Results. During the entire observation period, the electrocardiographic indices noted a change in the phases of the development of an experimental myocardial infarction and the processes of remodeling of the cardiac tissue of anterior-lateral parts of the heart.

According to the analysis of the chromatogram of rat serum peptides, it was found that in an acute phase of myocardial infarction, the changes in molecular weight distribution in an acute phase of myocardial infarction were observed, which was reflected by a decrease of peak in the region of macromolecular peptides with m.w.> 10,000 from 61.5% to 3.3%, and the appearance of peaks in the region of low molecular weight peptides within the range of m.w. 290-527. Reducing the fluorescence intensity of probes in one day after the simulation of myocardial infarction indicates an increase in the loading of albumin by ligands.

Conclusions. Characteristic peptide molecular-mass distribution in blood serum and albumin loading with ligands for each stage of myocardium necrosis development and its remodeling in experimental myocardium infarction has been shown.

Key words: myocardial infarction, electrocardiography, blood serum, peptides, fluorescent probes.

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VASCULAR REMODELING IN HYPERTENSIVE PATIENTS WITH DIABETES AND OBESITY

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Introduction. The morbidity of diabetes over the past decade has increased several times and continues to grow steadily, becoming the most spread and economic-spending chronic diseases worldwide [1]. In Europe, at approximately 10,3% of males and 9,6% of females (aged over 25 years) suffer from diabetes, involving more than 66 million according to the [2]. The fasting glucose is linked with the mortality level, regardless of sex and age. Increased glucose level (100-125 mg/dL) is associated with increased mortality [3]. Diabetes mellitus is often accompanied by cardiovascular diseases that can affect its course and prognosis.

In recent years there have been lots of jobs indicating that diabetes mellitus may be a risk factor for the development of diseases, presumably influencing the reduction of patients` life expectancy [4]. The combination of AH with diabetes enhances the risk for cardio vascular diseases (CVD), retinopathy and nephropathy [5]. Diabetic patients have faster atherosclerosis development with premature vascular affection, manifested by increased contractibility of smooth muscle, higher rigidity and resistance. Consequently, these changes lead to the hypertension development [6]. According to the US data, the prevalence of arterial hypertension (AH) in patients with diabetes mellitus increases up to 74% [7].

One of the points of application of carbohydrate imbalance may be the vascular endothelium. The state of glucose metabolism is largely correlated with lipid abnormalities and blood pressure levels (BP). High glucose levels stimulate the proliferation of smooth muscular cells, vasoconstriction, impaired vascular endothelium integrity, the development of endothelial dysfunction (ED), increased stiffness of the arteries and, through these mechanisms, leads to progression of hypertension [8]. Violation of the endothelial vascular control activity is the initial stage of atherosclerotic vascular lesion. This leads to an increase in rigidity of the arterial wall, which determines its rigidity, and an increase in the velocity of propagation of the pulse wave velocity (PWV). The thickening of the arterial walls due to hypertrophy and hyperplasia of smooth muscular cells of the media, the excitation of the connective tissue matrix of the poor elastin significantly aggravates the rigidity of the arteries leading to the decrease in their ability to change the diameter in response to fluctuations in blood pressure [9]. It has been established that the rigidity of the aortic wall correlates with PWV. The measurement of this indicator is considered the “gold standard” for assessing vascular rigidity, and its increase is an independent predictor of cardiovascular death in hypertensive patients [10]. In recent years, it has been proposed to evaluate the elastic properties of arteries in patients with a high risk of developing cardio vascular events (CVE) and AH with the help of the cardio-ankle vascular index (CAVI) [11]. The interrelation of CAVI and atherosclerosis of the carotid arteries in patients with essential hypertension and left ventricular diastolic dysfunction was revealed. CAVI is considered to be a reliable and independent marker of the vascular function, in particular, its rigidity (rigidity) [11,12].

With increasing blood pressure, age-related involution changes in the vascular wall itself and the formation of atherosclerotic plaques accelerate. In addition to the age, the influence on the sex, body mass index, and smoking remains relevant. The study of AH in patients with diabetes mellitus is relevant to general medical practice. This combination is a common cause of disability and reduced life expectancy of patients.

