephrectomy, patohistologicly confirmed clear cell renal carcinoma.

CASE REPORT

A 72year female patient was referred to radiological department in our institution, for abdominal ultrasound with symptoms of occasional macroscopic hematuria, during 1 mounts, malaise and with privies history of arterial hypertension.On the abdominal ultrasound,fig1,a hipoehogenic well defined solid mass in the interpolar region of the right kidney,was reviled, other abdominal organs presented with normal findings, no free fluid in the abdomen was founded. For further deferencions and determination of the lesion, the patient was sent to computer tomography and magnetic resonance. On the computer tomography ofthe abdomen and pelvis, fig. 2 and 3,the lesion of the right kidney was confirmed, localized in the interpolar region , well defined, without invasion of other organs, solid with heterogeneous characteristic, with areas of hemorrhage and necrosis and with compression of the pielocalical system of the right kidney but without hydronephrosis.. Other CT findings presented normal. On MRI, fig.5and 6 with standard sequences and protocol, right kidney mass, was presented with heterosignal characteristics, mainly hiperintense, with prompt arterial enhancement, without restriction of diffusion. Based on CT and MR characteristics,diagnose of malignant renal neoplasm was made and with urological consultation radical nephrectomy was performed. On the follow up exams, fig.4, during two years after surgery, our patient iswell, US and CT exams are normal, withoutmetastatic disease.

DISCUSSION

Renal cell carcinoma or RCC is a type of cancer that has been quite common in recent years. The frequency has increased by 10 times compared to 50 years ago. The reasons for this are aging of the population that increases the incidence of cancer and more frequent use of ultrasound, tomography and MRI that increases incidental detection. Frequent use of these imaging modalities also allowed early detection of RCC. At present, 75% of RCC cases are detected at Stage 1a, which is the earliest stage (Tumor limited to kidney and less than 7cm).Initial toll in diagnosing, renal cell carcinoma is ultrasonography, noninvasive, available, easy method, sensitive in detecting renal mass, differentiated solid from cystic, but is not specific, provides less information about the characteristics of the mass and extent of disease than do CT or MRI.CT is used to diagnose, stage renal cell carcinomas and in follow up procedure. CT protocol includes abdominal and pelvic area, non-contrast and with iv contrast. The lesions are soft tissue attenuation between 20-60HU, with areas of necrosis and 1/3 with calcification. Corticomedullary phase 25-60 seconds after administration of contrast, renal cell carcinomas show variable enhancement, usually less than the normal cortex, small lesions may enhance a similar amount and homogeneously, whereas larger lesions have irregular enhancement due to areas of necrosis.The corticomedullary phase is also best for assessing vascular anatomy,tumor thrombus into the venous circulation, the prognosis is significantly worse for those with IVC involvement. The nephrogenic phase (80-160 seconds) is the most accurate for detection of abnormal contrast enhancement.Excretory phases important in assessing the anatomy of possible pathology in the collecting system. CT is diagnostic method used for follow-up imaging after treatment used also for the detection of solid organ metastases. MR

is superior method, excellent at imaging and staging tumors, but is also good in suggesting the likely histology T2 differences, T1 is often heterogeneous due to necrosis, hemorrhage and solid components. T2 appearances depend on histology:clear cell RCC: hyper intense,papillary RCC: hypo intense. MR is also useful for imagining IVC tumor thrombus,the presence of enhancement in the thrombus make the differences between bland and tumor thrombus .The use of diffusion-weighted sequences are important in small renal lesions, which canbe inflammatory or malignant , both showed restricted diffusion, but the restriction is more common with abscess than tumor. Another radiological method for diagnosing renal tumors is intravenous urography, sensitive but not specific, rarely used, toll, compared with CT and MR. Nonmalignant and malignant lesion can be differentiated radiographically, but in some cases surgery is needed for confirmation. Biopsy is recommended when the renal mass may be a metastasis from another known cancer, in cases where tumor has infiltrative instead of a discrete pattern, or sometimes to confirm a diagnosis before chemotherapy for metastases is given.

Information's from radiological methods are important for staging RCC, following TNM (tumor, node, metastasis) system, where the size and extends are classified separate

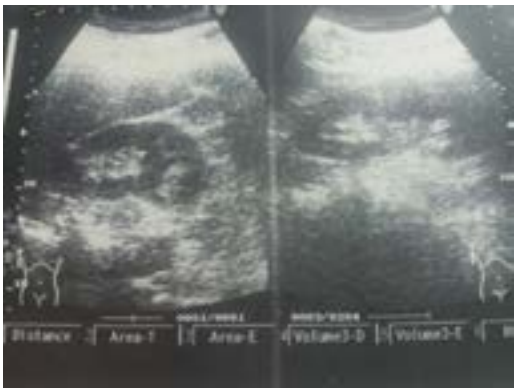


Figure 1:ultrasound,solid mass.

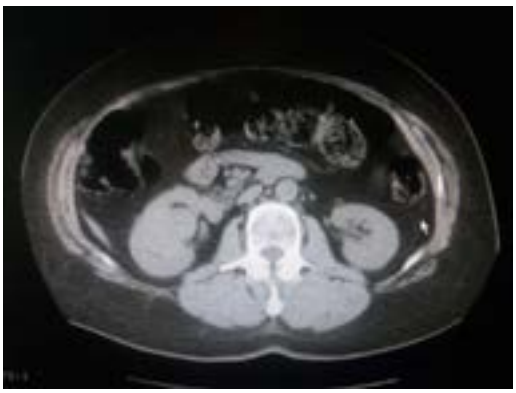


Figure 2:CT native phase

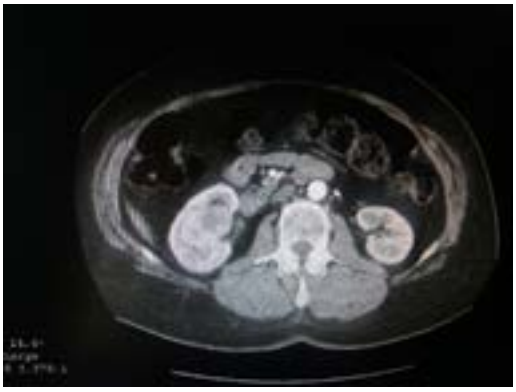


Figure 3:arterial post contrast enhansment

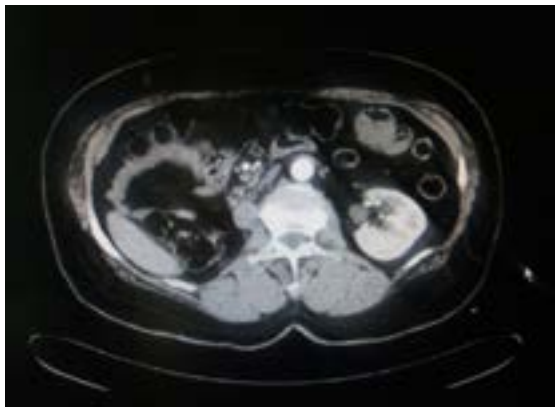
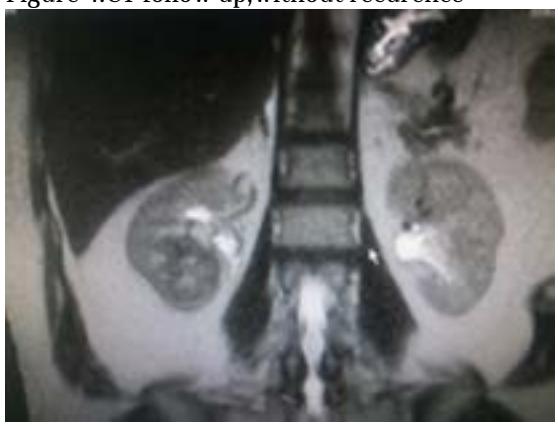


Figure 4:CT follow up,without recurence



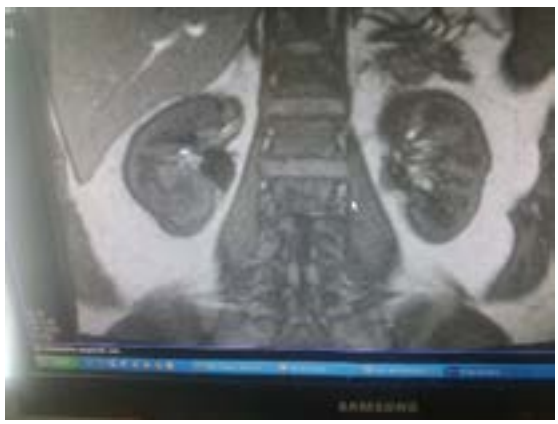


Figure 5 and 6:T1 and T2,standard, coronal,heterogeneous lesion,due to necrosis and hemorage, in the interpolar region of right kidney.

CONCLUSION

The incidence of renal cell carinoma has been increasing. Imaging plays a central role in its detection, staging, and treatment evaluation and follow-up.

