DOI 10.26724/2079-8334-2022-2-80-24-29
UDC 616.61-008.6-07:[616.12-008.331.1+616.379-008.64]

O.M. Bilovol, I.I. Kniazkova, O.M. Kirienko, N.V. Kuzminova[1], V.O. Golovachova, D.O. Kirienko, L.P. Abramova
Kharkiv National Medical University, Kharkiv
[1]National Pirogov Memorial Medical University, Vinnytsya

FUNCTIONAL CONDITION OF KIDNEYS IN PATIENTS WITH ARTERIAL HYPERTENSION IN COMBINATION WITH TYPE 2 DIABETES MELLITUS

e-mail: sskripka72@gmail.com

The purpose of the study was to clarify the diagnostic significance of neutrophil gelatinase-associated lipocalin and cystatin C in the blood of patients with arterial hypertension and type 2 diabetes mellitus and their correlation with intrarenal hemodynamic parameters. It was installed that in comparison with persons without diabetes in patients with arterial hypertension and type 2 diabetes mellitus at the stage of preclinical kidney damage found a more significant increase in neutrophil gelatinase-associated lipocalin and cystatin C in the blood. This allows us to consider these indicators as diagnostic manifestations of early detection of diabetic nephropathy. It was determined that a significant decrease in the final diastolic arterial blood flow velocities and a significant increase in the resistance index are diagnostic markers of morpho-functional changes in the kidneys during duplex scanning of the renal arteries in patients with arterial hypertension and type 2 diabetes mellitus.

Key words: neutrophil gelatinase-associated lipocalin, cystatin C, duplex scanning of renal arteries, arterial hypertension, type 2 diabetes mellitus

О.М. Біловол, І.І. Князькова, О.М. Кірієнко, Н.В. Кузьмінова[1], В.О. Головачова, Д.О. Кірієнко, Л.П. Абрамова

ФУНКЦІОНАЛЬНИЙ СТАН НИРОК У ПАЦІЄНТІВ З АРТЕРІАЛЬНОЮ ГІПЕРТЕНЗІЄЮ У ПОЄДНАННІ З ЦУКРОВИМ ДІАБЕТОМ 2 ТИПУ

Метою роботи було вивчення діагностичної значущості вмісту ліпокаліну, асоційованого з желатиназою нейтрофілів та цистатину С у крові та їх кореляцію з показниками внутрішньониркової гемодинаміки у пацієнтів з артеріальною гіпертензією та цукровим діабетом 2 типу. Встановлено, що у пацієнтів з артеріальною гіпертензією та цукровим діабетом 2 типу на стадії доклінічного ушкодження нирок при порівнянні з особами без діабету виявлень суттєво більше підвищення вмісту ліпокаліну, асоційованого з желатиназою нейтрофіл та цистатину С у крові, що дозволяє розглядати їх у якості діагностичних показників для раннього виявлення діабетичної нефропатії. Визначено, що значне зниження кінцевої діастолічної швидкостій артеріального кровотоку і значуще підвищення індексу резистентності є діагностичними маркерами морфо-функціональних змін нирок при проведенні дуплексного сканування ниркових артерій у пацієнтів з артеріальною гіпертензією та цукровим діабетом 2 типу.

Ключові слова: ліпокалін, асоційований з желатиназою нейтрофілів, цистатин С, дуплексне сканування ниркових артерій, артеріальна гіпертензія, цукровий діабет 2 типу.

The study is a fragment of the research project: "Development of methods for early diagnosis and drug prevention of fibrosing processes in patients with combined pathology (hypertension and type 2 diabetes mellitus) based on the assessment of cardiohemodynamics and renal function", state registration No. 0120U102062.

Numerous data indicate a high prevalence of arterial hypertension (AH) in patients with type 2 diabetes mellitus (DM-2) [12]. The combination of AH and type DM-2 leads to mutual influence on the course of the disease, the nature and severity of complications, often complicates the diagnosis, determines the features of the choice of drug therapy. It is well known that the combination of AH and type DM-2 is associated with earlier disability of this cohort of patients, increased risk of cardiovascular complications and higher mortality compared to the general population [12]. Hemodynamic disorders together with metabolic deviations in the patients lead to damage to target organs with macro- and microangiopathy. Diabetic nephropathy (DN) is considered to be one of the most severe complications of diabetes, affecting 20 to 40 % of patients [6].

