THE COURSE OF CHRONIC HEART FAILURE IN PERSONS WITH POST-INFARCTION CARDIOSCLEROSIS AND TYPE 2 DIABETES MELLITUS AND OBESITY ACCORDING TO A NUMBER OF METABOLIC AND HORMONAL INDICATORS

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Diseases of the cardiovascular system remain the leading cause of overall morbidity and mortality [1, 2]. Over the past three decades, some reduction in cardiovascular mortality has been associated with improved control of risk factors such as cholesterol, hypertension (AH), and smoking [3]. At the same time, there is an increase in obese people, type 2 diabetes mellitus (DM), the severity of metabolic shifts in which leads to vascular accidents [4].

The leading etiological factor in the development of chronic heart failure (CHF) is coronary heart disease (CHD), which according to many studies develops in almost 70% of cases [4, 5].

The pathogenesis of CHF is multifactorial and very complex, which includes the impact on the cardiovascular system of etiological factors and the activation of a complex of compensatory mechanisms. Risk factors for CHF include: left ventricular myocardial hypertrophy, type 2 diabetes, obesity [6-9].

It should be noted that the evolution of views on the pathogenesis of CHF resembles a spiraling movement — at each new round of obtaining new knowledge there is a return to old truths with modern analysis and combining them with the current paradigm.

To identify the stage of CHF, it is important to search for non-invasive methods of early differential diagnosis, risk assessment, disease prognosis, treatment dynamics.

Clusterin and fractalkin are among the biomarkers that indicate a predisposition to the development of CHF and early diagnostic indicators of the disease, especially in the asymptomatic course.

The role of clusterin in lipid transport and inhibition of inflammation has now been proven, making this molecule a potential candi-

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date as a marker of cardiovascular disease, diabetes, and obesity [10–12].

There is evidence of fractalkin — the only chemokine that exists in soluble and fixed forms in the pathogenesis of cardiovascular disease [13–16], which allows us to consider it as a marker of activation of the inflammatory process associated with chemotaxis of various leukocytes, primarily monocytes and lymphocytes in the area of inflammation. It is possible that the results of further studies will prove the possibility of using fractalkin as a target for therapeutic effects in patients with CHF. Global studies demonstrate the uncertainty of a number of issues regarding the progression of CHF in patients with postinfarction cardiocles-rosis and concomitant metabolic disorders and dictate the need to find new modern markers.

The aim: To determine the role of lipid metabolism and fractalkin and clusterin in the progression of CHF in patients with postinfarction cardiocles-rosis with concomitant type 2 diabetes and obesity.

**MATERIALS AND METHODS**

In accordance with the purpose of the work, a retrospective analysis of a comprehensive examination of 67 patients with postinfarction cardiocles-rosis with concomitant type 2 diabetes obesity. The study has been carried out in compliance with the main bioethical provisions of the Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine by the Council of Europe (dated April 4, 1997), the World Medical Association (WMA) Declaration of Helsinki — Ethical Principles For Medical Research Involving Human Subjects (1964–2008), as well as the Order of the Ministry of Health of Ukraine No. 690 dated September 23, 2009. All patients signed informed consent to participate in the study.

All patients were divided into 3 groups depending on the functional class (FC) of CHF:
- 1 group (n = 22) — patients with CHF II FC;
- 2 group (n = 23) — patients with CHF III FC;
- 3 group (n = 22) — patients with CHF IV FC.

All patients were examined clinically, they were instrumental, biochemical and hormonal examination. Echocardiographic examination was performed according to the standard method of H. Feigenbaum on an ultrasound device Radmir (Ultima Pro 30, Ukraine). Biochemical examination was performed by the peroxi-dase method using the Cholesterol Liquicolor reagent kit from Human (Germany), which included the determination of total cholesterol (CH), high-density lipoprotein (HDL) in heparin-stabilized serum. The level of triglyce-rides (TG) in the serum was determined by enzymatic colorimetric method using a set of reagents «Triglycerides GPO», company «Hu-man» (Germany). The coefficient of atherogeni-city (CA) was calculated by the formula of AM Klimov: firm «Human» (Germany). The coefficient of atherogenicity (CA) was calculated by the formula of AM Klimov: firm «Human» (Germany). The coefficient of atherogenicity (CA) was calculated by the formula of AM Klimov:

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CA = \frac{(CH – HDL cholesterol)}{HDL cholesterol}.
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The level of very low density lipoproteins (VLDL cholesterol): in mmol/l. The level of low-density lipoproteins (LDL):

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LDL cholesterol = CH – (LDL cholesterol + + HDL cholesterol) in mmol/L.
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Body mass index (BMI) — Kettle index — was determined by the formula:

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BMI = \frac{weight (kg)}{growth (m^2)}
\]

The clusterin level was determined by en-zyme-linked immunosorbsent assay using the Human Clusterin Elisa test system manufac-tured by Bio Vender (Czech Republic).

Serum concentration of fractalkine was per-formed by enzyme-linked immunosorbsent as-say using a set of reagents Human Fractalkine Elisa Kit «RayBio®» (Georgia).

The research was carried out in the bio-chemical department of the Central Research Institute of Kharkiv National Medical Uni-versity of the Ministry of Health of Ukraine.
on the enzyme-linked immunosorbent assay «Labline Go» (Austria). The obtained results are presented as the mean ± standard deviation from the mean (M ± m). Statistical processing of the obtained data was carried out using the statistical software package Statistica, 8.0 (Stat Soft Inc, USA), Microsoft office Excel-2003. Evaluation of differences between groups in a distribution close to normal was performed using Pearson’s test. Differences at p < 0.05 were considered statistically significant.