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COCHLEAR IMPLANTATION AND VERTIGO- A CASE REPORT

Marija Dokoska[1] , Irena Duma - Vasovska[1] , Marina Davcheva–Chakar[1], Jane Netkovski[1]

[1]University Clinic of Otorhinolaryngology, Medical Faculty –Skopje, R.N. Macedonia

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ABSTRACT

Introduction: Cochlear implantation (CI) is a standard of care for the patients with moderate to severe sensorineural hearing loss in the past more than 20 years. Postoperative vertigo it's one of the well-known complications and has a considerable impact of patient life. Children really suffer from this complication, usually in milder form and almost never long-term vertigo. The aim of presenting this case is to pint out the need to examine the vestibular function in each patient preoperatively. Case report: A 9-year-old child, with recurrent episodes of vertigo appearing for the first time 6 years after the implantation. Vestibular assessment function was done with caloric irrigation bitermal test that showed asymmetry between two labyrinths. Romberg showed deviation on the right side. Haed impuls test was positive on the right side and Dix –Hallpike's maneuver test was negative. There was no neurological signs and symptoms. Every next episode of vertigo was milder than the previous one and he well responded to standard vestibular therapy with Beathistine or Sulpiride. Vertigo did not affect implant performance,

Conclusion: Patients which are candidates for CI it's necessary to be informed about possibility and quality of post-operative vertigo. Implementing a protocol for preoperatively evaluation of the vestibular function of specially designed questionnaires and objective tests for assessment of the vestibular function should be standard procedure for each patient who is candidate for CI.

Key words: cochlear implantation, vertigo, vestibular therapy

INTRODUCTION

The very first beginning of CI as a possible solution of hearing rehabilitation in completely deaf patients dating back to the early 60's of last century and in the last more than 20 years CI has become a standard of care for the patients not only with severe but also with moderate sensorineural hearing loss.

The cochlear and vestibular systems share common anatomical and embryological origin with continuous membranous structure. This close proximity in vascular supply and innervation predisposes them to same noxious or developmental factors. Thus prenatal, perinatal, or postnatal injury and trauma may cause damage and affect one or both systems.

Although it's a reliable and safe procedure postoperative vertigo it's one of the well - known complications after cochlear implantation. Even it's not a live treating, postoperative vertigo has a considerable impact of patient quality of life. Therefore,in time when the indications for CI are significantly expanded and we have wide use and application of cochlear implant as well as implementing the bilateral implantation as a standard concept especially in children it is already becoming very important to understand, critically analyze and evaluate the risk of CI-induced vestibular impairment.

Published data regarding the incidence of post-operative vertigo varies widely and usually ranges between 30-60% (1-4). Postoperative vertigo it's more common in adults, especially in one who have a history of preoperative balance disorders and long lasting deafness. A review of the available literature also shows that patients undergoing cochleostomy have a significantly higher risk of postoperative vertigo compared with RW approach (1,7). Interestingly, children really suffer from this complication andit's usually in milder form thanin adults.

The postoperative vertigo may be result of the traumatic labyrinth damage during electrode insertion, intraoperative perilymph loss–gusher, foreign body reaction with labirynthitis, endolymphatic hydrops,

electrical co-stimulation of the sacculus-Sound induced vertigo, inflammation induced by the surgical procedure or vibration trauma during cochleostomy- which leads to dislodge the otoconia, introducing of bone dust into the labyrinth during the surgery (3,8-10).

The complaints can appear directly after cochlear implantation surgery or after a period of timelike a single attack or multiple episodes with transit occurrence and very rare as a permanent and chronic process. Clinically they are usually presented as unsteadiness, imbalance, instability and disequilibrium or rotatory/ sway vertigo with nausea and vomiting, but also there are forms of positional vertigo (BPPV) or Meniere-type of disorders(11)

CASE PRESENTATION:

A 9-year-old male patient (T.L) with congenital bilateral profound SNHL, implanted on the right at the age of 4, well rehabilitated with developed speech, experienced several recurrent episodes of vertigo, with transient occurrence, six years after the implantation.

First episode occurs on March 2018 and main complains and symptoms were dizziness, nausea and vomiting as well as headache in the occipital region. Also on getting up at the morning he felt "the things are turning around" more pronounced when turning his head from right to left. Vestibular assessment function was done and Caloric vestibular stimulation showed significant asymmetry between irritability of both labyrinths with reduced vestibular response to caloric stimulation of the right side. Standard symptomatic therapy, including Sulpiride (Eglonyl), Beathistine in combination with vitamins (B complex),was prescribed and initial improvement in the condition right after starting the treatment was evidenced. Two weeks later, just day before the scheduled checkup, there is a worsening of the condition and patient complains on intense dizziness, vomiting and headache. Detailed examination was done and no oblique deviation and spontaneous Ny were recorded but when rotating on left in lying position he complained of dizziness. From the vestibular testing on caloric stimulation we got hyporeflexia of the right hSCC. Romberg was positive towards right and on blood testing – mild Leukocytosis was present. The CT scan was clear with implant on place, The patient was detained for hospital treatment and antibiotics and symptomatic therapy (Eglonyl) was prescribed. After significant improvement over the next three days was discharged form hospital with negative Romberg, normal vestibular test results and negative head impulse test .Second episode appears three mount later, after a period of time without any complain there is a new onset of vertigo same as the previous episode. This time patient complains on unpleasant buss and noise first half an hour in the morning after switching on the audio processor and spontaneous nystagmus on left was detected. Vestibular testing showed hyporeflexia of the hSCC bilateral most intense in right side. Control check of the audio processor was fine and fitting was done one again. Standard symptomatic therapy with Betahistine and vitamins(B-complex) was prescribed and complete resolution of the symptoms and normalization of the test was achieved after 5 days. Third and the last episode of vertigo appeared four mounts after but this time in milder form, symptoms lasted only two days and resolved spontaneously. The patient is coming every 6 mounts on routine control and in the last 18 mounts he is free of symptoms.

DISCUSSION

Postoperative vertigo it's one of the well - known and most frequent complications (complaints) after cochlear implantation. It has a considerable impact of patient quality of life and can be a consequence of many causes. The complaints can appear directly after cochlear implantation surgery or after a period of time. From the published data risk of vertigo resulting from CI ranges between 30-60% and it's more common in adults, especially in one who have a history of preoperative balance disorders and long lasting deafness. Children really suffer from this complication which usually occurs in milder form.

CI program in R.N. Macedonia was established 15 years ago and first implantation was done at the University Clinic of Otorhinolaryngology, Medical Faculty, Skopje in 2006 y. So far we have implanted 82 patients (children and adults) and this is the first and only case where postoperative vertigo was reported which means that the Incidence of postoperative vertigo in our group of implanted patients is 1.2%.

Exposing patient to the risk of possible balance disorders associated with CI its justified in view of the hearing rehabilitation achieved. In any case it's necessary to inform the patient about possibility and quality of post-operative vertigo symptoms. Implementing a protocol for preoperative and postoperative evaluation of the vestibular function, which includes specially designed questionnaires and objective tests for assessment of the

vestibular function, should be standard procedure for each patient who is candidate for a cochlear implant. Even if cochlear implant presents minor risk for ipsilateral subjective vestibular affection, it is recommended though to implant the ear with lower vestibular function in unilateral cochlear implantation if all other factors are equal in order to avoid postoperative vestibular loss.

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ЛЕБЕР КОНГЕНИТАЛНА ОПТИЧКА НЕВРОПАТИЈА- ПРИКАЗ НА СЛУЧАЈ

Трпевска Шекеринов Наташа, Иванова Маја, Голубовиќ Милена

Универзитетска клиника за очни болети, Скопје, Р. Северна Македонија

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РЕЗИМЕ

Лебер конгенитална оптичка невропатија (Leber hereditary optic neuropathy-LHON) е хередитарно, неуродегенеративно, митохондријално заболување. Трансмисијата е преку мајката, затоа што болеста е резултат на мутации во гените на митохондријалната ДНА. Претставува многу ретко заболување, со инциденца 1:50 000, повеќе кај мажи и обично на возраст од 10 до 30 години. Дијагнозата се темели врз основа на клиничката слика и генетските истражувања. До сега не е откриен специфичен третман. Идебенон е лек кој овозможува неутрализирање на слободните радикали кои го пореметуваат целиот енергетски метаболизам на клетката, како резултат на нарушување во митохондриите.

Цел на трудот: Презентираме случај, пациент на 44 год. возраст, со прогресивно, безболно, билатерално губење на видот и направени генетски иследувања кои упатуваат на Лебер - оптикопатија. Целта на трудот е да се укаже на ова ретко заболување и да се поттикнат лекарите офталмолози на подетални истражувања, особено кај пациенти со слаба видна острина, која не кореспондира со клиничкиот наод. Иако ретка болест, Лебер оптикопатијата треба да се има предвид во нашите подрачја. Да се потенцира важноста на периметријата како дијагностичка метода и да се насочи вниманието кон невролошките (ВЕП, СЕП) и генетските истражувања во истите случаи.