At the present stage one of the important problems of practical medicine is the early diagnosis of DN, when morphological renal changes are reversible, and therapeutic interventions are most effective. It has been determined that in one third of patients with normoalbuminuria, glomerular lesions are histologically determined [5]. In this regard, the search for non-invasive biomarkers that reflect early structural renal changes in the comorbidity of AH and DM-2 diabetes is of particular importance.

Recent studies have shown that renal tubular damage plays an important role in the pathogenesis of DN. It has been determined that a number of molecules expressed by tubular epitheliocytes, in particular, neutrophil gelatinase-associated lipocalin (NGAL), renal damage molecule-1 (KIM-1), etc. reflect the degree of tubulointerstitial damage and fibrosis [8]. The use of these indicators in DM-2 can help detect early kidney damage.

© O.M. Bilovol, I.I. Kniazkova, 2022

Most of the work on the study of early biomarkers of renal damage in DM-2 has been conducted in experimental studies [4]. In the available literature to date, there is virtually no data on the status of markers of tubular and glomerular lesions in comorbidity of AH and DM-2. The use of biomarkers for early detection of tubulointerstitial renal damage in combination with visual imaging of the kidneys (duplex scanning of the renal arteries) can accurately diagnose these changes in the early stages of renal dysfunction, which is a promising direction in patient management.

The purpose of the study was to investigate the diagnostic significance of neutrophil gelatinase-associated lipocalin and cystatin C levels in the blood and their correlation with intrarenal hemodynamic parameters in patients with arterial hypertension and type 2 diabetes mellitus.

Materials and methods. 83 patients (35 men and 48 women) aged 40 to 54 years (mean age was 50.2±4.3 years) were examined. 43 patients (18 men, 25 women, mean age 51.5±3.1 years) had stage II AH, grade 2 and DM-2 of moderate severity, subcompensated (group 1), and 40 patients (17 men and 23 women, mean age 51.3±3.7 years) had stage II AH, without concomitant diabetes (group 2). The control group consisted of 20 healthy individuals (mean age 50.1±2.8 years).

All patients were examined in accordance with the recommendations of the European Society of hypertension and the European Society of Cardiology (ESH/ESC, 2018), The American Diabetes Association (ADA) 2019 and the International Diabetes Federation (IDF) 2018. All respondents were informed and signed an agreement to participate in the study.

Criteria for excluding patients from the study were: type 1 diabetes mellitus, secondary hypertension; myocardial infarction or cerebrovascular disorders less than 12 months old; heart failure III-IV functional class (NYHA); the content of glycosylated hemoglobin (HbA1c)> 8.0 %; retinopathy III-IV degree; stage III diabetic nephropathy; diabetic foot syndrome; clinically significant diseases of the respiratory system, gastrointestinal tract, nervous system, kidneys and blood systems in the acute stage, which require medical treatment or significantly affect the assessment of the studied parameters; malignant and autoimmune diseases.

All patients received antihypertensive therapy (a combination of common classes of drugs: ACE inhibitors, calcium antagonists, and beta-blockers (carvedilol) in moderate doses).

In addition, all patients received rosuvastatin (Sandoz, Slovakia) 20 mg and acetylsalicylic acid (Bayer Pharrma, Germany) 75 mg daily. A combination of metformin (Teva Pharmaceuticals, Slovenia) and gliclazide (Teva Pharmaceuticals, Slovakia) was prescribed to correct blood glucose.

All examined persons underwent a general clinical examination, measurement of office blood pressure, heart rate, determination of fasting serum glucose (GCG), HbA1c levels in whole blood, insulin, lipid profile; insulin resistance was assessed by the HOMA-IP index [1, 13]. The concentration of markers of renal dysfunction: cystatin C (Bio Vendor, Czech Republic) and NGAL (Hycult Biotech, Netherlands) was measured in commercial serum enzyme-linked immunosorbent assays.