The aim of the work was to study the peculiarities of endothelial vascular control activity and arterial wall stiffness in hypertensive patients in combination with diabetes mellitus.

Object and methods. 69 patients were examined, 39 of them were diagnosed with AH of the stage II in combination with diabetes, which made up the main (1st) group (19 men (48.7%), average age 56.7 ± 6.4 years.

The duration of AH was 8.1 ± 3.7 years, and diabetes mellitus – 6.1 ± 3.1 years. The level of HbA1c reached 6.78 ± 1.31 mmol/l in men and 6.89 ± 1.92 mmol/l in women. The experimental group (2nd) is represented by 30 patients with hypertension stage II without carbohydrate metabolism disorders – 14 (46.6%) men, average age 54.9 ± 6.1 years, duration of illness 6.3 ± 2.7 years. Patients did not differ according to blood pressure levels. HbA1c was determined in the reaction with a phosphorus-tungsten solution of «REAGENT» (Ukraine). The reliability of the results was checked on the control sera of the company «Biocont S» (Russia). The study also included 30 persons of similar age with no signs of AH and diabetes mellitus as a control group. The work was carried out in accordance with the provisions of the Helsinki Declaration of the World Medical Association, the Charter of the Ukrainian Association for Bioethics and the GCP norms (1992), in accordance with the requirements and norms of the Ministry of Health of Ukraine No. 66 of February 13, 2006. All patients signed an informed consent to participate in the study and were fully aware of the methods and scope of the study. The anthropometric study included the determination the body mass index (BMI), measurement of waist circumference (WC) and hips (WH), the ration between them (W-t-H). Obesity of grade I was detected in 28 patients, grade II – in 11 in the main group, the grade I was defined in 23 people, grade II – in 12 in the second group.

In the study the aortic stiffness index (ASI) was analyzed by the ratio of PAT/PP (mm Hg/ml), CIMT (mm), EDV and CAVI. The latest was determined by the method of reoplethysmography: PulseWaveVelocity (PWV) was determined on the shoulder-leg trunk and was calculated using the formula K. Shirai: CAVI = 2ρ ln (DBP/SBP) PWV2/ΔP: where ρ is blood viscosity; ΔP – pulse blood pressure, mm Hg; DBP – diastolic blood pressure, mm Hg; SBP – systolic blood pressure, mm Hg; PWV2 – the velocity of propagation of the pulse wave, m/s; ln is the natural logarithm (log); PWV = L/t, where L is the distance on the shoulder – shin segment (cm), and t is the time between the onset of blood supply to the brachial artery and the tibial artery [10]. Blood filling on the shoulder and the leg was recorded by computerized rheography (replethysmography) combined with simultaneous electrocardiogram recording. The aortic stiffness index was calculated using the method by Yu.M. Sirenko et al. [13]. The carotid intima-media thikness (CIMT) was determined by the method of Doppler sonography of the common carotid artery in the M and B modes using the Philips HD11XE device (USA) according to the generally accepted method with a frequency of 7.5 MHz ultrasound. For normal CIMT, values less than 1 mm were taken, CIMT of 1-1.2 mm were taken as intimal thickening, 1.3 mm and more were criteria for an atherosclerotic plaque. Endothelium depended vasodilatation (EDV) test with reactive hyperemia D. Celermajer et al. [14] was determined by measuring the increase in the diameter of the brachial artery (Δ%) during the period of reactive hyperemia. The normal reaction of the brachial artery is conventionally considered to be its expansion on the background of reactive hyperemia by 10% or more of the initial diameter. The endothelial dysfunction (ED) was ascertained when the vessel expanded in response to the sample of the significantly smaller size.

The level of ET-1 was determined by the immunoferment method using an ELISA system reagent kit. Total NO – for the total amount of nitrites and nitrates in the peripheral blood of the examined, a set of reagents from the company R & D Systems was used. The analysis was performed immediately after sample preparation. The functional state of the kidneys was assessed using glomerular filtration rate (GFR), which was calculated using the Cockroft – Gault formula. GFR in patients of the 1st and 2nd groups was comparable and ranged from 89 to 107 ml/min.