Клучни зборови: Лебер заболување, оптичка невропатија, наследни заболувања, генски тестирања, Идебенон

ВОВЕД

Лебер конгенитална оптичка невропатија (LHON) се карактеризира со билатерално, безболно, субакутно губење на видот кое обично се јавува кај млади адулти. Мажите имаат четири до пет пати повеќе ризик за разој во однос на жените. (1) Обично пациентите се целосно асимптоматски, се додека не се појави заматување на централниот вид на едното око, а слични симптоми се појавуваат и на другото око во просек два до три месеци подоцна. (1) Според некои автори кај околу 25% од случаите, губитокот на видот може уште во почетокот да е билатерален.(1)

При фундоскопијата често може да се манифестира псеудоедем на дискот и хиперемија, дилатација на артериоли, тортуозни крвни садови и перипапиларна телеангиектазија. Не е исклучено губитокот на видот да биде поврзан и со одредени кардиолошки, скелетни и невролошки промени. (1) Обично почнува на едното око, наеднаш, со значително намалување до 0.05 или помалку за неколку дена, или пак може да се намалува постепено во период од 2-3 месеци. Кај околу 50% од случаите другото око е зафатено симултано, додека кај остатокот видот се намалува во период од 9 месеци подоцна. Преваленцата на LHON не е јасно дефинирана, меѓутоа се проценува дека изнесува 1:50 000. (1)

LHON е класично поврзан со мутации на митохондријалниот основен пар G11778A (гванин до аденин на позиција 11778), T14484C (тирозин до цитозин) и G3460A.

Овие мутации првенствено влијаат на гените на респираторниот ланец I, митохондријалните гени ND1, ND4 и ND6 меѓу другите. (2)

Нарушувањето настанува заради „ point“ (точкасти) мутации во митохондријалната DNK и последователна митохондријална дисфункција. Примарниот тип на клетки кои се губат во LHON се ганглиските клетки

на ретината, кои се многу подложни на нарушеното производство на АТР и на оксидативен стрес.

Наследувањето на LHON го следи патот на митохондријалната генетика, т.е се наследува преку мајката и има многу варијабилен клинички фенотип, бидејќи другите генетски и еколошки фактори исто така играат улога. (3)

Според истражување во Кина, во однос на прогнозата по видната острина покажано е дека кај различните генотипови е различна. Генотипот T14484C има најдобра прогноза, а G11778A генотипот најлоша. Не се покажани релации меѓу генотипот и видната острина на почетокот, разлика во полот и разлика во возраста на јавување. (4)

ПРИКАЗ НА СЛУЧАЈ

Маж на 44 годишна возраст, прв пат се јавува на Клиниката за очни болести во декември 2018 година. Дал податок за постепено губење на видот на двете очи во последните 6-7 месеци, прво на десното, потоа на левото око. Хиперметроп +5.00 Dsph обострано. Видна острина обострано: брои прсти пред око бк/нк. Интраокуларниот притисок (IOP): 17.3 mmHg.

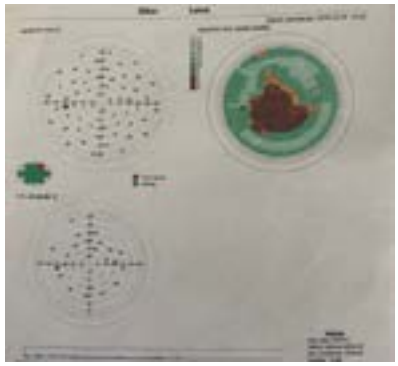
Во јули 2019, надобро корегираната видна острина (BCVA) на десното око е 0.01 (+6.00), и на левото око 0.05 (+6.00). Периметријата покажа обострано присутен централен и парацентрален скотом. (сл.1)

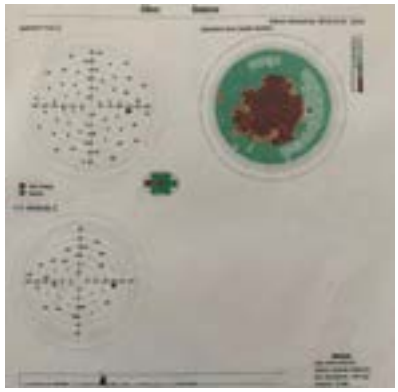
Наодот од оптичка кохерентна томографија (ОСТ) на задниот сегмент на окото, покажува истенчување на слојот на нервни влакна во супериорен и темпорален сектор. Макулата обострано со уреден наод. Слојот на папиларните ретинални нервни влакна (RNFL) со дебелина, на десно (ATT OD) 98 микрометри и лево (ATT OS) 96 микрометри. Макула со дебелина на десно (ATT OD) 262 микрометри и лево (ATT OS) 282 микрометри. (сл. 2,3)

Пациентот е дијабетичар, последните неколку месеци на инсулин.

Топографија на преден сегмент (модел Tomey Casia 2.Ver.3E.2): покажа кератометриски вредности десно, OD: K1: 47.5 и K2: 45.1. Пахиметрија (Pachy) 641 микрометри и лево OS: K1: 47.5, K2: 45.1; Pachy : 632 микрометри.

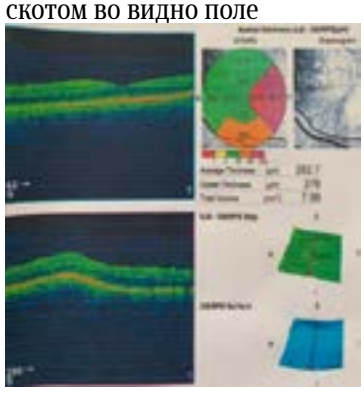
Останатите дополнителни иследувања како компјутеризирана томографија (КТ) и магнетна резонанца (МР) на глава беа уредни.

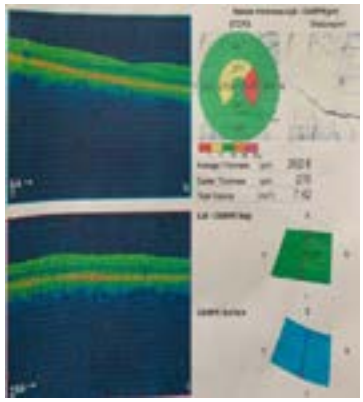




Слика 2: а) периметрија на десно око, централен и парацентрален скотом во видно поле

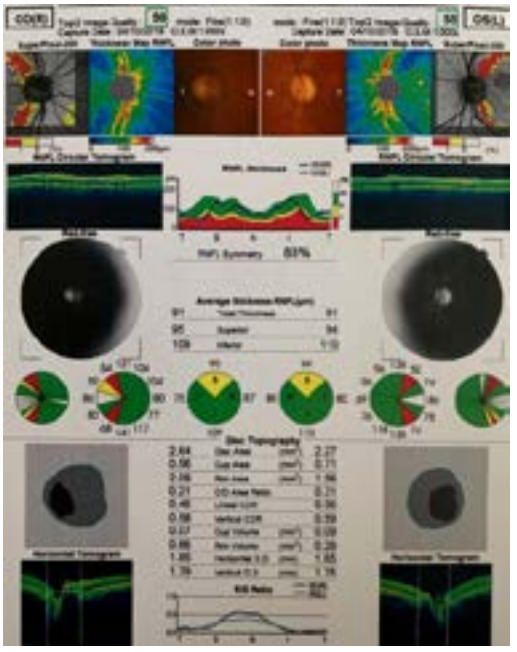
б) периметрија на лево око, централен и парацентрален скотом во видно поле





Сл. 1. а) десно око: ОКТ на макула со лесно истенчени

слоеви б) лево око: ОКТ на макула со лесно истенчени слоеви



Сл. 2 ОКТ на диск, обострано видливо истенчување на RNFL во темпорален сектор

Невролошките иследувања опфаќаа: визуелни евоцирани потенцијали (VEP) на десното око со отсутен одговор; на левото P100 нисковолтиран, пролонгиран, наод кој упатува на дефект во кондукцијата билатерално: и сензорни евоцирани потенцијали (SEP) обострано со уреден наод. MRI на глава со уреден наод.

Како понатамошно иследување беше назначено молекуларно-генетска анализа во Македонска академија на науките и уметностите (МАНУ), во Скопје.

Анализата била направена со метод: изолација на ДНК со фенол-хлороформ екстракција/етанол преципитација и PCR амплификација и ДНК секвенционирање на митохондријалните гени: MT –ND 4 (NP_536852.1), MT-ND1 (NP_536843.1) I MT –ND6 (NP_536854.1). Резултатот покажа присуство на патогена варијанта m.11778G>A; p.Arg340His во MT-ND4 генот, кој ја потврди дијагнозата за Лебер наследна оптичка неуропатија (LHON).

ДИСКУСИЈА

LHON е впрочем првата митохондријална болест прикажана од страна на докторот Албрехт фон Грефе пред повеќе од 150 години, меѓутоа името го добива според докторот Теодор Лебер кој подоцна опишал 15 пациенти со ова заболување во четири различни семејства. Подоцна се докажало дека мутацијата е во митохондријалната ДНА (mtDNA) и дека заради тоа се наследува преку мајката. (5)

Според истражувањата LHON најчесто настанува заради мутацијата m.11778G> A и од овој тип на мутација, според истражувањата, 90% се од Азиска популација и од 50 до 70% од белата раса. Од мутацијата m.14484T> C, 86% се случаи во Квебек, Канада. А од фреквенцијата на m.3460 G>A околу 20% се европски пациенти со LHON. Генските истражувања се насочени кон MT-ND1, MT-ND4, MT-ND6 гените. (6)

Кај повеќе од 90% од дијагностицираните пациенти било откриено присуство на една од трите “missense” мутации: m.11778G>A во MT-ND4 генот, m.14484T>C во MT –ND6 генот, и/или m.3460G>A во MT-ND1 генот, од кои најтешка форма е m.11778G>A, која што се потврди во молекуларната анализа и кај нашиот пациент.