Chronic kidney disease (CKD) was determined according to KGIGO 2012. The functional state of the kidneys was assessed by glomerular filtration rate (GFR) using the formula CKD-EPI. Cystatin C was used as a more sensitive and specific biomarker of renal damage.

Duplex scanning of the renal arteries was performed in the distal parts of the main trunk of the renal artery on an ultrasound scanner GE Medical Systems (Germany) convex sensor with a frequency of 2.25–3 MHz and a sensor with a frequency of 1–7 MHz in color Doppler mapping and pulse wave modes. To determine the state of renal hemodynamics, the peak systolic (Vps, cm/s) and final diastolic arterial blood flow velocities (Ved, cm/s) were evaluated. The resistance index was determined by the formula RI=(Vps-Ved)/Vps.

Statistica software package for Windows 10 was used for statistical analysis. All data are presented as mean (M), standard deviation (±SD), median (Me), quartile interval (MCI). To compare the statistical characteristics in different groups, multiple comparisons were used according to the one-factor variance analysis of Kruskal-Wallis (Kruskal-Wallis ANOVA), with steam comparison according to the Mann-Whitney test (Mann-Whitney U Test). The method of correlation analysis with the calculation of Spearman's coefficients was used to analyze the direction and strength of the relationship between certain indicators. Differences were considered significant at values of $p<0.05$.

Research results and their discussion. Clinical data of patients showed no statistical differences between groups by age, sex and body mass index. No significant differences were found between the groups of examined patients in the duration of hypertension and disorders of lipid metabolism. The concentration of urea and creatinine in the blood, GFR did not differ significantly between the two groups of examined patients.

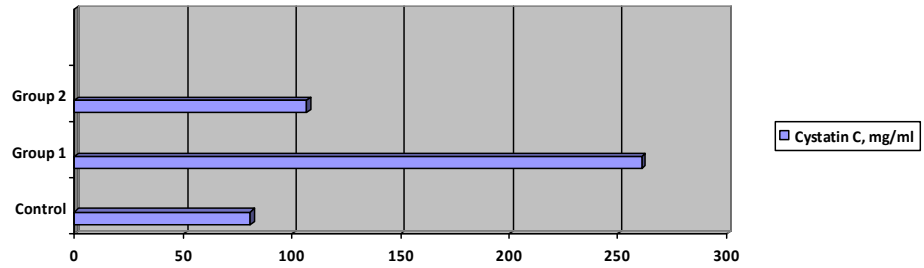

Fig.1. Serum cystatin C concentration (mg/ml) in patients with a combination of AH and DM-2 (group 1), patients with AH (group 2) and the control group.

The content of cystatin C in the blood of the surveyed persons representations in Figure 1.

As shown in Figure 1, in patients with hypertension (group 2) the content of cystatin C in the serum averaged 107.0 [93.12–123.45] mg/ml, which was 32.1 % significantly higher than the values of the control group, in which this indicator was 81.3 [71.63–91.27] mg/ml ($p<0.001$). The maximum value of the level of cystatin C in the serum was observed in patients with DM-2 in combination with AH (group 1), here the level was 261 [247.32–280.43] mg/ml, that was 3.2 times higher than the control group ($p<0.001$). With the comorbidity of diabetes and hypertension (group 1), the content of cystatin C in serum was 2.4 times higher ($p<0.05$) compared with patients with hypertension (group 2).

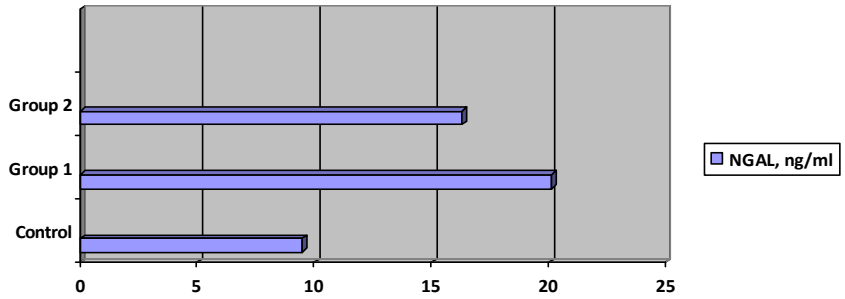

Fig.2. The content of NGAL (ng/ml) in the serum of patients with a combination of AH and DM-2 (group 1), patients with AH (group 2) and the control group.