All patients received the necessary drug therapy according to the standards of the treatment, with the greatest importance attached to the influence of drugs not only on the level of blood pressure, but also on the lipid and carbohydrate metabolism. Based on these provisions, patients of the main group took calcium antagonists (amlodipine) or AT1 angiotensin II receptor blockers (losartan, candesartan) as antihypertensive drugs, and diuretics and β-blockers were excluded from the treatment regimen. Metformin has been used to treat the diabetes of the second type. Statistical data processing was performed using the Statistica 6.0 program and the Microsoft Excel statistical functions package. Since the distribution of quantities in all compared groups was close to normal, parametric methods were used. The critical value of the significance level p is 0.05. The statistical hypothesis about the absence of differences between the two compared groups was tested using the corresponding variant of Student's criterion (for dependent or independent samples). In a selective analysis, qualitative and quantitative indicators were estimated using absolute and relative (in percent) frequencies, the central pattern and variability of quantitative indicators were calculated by finding the mean arithmetic value (M) and standard error of the mean (SEM), the results were represented as following: M ± SEM.

Results and discussion. In the 1st and 2nd groups, systolic blood pressure (by 18.1%; $p < 0.05$) and diastolic blood pressure (by 15.7%; $p < 0.05$) differed significantly from those in the control group, but between groups significant differences were absent. There are several mechanisms underlying the relationship between hyperuricemia and increased blood pressure. As already noted, high HbA1c stimulates the proliferation of smooth muscular cells and increasing stiffness of the arteries, impaired integrity of the vascular endothelium and the development of DE, induces an inflammatory process and the release of a number of mediators, including those that have vasoconstrictor properties. The inflammatory process and ischemia of the renal tissue contribute to the activation of the renin-angiotensin system, which leads to the destabilization of the blood pressure.

Indicators of the tough-elastic properties of arteries in both, the main and in the comparison group, differed significantly from the data of the control group. So, in the 1st, the ASI was increased by 18.9% comparing to the indicators of the healthy people. ASI in the 2nd group was higher – by 15.1% when compare to controls ($p < 0.01$), CIMT exceeded by 9.95% ($p < 0.01$) in patients of the 2nd group and 12.1% ($p < 0.01$) of the 1st one. The level of ET-1 in the examined from the 1st group was higher than in the control, by 5.51 pg/ml ($p < 0.01$), and in the 2nd – by 5.23 pg/ml ($p < 0,01$). Endothelium-de-