Митохондриите се ситни органели во цитоплазмата на клетката кои имаат сопствена ДНА (mtDNA) со 16 569 парови, 37 гени, кои се пренесуваат од мајката на децата. Мутацијата во гените е со различна пенетрантна способност. Кај некои луѓе болеста воопшто не манифестира симптоми. Доколку мајката која е носител на болеста не манифестира симптоми не може да ја пренесе болеста на детето. Покажано е дека одредени фактори од средината како што е пушењето можат да ја зголемат пентрантноста. (7)

LHON е најчестото митохондријално наследно заболување кое обично се јавува кај млади мажи. Обично се јавува помеѓу 10-30 години. Иако ретко, индивидуи манифестираат LHON и во седмата и осмата деценија од животот. (8) Авторите потенцираат дека мажите имаат четири до пет пати поголема веројатност да бидат заболени од жените, но ниту полот, ниту мутациониот статус не влијаат значително на времето и сериозноста на почетната загуба на видот, како и во презентираниот случај. (8)

Хормоналните разлики помеѓу мажите и жените, влијаат врз доминантноста на мажите во јавувањето на LHON.(9) Се смета дека естрогените хормони кај жените влијаат на митохондријалната дисфункција, вклучително и во неправилната синтеза на ATP, оксидативниот стрес и апоптозата.(9) Студии покажале дека во хибридни мобилни линии кои содржат хомоплазматски LHON мутации, додавање на 17 ɣ-естрадиол доведува до активирање на

митохондријална биогенеза, зголемена активност на супероксид дисмутаза 2 (SOD2), намалено производство на ROS и намалување на апоптозата.(9)

Автори вбројуваат и други инволвирачки фактори како траума на главата, индустриски токсини и лекови кои имаат митохондријална токсичност, како што се препарати за ретровируси и етамбутол. (10) Нутриционистичките недостатоци исто така се вклучени како можни причинители за губиток на видот кај LHON, потенцирајќи го ниското ниво на витаминот Б12. (11)

Митохондриите како клеточни органели ја произведуваат потребната енергија за функционирање на клетките преку процес наречен „клеточно дишење“ за кој е потребен кислород и каде се произведува енергија. За време на клеточното дишење, некои токсични форми на кислород може да се произведат (наречени слободни радикали); кои мора да бидат неутрализирани од други супстанции за да се избегне оштетување на клетките.

Кај LHON примарно се афектираат ретиналните ганглиски клетки, кои се подложни на нарушувањето на продукцијата на ATP и оксидативниот стрес. Наследувањето на LHON е во корелација со митохондријалната генетика и има многу варијабилни клинички фенотипови, бидејќи и други генетски и надворешни фактори исто така играат улога.

OCT овозможува реална слика на ретиналното ткиво во моментот на иследувањето.

Во акутната фаза, задебелувањето на ретиналните нервни влакна (RNFL) започнува најпрво во темпоралниот и инфериорните квадрант, потоа во супериорниот и назалниот. (12) Тоа се должи на раното инволвирање на ретиналните ганглиски клетки во папиломакуларниот сноп, а задебелување на RNFL е последователен на едемот резултат пак на нарушена митохондријална функција и аксонски транспорт. (13) RNFL потоа се истенчува во тек на хроничната фаза после месеци од почетокот на губитокот на видот. (14)

Повеќе детални иследувања покажале дека може да дојде и до суптилно нарушување на функцијата на оптичкиот нерв, вклучувајќи ги губитокот на видот, нарушување на колорниот вид, намалена чувствителност во контрастот, субнормален електроретинограм и визуелно евоцирани потенцијали. (15) Тешко е да се направи разлика помеѓу LHON и оптичката атрофија секундарна од други причини, како што е предната исхемична оптичка невропатија или глауком кај постарите лица, дури и ако постои јасна семејна историја на LHON. (15)

Кај повеќе пациенти со LHON, губитокот на видот обично е комплетен и траен, со видна острина обично полоша од 20/200 на двете очи, како и во случајот кој го презентираме (16)

Повраток на видот може да се случи по акутното губење, и понекогаш да се манифестира како „фенестрација“ најчесто како дефект во видното поле или со поголема регресија на централната видна острина и боја, обично билатерално. (17) Студии прикажуваат дека регресијата во видот обично се случува полека, меѓу 6 и 12 месеци од почетокот, но сепак, ненадејно драматично подобрување може да се случи многу години по почетокот на симптомите. (17)

Магнетната резонанца на мозокот и орбитите обично се нормални кај пациенти со LHON, што повторно се потврдува во нашиот случај. (17) Сепак има прикажани случаи со неспецифичен пролонгиран сигнал ретробулбарно на T2 сигналот, во краток период после губитокот на видот или со лезии на белата маса. (18)

Во одредени случаи, пациенти со LHON демонстрирале подобрување на оптичкиот нерв на постконтрасните слики, што укажува дека може да има воспалителна компонента во патогенезата на LHON (18). Визуелните евоцирани потенцијали (VEPs) и електроетиограмот (ERG) обично се абнормални кај пациентите со LHON, впрочем тие рефлектираат дегенерација на оптички нервни влакна и губиток на ретиналните ганглиски клетки (RGC).

Во нашата студија се потврди патолошки VEP наод обострано, на десно отсутен одговор, а лево P100 бранот изразито ниско волтиран, до аплатиран со изразито пролонгирана латенца-наод кој упатува на дефект во кондукцијата на визуелните патишта билатерално.

Во студијата на Dorfman и сор. се прикажуваат двајца браќа заболени со LHON со нормални VEP латенции и конфигурации пред почетокот на симптомите, и рани абнормалности кои вклучуваат продолжена VEP латентност и абнормална морфологија на VEP, односно со прогресија на симптомите, имало и прогресивно пролонгирање на латенцата на VEP. (19)

Друга студија прикажува дека пациенти со LHON имаат зголемена латентност на VEP и намалена амплитуда,

што е поврзано со намалена амплитуда на моделот на ERG N50-N95. (20) Секако се потврдува дека VEP и ERG се неопходни во дијагностицирање и следење на напредокот на болеста кај заболените пациенти со LHON.

Останати чести невролошки карактеристики поврзани со LHON се невролошки абнормалности како постурален тремор, периферна невропатија, неспецифична миопатија, нарушувања на движењето и синдром Леј. (20)

Некои лица со LHON, обично жени, можат да развијат прогресивно мултиплекс склероза (MS). Губитокот на видот во тој случај LHON-MS се јавува поинаку од класичниот LHON, обележан со повторливи епизоди на губиток на видот кои можат да бидат поврзани со окуларна болка, но со некомплетен повраток на видот и прогресија на слепилото кај речиси половина од сите засегнати лица (21) Имено, покрај сериозната билатерална оптичка невропатија, овие лица манифестираат дисеминирана демиелинација на централниот нервен систем, со карактеристични перивентрикуларни лезии на белата маса. (22)

Третмани кои моментално се испитуваат и ветуваат позитивен ефект ги вклучуваат аналозите на убиквинон, како што е идебенон, потоа генската терапија и матични клетки со цел да се поврати синтезата на АТР и да се обезбеди невропротекција на преживеаните ретиналните ганглиски клетки.

Идебенон се очекува да дејствува како неутрализатор на овие токсични форми на кислород и да има антиоксидантно дејство и, следствено, да спречи оштетување на клетките. (23)

Во лекувањето на LHON во истражување е и генската терапија. Бидејќи е тешко да се внесе ген директно во митохондријалниот геном, заради двојната мембрана, истражувачите пронашле нова техника алотопична експресија со трансфекција на посакуваниот ген во нуклеарниот геном. Новосоздадениот ,,див,, протеин е создаден со специфичен митохондријален таргет и така е импортиран во митохондријата. Понатаму е трансфектиран во нуклеусот како адено асоциран вирус (AAV) вектор. Еден од првите обиди на хибридни клетки, на мутацијата 11778 на ND4, покажано е подобрување во синтезата на АТП. Друг од гените што е алотопотски изразен во клетките со мутација на 11778 во генот SOD2, прави детоксикација на слободните радикали во митохондриите. (13)

Заклучок

LHON спаѓа во групата на ретки болести. Од посебно значење е да се зголеми свесноста кај офталмолозите за негова навремена детекција. Всушност секогаш кога постои неусогласеност меѓу клиничкиот наод и видната острина неопходно е да направат неврофизиолошки, како и генетски иследувања.

Управувањето со засегнатите лица со LHON подразбира пред се поддршка, како и обезбедување на визуелни помагала, помош при професионална рехабилитација и помош при релевантните социјални услуги.

Неопходен е и мултидисциплинарен пристап заедно со невролозите, кај пациентите со екстраокуларни невролошки карактеристики со цел да се минимизираат функционалните последици од дополнителни компликации и да им се овозможи на овие пациенти да функционираат колку што е можно пооптимално во средината.