Figure 2 presents the content of NGAL in the serum of patients.

It was found that the concentration of NGAL in the serum of patients in group 2 was 16.35 (14.52–19.57) ng/ml, which was 1.7 times ($p<0.001$) higher than the control group 9.51 (5.41–12.67) ng/ml. In patients of group 1 there was a significant increase in serum NGAL to 20.15 (18.23–24.12) ng/ml, which was significantly higher by 2.1 times ($p<0.001$) compared with the control group and 1.2 times ($p<0.05$) with group 2. Gender differences in the concentration of the studied biomarkers in the subjects were not observed.

The results of duplex scanning of the renal arteries in the examined patients and healthy individuals are presented in table 1.

Table 1

Duplex scanning of the renal arteries

Respondents group	Vps, cm/s	Ved, cm/s	RI
Control group (n=20)	92.5±3.0	36.9±1.1	0.61±0.03
Group 1 (n=43)	107.0±4.0¹*	27.0±1.2¹*** 2*	0.80±0.04 ¹*** 2*
Group 2 (n=40)	110.5±4.3¹*	31.5±1.3¹***	0.72±0.03¹***

Notes: 1*–significant differences compared with the control group $p<0.05$; 1***–significant differences compared with the control group $p<0.001$; 2*–significant differences between group 1 and group 2 ($p<0.05$).

Duplex scanning of the renal arteries showed that the peak systolic blood flow rate (Vps) was significantly increased in patients from groups 1 and 2 compared with the control group. At the same time, no differences in Vps between patients of groups 1 and 2 were observed.

The above data show that the final diastolic rate of arterial blood flow (Ved) was significantly reduced in patients from group 1 ($p<0.001$) and in patients from group 2 ($p<0.001$) compared with the control group. The decrease in Ved in patients of group 1 compared with group 2 was also significant ($p<0.05$). This corresponded to a significant increase in the resistance index (RI) in patients of both study groups compared with the control group ($p<0.001$). The RI was probably higher in group 1 compared with group 2 ($p<0.05$).

Thus, in patients in group 1, decreased Ved ($p<0.001$) and increased RI ($p<0.001$) could serve as markers in the diagnosis of preclinical renal dysfunction.

A correlation analysis showed a statistically significant correlation between NGAL content and serum creatinine concentration ($r=0.37$; $p<0.05$) in patients of group 1. In the same patients, there was a statistically correlation between cystatin C levels and serum creatinine concentration ($r=0.39$; $p<0.05$) and a negative correlation with GFR CKD-EPI ($r=-0.30$; $p<0.05$).

In patients of group 1 there were statistically significant positive correlations between RI and serum cystatin C concentration ($r=0.41$; $p<0.05$), serum NGAL content ($r=0.40$; $p<0.05$), serum creatinine

concentration (r=0.37; p<0.05), and between Ved and GFR CKD-EPI (r=0.32; p<0.05)._Significant negative correlations were also found between Ved and serum cystatin C (r=-0.40; p<0.05), NGAL (r=-0.41; p<0.05) and between RI and GKF CKD-EPI (r=-0.31; p<0.05).

According to the first global report on the prevalence of kidney disease (2017), among 125 countries (93 % of the world's population) the prevalence of these diseases was 10 % [5]. The most common therapeutic nosologies that lead to the development and progression of CKD are AH and DM-2. As mentioned earlier, 30-40 % of patients with type 2 diabetes develop CKD [10], and the combination of diagnoses in the absence of alternative causes of kidney disease increases the risk of cardiovascular events and associated mortality [9].