pended vasodilatation (EDV) is reduced compared with its level in healthy by 24.54% (p> 0.1) in patients of the 1st group and by 9,12% (p> 0.1) – in the 2nd group. Total NO was less by 5.8 μmol/L in the 1st group and by 4.4 μmol/L in the 2nd group. PWV in the 1st group increased by 16%, in the 2nd – by 9.1% compared with the control group (p <0.01). CAVI in the comparison group exceeded the normal level by 9.17% (p <0.01), and in the main group – by 16.9% (p <0.01). When comparing the indices of ED and stiffness of the arteries in the patients of the comparison group and the main group, the following changes were found: ASI in the patients of the main group turned out to be higher than in the comparison group, by 3.65% (p> 0.1), the level of ET-1 was higher by 5.12% (p> 0.1), Total NO in the main group is 12.5% less than in the comparison group. In patients with arterial hypertension with diabetes mellitus, the brachial artery EDV was less by 9.15% than in patients with hypertension, and significantly differed from the control group by 45.19% (p <0.05) and 39.61% (p <0.05) respectively. These data show that impaired endothelial function of the vascular wall is the first link in the development of atherosclerosis. PWV in the main group increased by 37.13% comparatively to the control group (p <0.001). The level of PWV in patients with essential hypertension combined with diabetes mellitus is exceeded by 5.11% (p> 0.1) comparing to the group without diabetes. At the same time, CAVI was increased in the main group by 8.3% (p> 0.1) comparing to the 2nd group. Analyzing the results of the evaluation ED of the endothelial function of the endothelium and the stiffness of the arteries in the whole, it should be noted that levels of ASI, CIMT, ET-1, PWHP and CAVI in the main observation group are higher than in the group without concomitant diabetes mellitus. All studied parameters, directly (ET-1) or indirectly (PWV, CAVI), or through increased rigidity (ASI, CIMT) have an adverse effect, worsening the function of the vascular wall. The identified structural changes in the arteries indicate about the presence of an early atheromatous process in the arterial wall in hypertensive patients with diabetes mellitus. These changes occur both due to the violation of the internal elastic properties of the artery wall, and the geometric properties associated with its thickening (remodeling), i.e. there is a more pronounced decrease in elasticity and development of rigidity of the arteries in patients with hypertension and diabetes. One of the points of application of elevated HbA1c may be the vascular endothelium. The impairment of endothelium vasoreacting activity caused by dyslipidemia and oxidative stress is the initial stage of atherosclerotic vascular lesion and a predictor of severe CVE. It has been shown [15] that the extensive control of carbohydrate metabolism, through normalization of HbA1c, has a positive effect on endothelial function improving such complications as nephropathy and neuropathy. Clinical and experimental data are accumulating, indicating an increase in the level of many metabolic biomarkers associated with the risk of atherosclerosis, including the patients with diabetes mellitus [16,17,18]. It becomes obvious that the endothelial lining of blood vessels regulates local processes of homeostasis, proliferation, migration of blood cells into the vascular wall and, finally, the value of local blood flow and vascular tone regulating blood pressure. In DE, an imbalance occurs between these factors ensuring all these processes. In some diseases, endothelial function is actively studied [5,8], but the problem is to study it in patients with comorbidities.

Conclusion. The addition of diabetes mellitus significantly affects the functional and structural changes in the arterial wall, contributes to ED and worsens the course of hypertension. The most unfavorable effect on the course of hypertension with diabetes mellitus is exerted by such indicators as PWV, CAVI and the level of ET-1. The definition of CAVI, PWV, ET-1, ASI, along with such additional criteria as EDV and CIMT, can be used as criteria for the risk of CVE in patients with hypertension combined with diabetes mellitus.

Prospects for further research. The further studies of vessel wall remodeling values in patients with arterial hypertension combined with type 2 diabetes and obesity are necessary, since they are important for improving the quality of diagnosis of target organ damage in people with high and very high cardiovascular risk. A deeper assessment of the state of the vascular wall will contribute to the more distindt patient's state of such patients and will allow to correct the therapy in order to prevent the onset of adverse cardiovascular events.

There is no conflict of interest.

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РЕМОДЕЛЮВАННЯ СУДИН У ГІПЕРТЕНЗИВНИХ ХВОРИХ НА ЦУКРОВИЙ ДІАБЕТ З ОЖИРІННЯМ

Шелест Б. О.

Резюме. У статті розглядається питання зміни судинної стінки артерій у хворих з гіпертонією, поєднаною з цукровим діабетом 2 типу та ожирінням. Вивчаються такі структурно-функціональні показники як швидкість поширення пульсової хвилі (ШППХ), товщина комплексу інтима-медіа сонної артерії (ТКІМ), серцево-лодижечно індекс (CAVI), індекс жорсткості аорти (ІЖА) і лабораторні дані, а саме ендотелін-1 та ендотелій залежна вазодилатація (ЕЗВД). Визначення рівня ІЖА, ШППХ можна використовувати в якості критеріїв ризику розвитку серцево-судинних ускладнень у пацієнтів з поєднаним перебігом АГ і цукрового діабету. Необхідні подальші більш глибокі дослідження функції ендотелію і ремоделювання стінок артерій у пацієнтів з артеріальною гіпертензією в поєднанні з діабетом. Пошук нових додаткових діагностично значущих маркерів у пацієнтів цієї когорти представляється перспективним.

Ключові слова: гіпертонічна хвороба, цукровий діабет, жорсткість судинної стінки, ендотеліальна функція.