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PËRDORIMI I OMENTUMIT PËR MBULIMIN E PLAGËS ME VASKULARIZIM TË DËMTUAR NGA RREZATIMI I HEMITORAKSIT TË MAJTË - RAPORTIM RASTI

Artan Dika, Gjorgje Xhokiq, Natasha Dosevska, Ermira Bexheti

Klinika universitare e Kirurgjisë plastike dhe rekonsktruktive – Shkup, Spitali i përgjithshëm "8 shtatori" – Shkup, Spitali klinik – Tetovë

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ABSTRAKTI

HYRJE: Megjithë lokalizimin brenda kavitetit të barkut, omentumi i madh përbën një strukturë që mund të përdoret për rekonstruksionin e pjesëve tjera të trupit, në radhë të parë murit të krahërorit. Ai mund të përdoret si lembo e pedunkular apo si lembo e lirë. Në literaturën në Maqedoni nuk ka të dhëna për raste të tjera të përdorimit të omentumit për mbulimin e plagëve të ndryshme.

RAPORTIM RASTI: Pacientja 63 vjeçare u operua në klinikën tonë për shkak të një formacion ulcerativonekrotik te gjirit të majtë, 25 vite pas operacionit për heqjen e karcinomës së gjirit të majtë shoqëruar me radioterapi postoperative. Biopsitë e bërë përjashtojnë recidivën e kancerit. Pasi herën e parë dështon mbulimi i plagës me lembo kutane, e cila nekrotizoi në pjesën e sipërme, në operacionin e dytë bëhet mbulimi me lembo të pedunkuluar të omentumit të madh. Omentumi u transpozua në toraks përmes një tuneli të vogël në murin e barkut dhe për mbulimin e tij u përdor transplant kutan me trashësi të pjesëshme. Shërimi kaloi pa probleme.

DISKUTIMI DHE PËRFUNDIMI: Mbulimi i plagëve të murit të krahërorit mund të bëhet në shumë mënyra. Omentumi i madh është një nga opsionet që duhet të merren në konsideratë për mbulimin e plagëve të kafazit të kraharorit, sidomos në rastet kur bëhet fjalë për inde me vaskularizim të dëmtuar dhe fibrozë të shprehur, ku mundësia e përdorimit të indeve lokale apo atyre fqinje është e kufizuar.

FJALËT KYÇE: omentumi, lembo, krahërori, mbulim plage.

HYRJE

Omentumi i madh përbën një palosje të peritoneumit të mbushur me ind fibroz, dhjamor dhe limfatik. Ai mbahet i lidhur me kolonin transvers, stomakun, dhe pjesën fillestare të duodenit dhe furnizohet me gjak nga arteria gastroepiploike e djathtë dhe e majtë, të cilat krijojnë pastaj një rrjet të zhvilluar që i japin omentumit vaskularizim të shprehur. Omentumi i madh njihet ndryshe edhe si polici i barkut. Ai përbën një strukturë që mund të përdoret në shumë raste për rekonstruksionin e defekteve indore dhe mbylljen e plagëve të ndryshme. Omentumi mund të përdoret si lembo e pedunkuluar për mbulimin e defekteve indore më në afërsi, duke e ruajtur lidhje dhe vaskularizimin origjinal ose si lembo e lirë për të mbuluar defekte indore në largësi, duke bërë anastomozimin e enëve të gjakut të omentumit me enët e gjakut afër zonës marrëse. Lemboja e parë e lirë është realizuar me omentumin e madh në vitin 1972 nga Buncke dhe McLean për të mbuluar një defekt të madh të skalpit me ekspozim të kockës. Në literaturën vendore nuk kemi hasur deri tani publikime të rasteve ku omentumi është përdorur për lembo në kirurgjinë plastike dhe rekonstruktive.

RAPORTIM RASTI

Pacientja 63 vjeçe paraqitet në klinikën tonë për shkak të një plage të madhe ulceronekrotike në gjirin e majtë (Foto 1). Pacientja referon se rreth 25 vjet më parë është operuar për shkak të karcinomës në gjirin e majtë dhe pas operacionit i është nënshtruar rrezatimit të shprehur të kësaj zone. Vet gjiri i majtë paraqitet si një strukturë e fortë fibrotike. Fillimisht u mor biopsi nga zona nekrotiko-

ulcerative dhe u dërgua për verifikim histopatologjik për të përjashtuar praninë e recidivës së kancerit të gjirit. Rezultati histopatologjik tregoi për inflamacion kronik ulcerative pa prani të qelizave malinje. Si në ekzaminimin fizik të pacientes ashtu edhe në rezonancën magnetike rezultoi atrofi e theksuar e muskulit latisimus dorsi dhe strukturave fqinje gjë që e bëri të pamundur rekonstruksionin e plagës me këtë muskul. Pas kompletimit me analizat e nevojshme pacientja iu nënshtrua intervenimit kirurgjik me antestezion të përgjithshëm. Në intervenimin e parë, pas heqjes së plotë të indeve nekrotike dhe pjesëve tjera pa vaskularizim të mirë (Foto 2), fillimisht u bë mbulimi i plagës me lembo të madhe kutane torakabdominale.

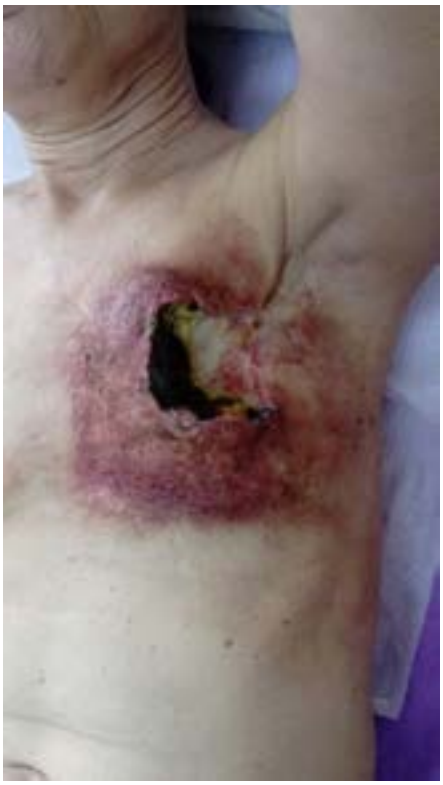

Foto 1

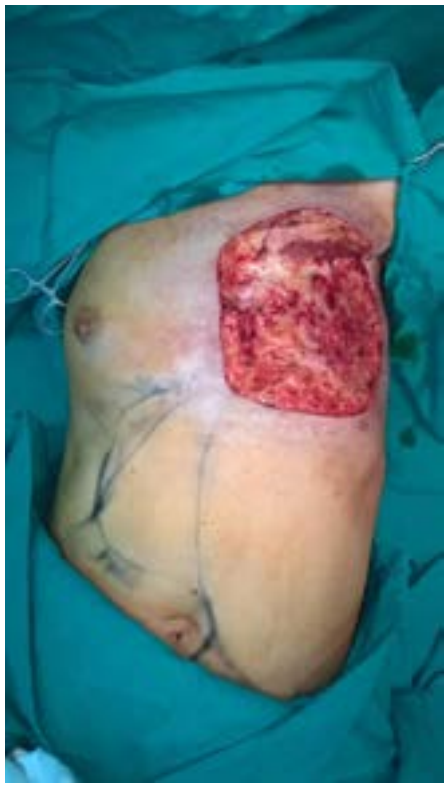

Foto 2

I gjithë materiali i hequr u dërguar për ekzaminim histopatologjik. Rezultati dëshmoi sërish për mungesë të qelizave malinje dhe prani të ulcerës trofike të gjirit me osteonekrozë. Fatkeqësisht mbulimi i plagës me lembo kutane dështoi për shkak të nekrozës në pjesën e sipërme të lembos, e cila mbulonte plagën e mbetur pas heqjes së gjirit të majtë, i cili ishte shëndërruar në një formacion fibronekrotike. Kjo shtroi nevojën për një intervenim të dytë. Meqë kishim të bëjmë me një regjioni me fibrozë të gjerë me pjesë edhe me osteonekrozë, si pasojë e rrezatimit të mëhershëm, u vendos që mbulimi i plagës të bëhet me lembo të omentum majus, si një zgjidhje më praktike e problemit në rastin konkret. Fillimisht u hap kaviteti peritoneal me laparotomi mediane. U bë identifikimi i omenumit të madh dhe mobilizimi i tij duke e ndarë atë nga koloni transvers. Më pas u kalua në përgatitjen e lembos së omentum majus duke e liruar pjesën e tij të majtë, ndërkohë që u ruajt vaskularizimi nga ana e djathtë e omentumit. Në rastin konkret kishim të bëjmë me paciente me konstrukt të dobët me omentum të hollë e jo të zhvilluar (Foto 3).