The high combined risk of CKD progression and cardiovascular complications leads to an unfavorable prognosis among patients with AH and DM-2 [6]. This is due to the common pathogenetic mechanisms of heart, kidney and vascular damage in patients with AH in combination with the inherent DM- 2 lipo- and glucose toxicity and insulin resistance. Of course, early detection of kidney damage in patients with AH in combination with DM-2 allows to optimize drug treatment to prevent or slow the progression of adverse effects of renal failure.

The “gold” standard in the diagnosis of DN and cardiovascular risk assessment is albuminuria. At the same time, this marker has many limitations, such as low sensitivity and significant variability, depending on the level of physical activity, postural load, diet, body temperature and others. [15]. In addition, increased albuminuria in DM-2 is nonspecific and may be a manifestation of concomitant AH [9]. The increase in the incidence of adverse cardiovascular and renal outcomes, which is observed in patients with normal albuminuria, confirms the earlier start of the pathological process. It is noted that the share of normoalbuminuria variant of CKD among patients with DM-2 with GFR<60 ml/min/1.73m2 varies from 40 to 70 % [6]. It has been shown that approximately 20 % of people with normoalbuminuria have progression of renal failure [12], which suggests the search for more sensitive and specific markers of tubulointerstitial pathology to detect kidney damage in the early stages of normoalbuminuria.

In our study to assess renal function, together with the assessment of albuminuria and GFR, we also measured serum cystatin C levels. Cystatin C is an inhibitor of cysteine protease with a molecular weight of 13 kDa and is produced by all nuclear cells at a constant rate [4]. In healthy cystatin C is almost freely filtered by glomeruli and almost completely reabsorbed and catabolized in the proximal tubules [7]. Unlike creatinine, the level of cystatin C in the blood depends little on gender, age, muscle mass and diet [9]. It is noted that in type 2 diabetes, the content of cystatin C is a more accurate marker of renal function than creatinine and can be used for early detection of GFR [2].

In our study in the examined patients of both study groups, the concentration of creatinine in the serum and the glomerular filtration rate (according to the formula CKD-EPI) in most cases corresponded to the reference values, which indicated favor of the low diagnostic value of these parameters to assess the functional status of the kidneys of this category of patients. In our study, it was shown that serum cystatin C levels increased in patients with AH and reached maximum values in the comorbidity with DM-2. It is possible that minimal changes in renal function, as determined by cystatin C, even at the stage of normoalbuminuria, will be the result of kidney damage and decreased reabsorption in the proximal tubules, which is associated with the progression of nephropathy.

NGAL is a representative of a large group of lipocalins, which are small extracellular proteins with various functions. Human NGAL consists of a single polypeptide chain containing 178 amino acid residues. The protein is released from neutrophil granules in the form of monomer, homo- and heterodimer; it is bound to matrix metalloproteinase-9 and has a molecular weight of 25 kDa. The NGAL molecule is expressed in the blood from secondary granules of activated neutrophils, but can be synthesized in different organs and in different cell types, including epitheliocytes of the renal tubules [13]. In fact, in renal tubules, NGAL production is enhanced in response to stimuli such as ischemia-reperfusion, inflammation, nephrotoxic compounds, etc., which indicates the important role of this protein in the regeneration and repair of tubules [13].

In acute renal failure, an increase in serum NGAL is observed, but the molecules of the compound are absorbed in the proximal tubules and are not excreted in the urine. Renal NGAL is synthesized in the thin ascending part of the Henle loop and in the collecting tubules and enters the urine. Serum NGAL, which enters the kidneys, helps to repair damaged cells, and NGAL, which is synthesized in the kidneys, has a bacteriostatic effect (prevents the entry of iron into bacterial cells) and prevents further development of urinary tract infections [3].

It has previously been reported that serum NGAL levels may be elevated in patients with CKD, infections, anemia, hypoxia, malignancies, etc. [2]. Some studies have shown a dependence of urinary excretion of NGAL on proteinuria [2].