РЕМОДЕЛИРОВАНИЕ СОСУДОВ У ГИПЕРТЕНЗИВНЫХ ПАЦИЕНТОВ С САХАРНЫМ ДИАБЕТОМ И ОЖИРЕНИЕМ

Шелест Б. А.

Резюме. В статье рассматривается проблема изменения качества сосудистой стенки артерий у больных с гипертонией, сочетанной с сахарным диабетом 2 типа и ожирением. Изучаются такие структурно-функциональные показатели как скорость распространения пульсовой волны (СРПВ), толщина комплекса интима-медиа сонной артерии (ТКИМ), сердечно-лодыжечный индекс, индекс жесткости аорты (ИЖА) и лабораторные данные, а именно эндотелин-1 и эндотелий зависимая вазодилятация (ЭЗВД). Определение уровня ИЖА, СРПВ можно использовать в качестве критериев риска развития сердечно-сосудистых осложнений у пациентов с сочетанным течением АГ и сахарного диабета. Необходимы дальнейшие более глубокие исследования функции эндотелия и ремоделирования стенок артерий у пациентов с артериальной гипертензией в сочетании с диабетом, и поиск новых дополнительных диагностически значимых маркеров у пациентов этой когорты представляется перспективным.

Ключевые слова: гипертония, сахарный диабет, жесткость сосудистой стенки, эндотелиальная функция.

VASCULAR REMODELING IN HYPERTENSIVE PATIENTS WITH DIABETES AND OBESITY

Shelest B. O.

Abstract. The article deals with the problem of changing in the vascular wall in patients with hypertension, combined with type 2 diabetes and obesity. Structural and functional indicators such as the pulse wave velocity (PWV), the thickness of the carotid intima-media complex (CIMT), the cardio ankle vascular index (CAVI), the aortic stiffness index (ASI) and laboratory data, namely endothelin-1 and endothelium dependent vasodilation (EDVD) were studied.

Purpose of the study. Study of the characteristics of endothelial dysfunction and arterial wall stiffness in patients with arterial hypertension (AH) in combination with diabetes mellitus type 2.

Methods: 69 patients were examined, 39 consisted the 1st (main) group with AH of the stage II in combination with diabetes (19 men (60.6%), average age 56.7 ± 6.4 years. The comparison group (2nd) is represented by 30 patients with hypertension stage II without carbohydrate metabolism disorders - 17 (60.2%) men, average age 54.9 ± 6.1 years. Patients did not differ according to the levels of blood pressure (BP). HbA1c was determined by reaction with a phosphorus-tungsten. Enzyme immunoassay and Doppler methods of investigation of peripheral vasoregulation were used.

Results. The level of PWV in patients with essential hypertension combined with diabetes mellitus is exceeded by 5.11% (p>0.1) comparing to the group without diabetes. At the same time, CAVI was increased in the main group by 8.3% (p> 0.1) comparing to the 2nd group. Analysing the results of the evaluation ED of the endothelial function of the endothelium and the stiffness of the arteries in the whole, it should be noted that levels of ASI, CIMT, ET-1, PWV and CAVI in the main group are higher than in the group without concomitant diabetes mellitus. All studied parameters, directly (ET-1) or indirectly (PWV, CAVI), or through increased rigidity (ASI, CIMT) have an adverse effect, worsening the function of the vascular wall. The identified structural changes in the arteries indicate the presence of early atheromatous process in the arterial wall in patients with hypertension with diabetes. The addition of diabetes contributes to endothelial dysfunction and worsens the course of hypertension. An unfavourable prognosis for the course of hypertension with diabetes mellitus has an increase in such indicators as PWV, ASI, ET-1 level.

Conclusion. Determination of ASI, PWV, ET-1 level along with such additional criteria as EDV and CIMT can be used as risk criteria for the development of cardiovascular complications in patients with combined course of AH and diabetes mellitus. The further deeper studies of endothelial function and artery wall remodelling in patients with hypertension combined with diabetes are necessary, and searching for new additional diagnostically significant markers in patients of this cohort seems to be perspective.

Key words: hypertension, diabetes mellitus, arterial stiffness, endothelial function.

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