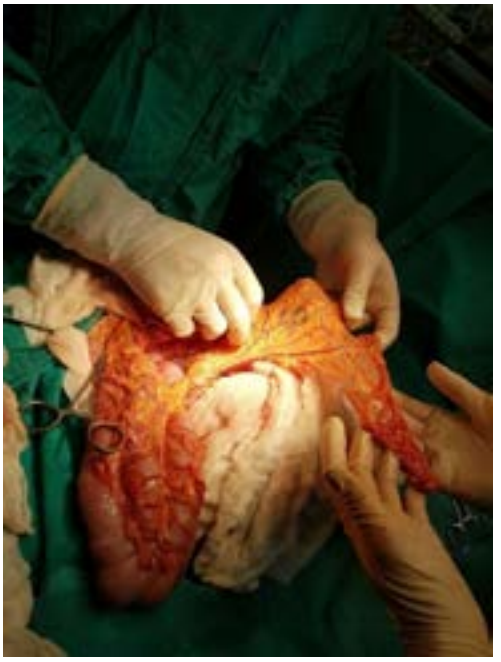

Foto 3

Megjithatë, pas provës nëse lemboja arrin të defektin e hemitoraksit të majtë rezultoi se materiali ishte i mjaftueshëm për të arritur dhe mbuluar plagën e hapur në tërësi (Foto 4). Plani ishte që lemboja të jetë e pedunkuluar duke e ruajtur vaskularizimin nga ateria gastroepiploike e djathtë, duke e nxjerrë lembon omentale përmes një tuneli të vogël në murin e sipërm të barkut. Më tej u bë fiksimi i lembos në pjesët anësore të plagës së hapur, të cilat paraprakisht u rifreskuan.

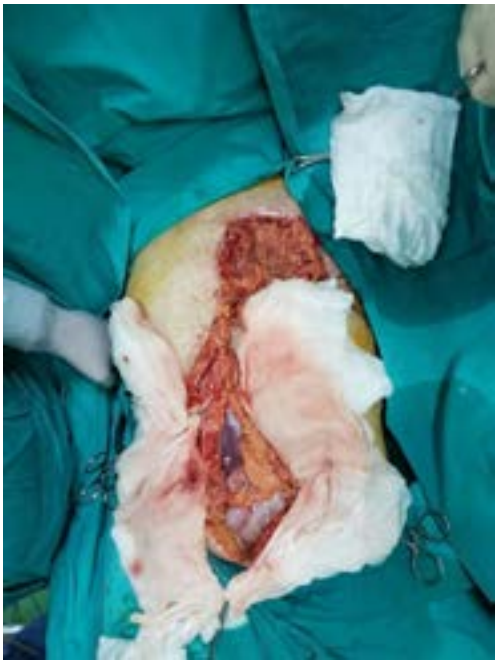

Foto 4

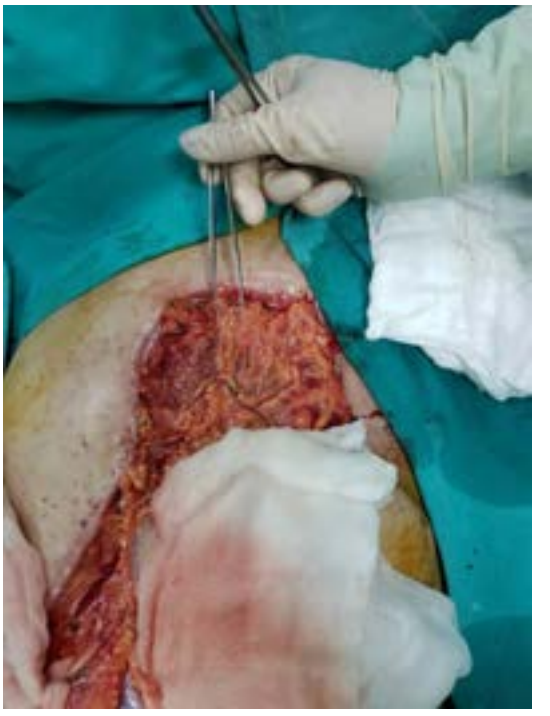

Foto 5

Fiksimi i lembos u bë me disa qepje me vikryl 3.0 (Foto 5). Mbyllja e laparotomisë, me përjashtim të tunelit rreth 3 cm përmes të cilit kalon omentumi për në murin e gjoksit, u realizua me sutura të veçanta të paabsorbueshme polipropileni 0, ndërsa mbi lembon e omentumit që mbulon plagën në gjysmëkrahërorin e majtë u vendos transplant lëkure me trashësi të pjesshme. Ecuria postoperatore ishte e mirë dhe shërimi i plagës nuk pati komplikime (Foto 6).

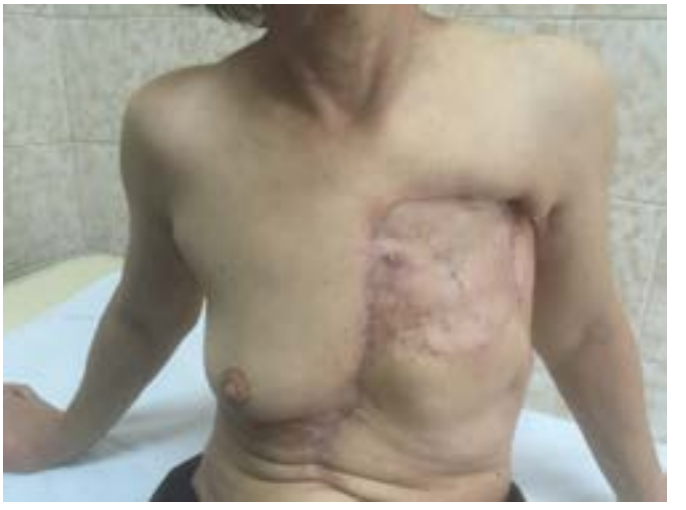

Foto 6

DISKUTIM

Defektet e murit të krahërorit mund të mbulohen me lembo

të ndryshme lokale apo në distancë, të pedunkuluara apo të lira, kutane apo muskulokutane. Në rastet si ky i yni me rrezatim të shprehur dhe me ndryshime fibro-nekrotike e osteonekrozë të indeve të murit të gjoksit përdorimi i lembove kutane apo muskulokutane është me prognozë të rezervuar. Vaskularizimi i shprehur i omentumit të madh nga dy arteriet gastroepiploike e bënë atë të përshtatshëm për mbulimin e plagëve të tilla, sidomos pas rrezatimit apo edhe në raste të nekrozave me natyrë të ndryshme. Në raste me defekte të të gjithë trashësisë së murit torakal mund të lind nevoja e vendosjes së rrjetës. Përparësitë e përdorimit të omentumit si lembo përfshijnë lehtësinë e ngritjes së lembos, furnizimin e mirë me gjak të saj, sipërfaqen e madhe, mundësinë për të mbuluar plagë në pjesë të ndryshme të trupit, qoftë si lembo e pedunkuluar apo e lirë, etj. Kundërindkacionet për përdorimin e omentumit si lembo përfshijnë rezeksionet e mëhershme kirurgjike të tij apo praninë e karcinomave ose metastaza në omentum. Kujdes duhet patur në rastet me adhezione të organeve të barkut nga operacionet e mëhershme si dhe në pacientët e dobët ku përmasat e omentumit mund të jenë të pamjaftueshme. Komplikimet përfshijnë humbjen e pjesshme apo të plotë të lembos nga komplikimet vaskulare, dehisciencën, seromat, hematomat, absceset, herniet e murit të barkut, obstruksionin e stomakut dhe ileusin.

Si PËRFUNDIM mund të thuhet se megjithë nevojën për hapjen e kavitetit peritoneal dhe të ndonjë disavantazhi tjetër, me përparësitë e saj të tjera kjo lembo mund të jetë një opsion i vlefshëm për zgjidhjen e rasteve recidivuese dhe shumë të komplikuar të defekteve postoperatore, por për këtë është e nevojshme edhe njohja e mirë e anatomisë kirurgjikale të kësaj zone dhe përvoja e ekipit kirurgjikal.

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2. Metodat & Materialet: Ky paragraf duhet të përfshijë atë informacion që ishte në dispozicion në kohën që plani apo protokoli i studimit po shkruhej. Të gjitha informacionet e marra gjatë studimit i takojnë paragrafit të Rezultateve.

Përshkruani përzgjedhjen tuaj të pjesëmarrësve së vrojtimit ose eksperimentit (pacientët ose kafshët laboratorike, përfshirë kontrollat) qartë, duke përfshirë kriteret e përshtatshme (inkluzive) dhe përjashtuese (ekskluzive).

Parimi udhëheqës duhet të jetë i qartë se si dhe pse studimi është bërë në një mënyrë të caktuar. Jepni detaje të mjaftueshme për metodat, mjetet dhe materialet (jepni emrin dhe adresën e prodhuesit në kllapa), dhe procedurat për të lejuar të tjerët të kuptojnë dhe riprodhojnë rezultatet tuaja.

Nëse një metodë e caktuar që është përdorur është e njohur, atëherë nuk është e nevojshme të jepet përshkrim komplet i saj. Mund t'i referoheni punimit në të cilin së pari herë është përshkruar dhe të

Additional Information for Authors

I. First page - *front page*: It should contain: (a) title of paper, a short, but informative; (b) the first name, initials of middle name and last name of each author; (c) the institution; (d) the name of the department that is attributable to the scientific work; (e) the name and address of the author with whom to correspond about the manuscript (f) source/support in the form of grants, equipment, drugs, or all.

II. Second page - *abstract and keywords*: The abstract should be written with a maximum of 150 words for unstructured abstracts and 250 words for structured abstracts (containing parts: objective(s) of study or research, basic procedures, such as selection of subjects or laboratory animals, observational and analytical methods, then, the main findings/results (data and their statistical significance, if possible), and the main conclusions. Emphasize the new and important aspects of the study or observation.