The main results of our study are that in AH and especially in the comorbidity it with DM-2, there was an increase in serum biomarker of kidney damage NGAL compared with healthy individuals. Other scientists [11, 14] have shown that urinary NGAL increases in AH and noted that this parameter is a sensitive biomarker, indicating tubulointerstitial damage in patients with hypertension without diabetes or kidney disease in the early stages of dysfunction. Taken together, these data suggest that NGAL may be a more sensitive marker of renal damage in patients with AH.

Most of the work on the study of early biomarkers of renal damage in type 2 diabetes has been performed experimentally on animal models [4]. But there is very little work on early biomarkers of kidney damage in people with DM-2.

Our study showed that the combination of AH and DM-2 leads to a significant increase in serum NGAL – a clinical biomarker of renal tubular damage. Prolonged expression of the NGAL gene in renal tubular cells may be directly involved in the progression of renal damage and be involved in pathological signaling pathways that cause the development of tubulointerstitial fibrosis [2].

It is known that among the molecular mechanisms underlying the damage of the renal tubules in the comorbidity of AH and DM-2, a significant role is played by oxidative stress and activation of the local renin-angiotensin-aldosterone system (RAAS). It has also been proven [4] that in DM-2 the intrarenal RAAS is especially activated, which determines the increase in the content of angiotensin II in the fluid of the proximal tubules. Decreasing of endocytic receptors involved in NGAL reabsorption may also play a role in increasing blood NGAL levels [2]. Also in experimental works it was shown that in DM-2 in the kidneys increases the activity of NADPH oxidase and decreases the activity of the antioxidant enzyme - superoxide dismutase [3].

According to our duplex scanning of the renal arteries, we found an increase of RI, which was more pronounced in patients with AH and DM-2, indicating an increase in intraglomerular pressure and accelerating the progression of renal failure. The rate of blood flow to systole (Vps) in patients of both study groups was significantly increased compared with the control group but did not differ significantly in patients of group 1 and group 2. Decreased Ved was observed in both group 1 ($p<0.001$) and group 2 ($p<0.001$) patients compared to the control group. Analysis between the groups of examined patients also showed that Ved was significantly lower ($p<0.05$) in the comorbidity of AH and DM-2 (group 1) compared with hypertension patients without diabetes (group 2). Thus, we see that patients in both study groups had an increase of Vps and a decrease of Ved, which was more pronounced in the comorbidity of AH and DM-2 diabetes.

Conclusions

1. In patients with AH and DM-2 at the stage of preclinical kidney damage in comparison with persons without diabetes found elevated levels of NGAL and cystatin C in the blood, which allows us to consider them as diagnostic indicators for early detection of diabetic nephropathy.

2. It was found that a significant decrease in Ved and a significant increase in RI during duplex scanning of the renal arteries are diagnostic markers of morpho-functional changes in the kidneys in patients with AH and DM-2.

Prospects of further research are to identify these and search for new biomarkers in patients who do not yet have signs of renal failure, will reveal the manifestations of renal damage in the preclinical stage.

References

1. Zhdan VM, Lebid VH, Ivanyts′kyy IV, Ishcheykina YU, Boryak KhR. Otsinka hepatotoksychnoho efektu tryvaloho pryyomu statyniv za rezultatamy zsuvnokhvylovoyi elastometriyi. Aktualni problemy suchasnoyi medytsyny. Visnyk Ukrayinskoyi medychnoyi stomatolohichnoyi akademiyi. 2022; T. 22, № 1 (77) :35–40. [in Ukrainian]

2. Abbasi F, Moosaie F, Khaloo P, Dehghani Firouzabadi F, Fatemi Abhari SM, Atainia B, et al. Neutrophil Gelatinase-Associated Lipocalin and Retinol-Binding Protein-4 as Biomarkers for Diabetic Kidney Disease. Kidney Blood Press. Res. 2020; 45 :222–232

3. Afroz T, Sagar R, Reddy S, Gandhe S, Rajaram KG. Clinical and histological correlation of diabetic nephropathy. Saudi J Kidney Dis Transpl. 2017; 28(4) :836–841

4. Barnett AM, Babcock MC, Watso JC, Migdal KU, Gutiérrez OM, Farquhar WB, et al. High dietary salt intake increases urinary NGAL excretion and creatinine clearance in healthy young adults. Am J Physiol Renal Physiol. 2022; 322(4): F392–F402. doi: 10.1152/ajprenal.00240.2021.