Below the abstract identify and write the keywords: 35 words or short phrases that will assist in indexing the paper and publication of the abstract.

Use terms from the list of Index Medicus for Medical Sub-Headings (MeSH); if there is no appropriate MeSH term for some newly introduced terms, we can use the given terms.

III. Third and further pages – *full text of the article*: The full text of research or observational articles should normally be, but not necessarily, divided into sections with the following headings: introduction, material and methods, results and discussion.

1. Introduction: Provide a context or background for the study (that is, the nature of the problem and its significance). To do this you must complete a literature review – searching for, finding and reading relevant papers, which must be referenced in your manuscript. Explain your hypotheses and the plan to test them, and describe your aims. Clearly state what you expect to find and the reasoning that led you to the hypotheses that you have made. The research objective is often more sharply focused when stated as a question. Do not include data or conclusions from the work being reported.

2. Methods & Material: This section should include only information that was available at the time the plan or protocol for the study was being written. All information obtained during the study belongs in the Results section.

Describe your selection of the observational or experimental participants (patients or laboratory animals, including controls) clearly, including eligibility and exclusion criteria.The guiding principle should be clarity about how and why a study was done in a particular way.

Give sufficient details of the methods, apparatus and materials (give the manufacturer's name and address in parentheses), and procedures to allow others to understand and reproduce your results.

If a particular method used is well known then there is no need to give a complete description. You can reference the paper in

përmendni ndonjë modifikim/ndryshim që keni bërë. Jepni arsyet për përdorimin e tyre dhe vlerësoni kufizimet e tyre. Në fund, përshkruani se si i keni analizuar të dhënat tuaja, duke përfshirë metodat statistikore dhe pakon programore që keni përdorur.

Autorët e doreshkrimeve të rishqyrtuara duhet të përfshijnë një paragraf që përshkruajnë metodat që kanë përdorur për lokalizimin, përzgjedhjen, ekstrahimin dhe sintetizimin e të dhënave. Përdorni formën joveprore të foljes, në vetën e tretë, kur dokumentoni metodat, gjë që do të fokusonte vëmendjen e lexuesit tek puna që është bërë e jo tek hulumtuesi (P.sh. Janë marrë, janë realizuar, janë prezantuar etj.)

2. a) Statistikat: Përshkruani metodat statistikore me detaje të mjaftueshme për t'ia mundësuar një lexuesi me njohje në atë fushë t'i qaset të dhënave origjinale për të verifikuar rezultatet e raportuara. Kur është e mundur, përcaktoni sasinë e zbulimeve dhe prezantoni ato me indikatorë përkatës të gabimeve në matje apo pasiguri (siç janë inter-valet e besueshmërisë). Evitoni mbështetjen vetëm në testet statistikore të hipotezave, siç janë vlerat p, që dështojnë të transmetojnë informacion të rëndësishëm mbi madhësinë e efektit. Jepni detaje rreth përzgjedhjes së rasteve (randomizimi) dhe përshkruani metodat dhe sukseset e vro¬jtimit gjatë realizimit të studimeve të verbuara. Definoni termet statis¬tikore, shkurtesat dhe më së shumti simbolet. Specifikoni programin kompjuterik që është përdorur.

3. Rezultatet: Ky paragraf duhet t'i bëjë gjetjet tuaja të qarta. Prezantoni rezultatet tuaja në rend logjik në tekst, tabela dhe ilustrime, duke dhënë së pari rezultatet kryesore ose më të rëndësishme. Mos i përsërisni të gjitha të dhënat në tabela apo ilustrime, në tekst. Nënvizoni ose përm-bledhni shkurtimisht vetëm vrojtimet më të rëndësishme.

Kur të dhënat përmblidhen në paragrafin e Rezultateve, jepni rezultate numerike jo vetëm si derivate (për shembull, përqindja) por gjithashtu si numra absolut nga të cilët derivatet janë llogaritur, dhe specifikoni metodat statistikore që janë përdorur për t'i analizuar ato.

Kufizoni tabelat dhe figurat në aq sa janë të nevojshme për të sqaruar argumentin e punimit dhe për të vlerësuar të dhënat ndihmëse. Duke përdorur grafikonet për të reprezentuar të dhënat tuaja si alternativë e tabelave, do të rrisë kuptueshmërinë e lexuesit. Mos i dyfishoni të dhënat në grafikone dhe tabela. Duhet të jeni të qartë se cili lloj i grafikoneve është i përshtatshëm për informacionet tuaja. Për shembull, për të reprezentuar korelimin mes dy ndryshoreve, preferohet grafiku vijëzor, krahasuar me grafikun rrethor apo në formë shtyllash.

Sa i përket të gjitha paragrafeve, qartësia dhe të qënit i thuktë është kyçe. Mos prezantoni të njëjtat të dhëna më shumë se një herë. Kufizojeni veten në të dhënat që ndihmojnë në adresimin e hipotezave tuaja. Kjo është e rëndësishme edhe nëse të dhënat i aprovojnë ose nuk i pranojnë ato. Nëse keni bërë analiza statistikore, duhet të jepni vlerën e proba¬bilitetit (p) dhe të tregoni se është shprehës (sinjig në nivelin që ju po testoni. Varësisht nga analizat e përdorura, gjithashtu mund të jetë e rëndësishme të jepni intervalet e besueshmërisë së rezultateve (Confidence Interval –

which it was first described and mentioned any modifications you have made. Give the reasons for using them, and evaluate their limitations. Finally,, describe how you analysed your data, including the statistical methods and software package used.

Authors submitting review manuscripts should include a section describing the methods used for locating, selecting, extracting, and synthesizing data.

Use the third person passive voice when documenting methods which would focus the readers' attention on the work rather than the investigator.(e.g. Were taken, was performed, were presented itd.)

2. a) Statistics: Describe statistical methods with enough detail to enable a knowledgeable reader with access to the original data to verify the reported results. When possible, quantify findings and present them with appropriate indicators of measurement error or uncertainty (such as confidence intervals). Avoid relying solely on statistical hypothesis testing, such as p values, which fail to convey important information about effect size. Give details about the randomization and describe the methods and success of observations while using blinded trials. Define statistical terms, abbreviations, and most symbols. Specify the computer software used.

3. Results: This section should make your findings clear. Present your results in logical sequence in the text, tables, and illustrations, giving the main or most important findings first. Do not repeat all the data in the tables or illustrations in the text. Emphasize or summarize only the most important observations.

When data are summarized in the Results section, give numeric results not only as derivatives (for example, percentages) but also as the absolute numbers from which the derivatives were calculated, and specify the statistical methods used to analyze them.

Restrict tables and figures to those needed to explain the argument of the paper and to assess supporting data. Using graphs to represent your data as an alternative to tables will improve the reader's understanding. Do not duplicate data in graphs and tables. You need to be clear what type of graphs is suitable for your information. For example, to represent the correlation between two variables, a line graph is preferred to a pie chart or a bar chart.

As with all sections, clarity and conciseness is vital. Don't present the same data more than once. Restrict yourself to the data that helps to address your hypotheses. This is important whether the data supports or disproves them. If you have carried out a statistical analysis, you should give the probability (P) value and state it is significant at the level you are testing. Depending on the analysis used, it may also be important to give the confidence intervals of the results, or the statistical parameters such as the odds ratios. Provide a caption for each figure making the gen¬eral meaning clear without reference to the main text, but don't discuss the results. Let the readers decide for themselves what they think of the data. Your chance to say what you think comes next, in the discussion.

3. Tables: Each table should be inserted at the point of the text where they have to be placed logically, typed by the same rules

CI), ose parametrat statistikorë si proporcionet e rastit (odds ratio). Bëni përshkrimin tek secila figurë duke bërë të qartë domethënien e përgjithshme pa referencë në tekstin kryesorë, por mos diskutoni rezultatet në të. Lëreni lexuesin të vendosë vetë se çfarë men-don për të dhënat. Mundësia juaj për të thënë se çfarë mendoni, është në vazhdim, tek diskutimi.

3. Tabelat: Secila tabelë duhet të vendoset në vendin e tekstit ku duhet të vihet logjikisht, e plotësuar me të njëjtat rregulla sikur teksti i plotë. Mos i dërgoni tabelat si fotografi. Secila tabelë duhet të citohet në tekst. Tabelat duhet të jenë me numra ashtu që të jenë në koordinim me refer-encat e cituara në tekst. Shkruani një përshkrim të shkurtë të tabelës nën titullin. Çdo sqarim shtesë, legjendë ose sqarim i shkurtesave jostan¬darde, duhet të vendoset menjëherë poshtë tabelës.

4. Diskutimi: Ky paragraf është pjesa ku ju mund të interpretoni të dhë-nat tuaja dhe të diskutoni duke ballafaquar dhe krahasuar gjetjet tuaja me ato të hulumtuesve të mëparshëm. Rishikoni referencat e literaturës dhe shihni nëse mund të përfundoni se si të dhënat tuaja përkojnë me atë që keni gjetur.

Ju gjithashtu duhet të llogarisni rezultatet, duke u fokusuar në mekaniz¬mat në prapavij të vrojtimit. Diskutoni nëse rezultatet tuaja mbështesin hipotezat tuaja origjinale. Gjetjet negative janë aq të rëndësishme në zhvillimin e ideve të ardhshme sikur gjetjet pozitive.

E rëndësishme është se, nuk ka rezultate të këqija. Shkenca nuk të bëjë me të drejtën dhe të gabuarën, por merret me zgjerimin e njohjeve të reja.

Diskutoni si janë paraqitur gabimet në studimin tuaj dhe çfarë hapa keni ndërmarrë për të minimizuar ato, kështu duke treguar se ju çmoni ku¬fizimet e punës tuaj dhe fuqinë e përfundimeve tuaja. Duhet gjithashtu të merrni në konsideratë ndërlikimet e gjetjeve për hulumtimet në të ardhmen dhe për praktikën klinike. Lidhni përfundimet me qëllimet e studimit, por evitoni qëndrimet dhe përfundimet e pakualifikuara, që nuk mbështeten në mënyrë adekuate nga të dhënat. Shmangni prioritetet deklarative apo të aludoni në punën që nuk është krahasuar.

5. Referencimi: Referencat janë baza mbi të cilën është ndërtuar raporti juaj. Shqyrtimi i literaturës dhe leximi i referencave gjithmonë duhet të jetë pikë fillestare e projektit tuaj. Ky paragraf duhet të jetë i saktë dhe të përfshijë të gjitha burimet e informacionit që keni përdorur.

Në formatin " Vancouver" , referencat numërohen një nga një, sikur që shfaqen në tekst dhe identifikohen me numra në bibliografi..

Shënoni të gjithë autorët kur janë gjashtë e më pak; kur janë shtatë ose më tepër, shënoni tre të parët, pastaj shtoni "et.al." Pas emrave të autorëve shkruhet titulli i artikullit; emri i revistës i shkurtuar sipas mënyrës së Index Medicus; viti i botimit; numri i vëllimit; dhe numri i faqes së parë dhe të fundit.

Referencat e librave duhet të jepen sipas emrit të autorit, titulli i librit (mund të citohet edhe titulli i kapitullit para titullit), vendi i botimit, botuesi dhe viti.

as for the full text. Do not send tables as photographs. Each table should be cited in the text.Tables should be numbered so that they will be in sequence with references cited in the text. Provide a brief explanation of the table below the title. Any additional explanations, legends or explanations of non¬standard abbreviations, should be placed immediately below the table.

4. Discussion: This section is where you interpret your data and discuss how your findings compare with those of previous researchers. Go over the references of your literature review and see if you can determine how your data fits with what you have found.

You also need to account for the results, focusing on the mechanisms be¬hind the observation. Discuss whether or not your results support your original hypotheses. Negative findings are just as important to the de¬velopment of future ideas as the positive ones.

Importantly, there are not bad results. Science is not about right or wrong but about the continuing development of knowledge.

Discuss how errors may have been introduced into your study and what steps you took to minimise them, thus showing that you appreciate the limitations of your work and the strength of your conclusions. You should also consider the implications of the findings for future research and for clinical practice. Link the conclusions with the goals of the study but avoid unqualified statements and conclusions not adequately supported by the data. Avoid claiming priority or alluding to work that has not been compared.

5. Referencing: The references are the foundation on which your report is built. Literature searches and reading of references should always be the starting point of your project. This section must be accurate and in¬clude all the sources of information you used.

In the Vancouver format, references are numbered consecutively as they appear in the text and are identified in the bibliography by numerals.

List all authors when there are six or fewer; when there are seven or more, list the first three, then add "et al." The authors' namer are fol-lowed by the title of the article; the title of the journal abbreviated ac-cording to the style of Index Medicus; the year of publication; the volume number; and the first and last page numbers.

References to books should give the names of any editors, place of publication, editor, and year.

In the text, reference numbers are given in superscript. Notice that issue number is omitted if there is continuous pagination through¬out a volume, there is space between volume number and page numbers, page numbers are in elided form (51-4 rather than 51-54) and the name of journal or book is in italics.The following is a sample reference:

Në tekst, numrat e referencave jepen me indeks të sipërm. Vëreni se çështja e numrave neglizhohet nëse ka numërtim të vazhdueshëm përg¬jatë gjithë vëllimit, ka hapësirë mes numrit të vëllimit dhe numrit të faqes, numrat e faqeve janë në këtë formë: 51-4 në vend të 51-54, dhe emri i revistës ose librit është në italic. Në vazhdim është një shembull i referencës:

Artikujt e revistave:

1. Lahita R, Kluger J, Drayer DE, Koffler D, Reidenberg MM. Antibodies to nuclear antigens in patients treated with procainamide or acetylpro¬cainamide. *N Engl J Med* 1979;301:1382-5.
2. Nantulya V, Reich M. The neglected epidemic: road traffic injuries in developing countries. *BMJ* 2002;324: 1139.
3. Murray C, Lopez A. Alternative projections of mortality and disability by cause 1990-2020: global burden of disease study. *Lancet* 1997;349: 1498-504.

Librat dhe tekste tjera:

4. Colson JH, Tamour NJJ. Sports in juries and their treatment. 2nd ed. London: S. Paul, 2006.
5. Department of Health. *National service framework for coronary heart disease*. London: DoH, 2000.

   www.doh.gov.uk/nsf/coronary.htm (accessed 6 Jun 2003).
6. Kamberi A, Kondili A, Goda A, dhe bp; *Udhërrëfyes i shkurtër i Shoqatës Shqiptare të Kardiologjisë për parandalimin e Sëmundjes Aterosklerotike Kardiovaskulare në praktikën klinike*, Tiranë, 2006
7. Azemi M, Shala M, dhe bp. *Pediatria sociale dhe mbrojtja shëndetësore e fëmijëve dhe nënave*. Pediatria, Prishtinë 2010; 9-25

Shmangni përdorimin e abstrakteve si referenca; "të dhëna të papub-likuara" dhe "komunikime personale". Referencat e pranueshme, por ende të papublikuara lejohet të merren, vetëm nëse shënoni se janë "në shtyp".

6. Mirënjohjet: Ju mund të keni dëshirë të falënderoni njerëzit që ju kanë ndihmuar. Këto mund të rangohen prej atyre që ju kanë përkrahur me teknika eksperimentale deri tek ata që ju kanë këshilluar deri në bër¬jen e dorëshkrimit final.

7. Formati i fajllit të të dhënave për **ilustrimet** (**figurat**): JPG

Nëse përdoren fotografitë e pacientëve, qoftë subjekti, qoftë fotografitë e tyre nuk duhet të jenë të identifikuara, ato duhet të shoqërohen me lejen e shkruar nga ta për përdorimin e figurës. Format e lejuara janë në dispozicion nga redaksia.

Nëse fajllet e të dhënave janë shumë të mëdha për t'u dërguar me e-mail, rekomandohet dërgimi me CD në adresën tonë.

8. Legjendat për Ilustrimet (Figurat)

Legjenda e tabelës duhet të vendoset mbi tabelë. Referenca e një tabeleje, e cila është marrë nga ndonjë publikim tjetër, duhet të vendoset poshtë tabelës. (Është përgjegjësi e autorit të sigurojë lejen e ribotimit nga botuesit e atij botimi) Legjenda e figurës duhet të vendoset në fund të faqes. Referenca e figurës e marrë nga ndonjë tjetër publikim vendoset në fund të legjendës. (Leja e ribotimit duhet të sigurohet nga botuesi i këtij botimi).

Journal articles:

1. Lahita R, Kluger J, Drayer DE, Koffler D, Reidenberg MM. Antibodies to nuclear antigens in patients treated with procainamide or acetylpro¬cainamide. *N Engl J Med* 1979;301:1382-5.
2. Nantulya V, Reich M. The neglected epidemic: road traffic injuries in developing countries. *BMJ* 2002;324: 1139.
3. Murray C, Lopez A. Alternative projections of mortality and disability by cause 1990-2020: global burden of disease study. Lancet 1997;349: 1498-504.

Books and other monographs:

4. Colson JH, Tamour NJJ. Sports in juries and their treatment. 2nd ed. London: S. Paul, 2006.
5. Department of Health. *National service framework for coronary heart disease*. London: DoH, 2000.

   www.doh.gov.uk/nsf/coronary.htm (accessed 6 Jun 2003).
6. Osler AG. *Complement: mechanisms and functions*. Englewood Cliffs: Prentice-Hall, 1976.

Avoid using as references abstracts; "unpublished data" and "personal communications". References to accepted but yet unpublished articles are allowed to be made, only if you note "in press".

6. Acknowledgements: You may wish to acknowledge people who have helped you. These can range from those who supported you with exper¬imental techniques to those who read or offered advice on your final manuscript.

7. Data file format for **illustrations** (**figures**): JPG

If photographs of patients are used, either the subjects should not be identifiable or their pictures must be accompanied by written permis-sion to use the figure. Permission forms are available from the Editor.

If data files are too big for transmission as an Email attachment submis¬sion of a CD to our address is recommended.

8. Legends for Illustrations (Figures)

The legend of a table has to be placed above the table. The reference of a table, which has been taken from another publication, must be placed below the table. (It is the author's responsibility to obtain the permission of reproduction from the publishers of the publication.) Figure legends are to be placed at the end of the paper. The reference of a figure taken from another publication stands at the end of the legend. (Permission of reproduction must be obtained from the publishers of this publication).