5. Chang J, Yan J, Li X, Liu N, Zheng R, Zhong Y. Update on the Mechanisms of Tubular Cell Injury in Diabetic Kidney Disease. Front. Med. 2021; 8: 661076. doi: 10.3389/fmed.2021.661076

6. Csaba P. Kovesdy Epidemiology of chronic kidney disease: an update 2022 Kidney International Supplements. 2022; 12: 7–11; https://doi.org/10.1016/j.kisu.2021.11.003

7. Cusumano AM, Tzanno-Martins C, Rosa-Diez GJ. The Glomerular Filtration Rate: From the Diagnosis of Kidney Function to a Public Health Tool. Front Med (Lausanne).. 2021;; 8: 769335. doi: 10.3389/fmed.2021.769335.

8. Greco M, Chiefari Eusebio, Mirabelli M, Salatino A, Tocci V, Cianfrone P, et al. Plasma or Urine Neutrophil Gelatinase-Associated Lipocalin (NGAL): Which Is Better at Detecting Chronic Kidney Damage in Type 2 Diabetes? Endocrines. 2022; 3: 175–186. https://doi.org/10.3390/endocrines3020016

9. Inker LA, Eneanya ND, Coresh J, Tighiouart H, Wang D, Sang Y, et al. New Creatinine- and Cystatin C-Based Equations to Estimate GFR without Race. N Engl J Med. 2021; 385(19): 1737–1749. doi:10.1056/NEJMoa2102953

10. Jia G, Sowers JR. Hypertension in Diabetes: An Update of Basic Mechanisms and Clinical Disease. Hypertension. 2021; 78(5): 1197-1205. doi: 10.1161/HYPERTENSIONAHA.121.17981.
11. Karoli R, Gupta N, Karoli Y, Kulshrwshtha MR, Twari V. Neutrophil Gelatinase-Associated Lipocalin (NGAL) as a marker of renal tubular injury in metabolic syndrome patients with hyperuricemia. J. Assoc Physycians India. 2022; 69(12): 11–12.
12. Klimontov VV, Korbut AI. Albuminuric and non-albuminuric patterns of chronic kidney disease in type 2 diabetes. Diabetes Metab Syndr.2019; 13(1): 474–479. doi: https://doi.org/10.1016/j.dsx.2018.11.014
13. Maslova GS, Skrypnyk RI, Skrypnyk IN. The role of L-ornithine-L-aspartate in prophylaxis of cytostatic-induced liver injury in patients with multiple myeloma.Svit medytsyny ta biolohiyi. 2021; 4 (78): 100–104. DOI: 10.26724/2079-8334-2021-4-78-100-104
15. Petrykiv S, de Zeeuw D, Persson F, Rossing P, Gansevoort R, Laverman G, et al. Variability in response to albuminuria-lowering drugs: true or random? Br J Clin Pharmacol. 2017; 83, No. 6: 1197-1204 doi: 10.1111/bcp.13217
14. Rysz J, Gluba-Brzozka A, Franczyk B, Franczyk B, Jabłonowski Z, Ciałkowska-Rysz A. Novel Biomarkers in the diagnosis of chronic kidney disease and the prediction of its outcome. Int. J., Mol. Sci. 2017; 18: 1702 DOI: 10.3390/ijms18081702

Стаття надійшла 20.05.2021 р.

DOI 10.26724/2079-8334-2022-2-80-29-33
UDC 616.153.915:616.72-007.24]-036.1-07-08

O.P. Bukach, I.O. Buzdugan
Bukovinian State Medical University, Chernivtsi

DYSLIPIDEMIA IN PATIENTS WITH RHEUMATOID ARTHRITIS DEPENDS ON COMORBID PATHOLOGY AND GENETIC PREDICTORS

e-mail: bukach06@gmail.com

The purpose of the study was to investigate the dynamics of the blood lipid spectrum under the influence of treatment depending on comorbid pathology and polymorphism of the gene T-786C endothelial nitric oxide synthase in patients with rheumatoid arthritis. 110 patients with rheumatoid arthritis and 20 practically healthy people were examined and treated. In the study, the concentration of high-density lipoprotein cholesterol decreased in patients with rheumatoid arthritis – by 22.3 %, rheumatoid arthritis, arterial hypertension – by 29.27 %, rheumatoid arthritis, arterial hypertension, abdominal obesity – by 33.61 %, rheumatoid arthritis, arterial hypertension, abdominal obesity, type 2 diabetes mellitus – by 44.55 %. The increase in total cholesterol, low-density lipoprotein cholesterol and triglycerides depending on the gene polymorphism is found in 87.5 %, 62.5 %, 100 % of patients with *CC* genotype, in 56.52 %, 47.83 %, 78.26 % of patients with *TC* genotype, 56.52 %, 37.93 % and in 75.86 % of patients with TT genotype. A comprehensive treatment of rheumatoid arthritis with comorbid pathology was proposed by adding telmisartan, rosuvastatin and L-arginine to the basic therapy.

Key words: rheumatoid arthritis, comorbid pathology, dyslipidemia, polymorphism of the T-786C gene of endothelial nitric oxide synthase, rosuvastatin, telmisartan, L-arginine

О.П. Букач, І.О. Буздуган

ДИСЛІПІДЕМІЯ У ХВОРИХ НА РЕВМАТОЇДНИЙ АРТРИТ ЗАЛЕЖНО ВІД КОМОРБІДНОЇ ПАТОЛОГІЇ ТА ГЕНЕТИЧНИХ ПРЕДИКТОРІВ

Метою роботи було вивчити динаміку ліпідного спектру крові під впливом лікування залежно від коморбідної патології та поліморфізму гена Т-786С ендотеліальної оксиду азоту синтази у хворих на ревматоїдний артрит.У роботі обстежено та проліковано 110 хворих на ревматоїдний артрит та 20 практично здорових осіб. При дослідженні концентрація холестерол ліпопротеїдів високої щільності знижувалась у пацієнтів із ревматоїдним артритом – на 22,3 %, ревматоїдним артритом, артеріальною гіпертензією – на 29,27 %, ревматоїдним артритом, артеріальною гіпертензією, абдомінальним ожирінням – на 33,61 %, ревматоїдним артритом, артеріальною гіпертензією, абдомінальним ожирінням, цукровим діабетом типу 2 – на 44,55 %. Підвищення вмісту загального холестеролу, холестерол ліпопротеїдів низької щільності та тригліцеролів залежно від поліморфізму гена виявляється відповідно у 87,5 %, 62,5 %, 100 % хворих *CC*-генотипом, у 56,52 %, 47,83 %, 78,26 % хворих *TC*-генотипом, у 56,52 %, 37,93 % та 75,86 % хворих ТТ-генотипом. Запропоновано комплексне лікування ревматоїдного артриту з коморбідною патологією шляхом додаванням до базисної терапії телмісартану, розувастатину і L-аргініну.

Ключові слова: ревматоїдний артрит, коморбідна патології, дисліпідемія, поліморфізм гена Т-786С ендотеліальної оксиду азоту синтази, розувастатин, телмісартан, L-аргінін.

The work is a fragment of the research project "Clinical and pathogenetic justification of differentiated treatment of patients with combined pathology of internal organs", state registration No. 0122U002209.

A timely diagnosis of rheumatoid arthritis (RA) and the earliest possible appointment for adequate therapy significantly improves the course of the disease. It contributes to the achievement of long-term clinical remission [13].

The interaction of genetic and environmental factors leads to a cascade of immune responses, which ultimately lead to the development of synovitis, joint destruction and structural bone damage. This, in turn, leads to pain, disability, and emotional, social, and economic problems [9].

© O.P. Bukach, I.O. Buzdugan, 2022