RESULTS AND THEIR DISCUSSION

The analysis of the obtained data (Table 1) shows that with the progression of CHF from FC II to FC III there is a deterioration of lipid metabolism: a significant increase in cholesterol levels by 5.5 %, TG — by 15.7 %, LDL cholesterol — by 74.4 %, VLDL cholesterol — by 15.9 %, reduction of HDL cholesterol — by 27.6 % (p < 0.05). These results demonstrate atherogenic progression of the blood lipid spectrum in patients with postinfarction cardiosclerosis and type 2 diabetes. At the same time, an increase in BMI by 8.8 % was noted, which indicates a more pronounced obesity in the group of patients with CHF III FC.

It should be noted that the level of Hb1Ac was the same in all three groups of patients.

At the same time, with the progression of CHF III FC to FC IV there is a decrease in CH — by 8.3 %, TG — by 27.4 %, LDL cholesterol — by 12.2 %, VLDL cholesterol — by 21.16 % and an increase in HDL cholesterol — by 15.7 % (p < 0.05), which is accompanied by a decrease in body weight — BMI decreases by 23.1 %.

Analysis of the level of fractalkin showed that in patients with CHF with an increase in its FC, it increases. On the contrary, the level of clusterin decreased: in patients with CHF II FC it was 14.0 % and 33.2 %, respectively, higher than in the groups of CHF III FC and CHF IV FC (p < 0.001).

The study shows the classic changes in patients with postinfarction cardiosclerosis with CHF and concomitant type 2 diabetes and obesity, which are the formation of disorders of lipid metabolism of atherogenic nature, which are associated with body weight, as well as changes in new indicators such as fractalkin and clusterin, indicating the role of these molecules in the progression of CHF.

The striking effect of type 2 diabetes on the development and prognosis of CHF is due to a whole set of interrelated mechanisms. First of all, these are factors of high cardiovascular risk that make up the syndrome of insulin resistance: dyslipidemia, hypertension, obesity, inflammation [17]. Hyperglycemia is a leading link in heart disease and the presence of type 2 diabetes contributes to the development of coronary atherosclerosis and realizes its negative impact on the progression of CHF due to the occurrence and severity of coronary heart disease [18, 19].

This paper reflects the concept of the effect of chemokines on myocyte contractility, as evidenced by the results of other researchers who demonstrate that fractalkin causes a decrease in cardiomyocyte contractility through the CXCR4 receptor [20, 21].

The obtained results suggest that type 2 diabetes, obesity, dyslipidemia, inflammation have common pathogenetic mechanisms of the development and progression of cardiovascular complications in patients with comorbid pathology, lead to summation and potentiation of cardiovascular risk, which is consistent with the results obtained by other studies, reflected in subsequent works [22–24].

CONCLUSIONS

1. Due to the progression of chronic heart failure in patients with postinfarction cardiosclerosis and concomitant type 2 diabetes and obesity, an increase in all fractions of lipoproteins at stage III functional class was diagnosed, and then their decrease (at stage IV functional class), which may indicate a deterioration in this category of patients, due to the progression of metabolic shifts, stagnation, dysfunction of the main parenchymal organs.

2. Increased circulatory levels of fractalkin and decreased clusterin content in patients with postinfarction cardiosclerosis with concom-
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The course of chronic heart failure in persons with post-infarction cardiосclerosis and type 2 diabetes mellitus and obesity according to a number of metabolic and hormonal indicators

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The aim of the study is to investigate the effect of lipid metabolism, biomarkers of fractalkin and clusterin inflammation on the development and progression of chronic heart failure (CHF) in patients with post-infarction cardiосclerosis, type 2 diabetes and obesity.

Materials and methods. A retrospective analysis of a comprehensive examination of 67 patients with postinfarction cardiосclerosis with concomitant type 2 diabetes and obesity. All patients were divided into 3 groups depending on the functional class (FC) of CHF: 1 group (n = 22) — patients with CHF II FC; Group 2

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(n = 23) — patients with CHF III FC; Group 3 (n = 22) — patients with CHF IV FC. All patients were examined clinically, they underwent instrumental, biochemical and hormonal examinations.

Results. With the progression of CHF from FC II to FC III there is a deterioration of lipid metabolism: a significant increase in cholesterol levels by 5.5 %, TG — by 15.7 %, LDL cholesterol — by 74.4 %, VLDL cholesterol — by 15.9 %, reduction of HDL cholesterol by 27.6 % (p < 0.05). An analysis of the fractal equation showing that ailing on CHF is advised by FC; and the level of clusterin — on the contrary decreases. Classical changes in patients with postinfarction cardiosclerosis with CHF and concomitant type 2 diabetes mellitus and obesity, which are the formation of atherogenic lipid metabolism disorders associated with body weight, as well as changes in the latest indicators such as fractalkin and clusterin, indicating the role of these molecules in the progression of CHF.

Conclusions. Due to the progression of chronic heart failure in patients with postinfarction cardiosclerosis and concomitant type 2 diabetes and obesity, an increase in all fractions of lipoproteins at stage III functional class was diagnosed, and then their decrease (at stage IV functional class), which may indicate a deterioration in this category of patients, due to the progression of metabolic shifts, stagnation, dysfunction of the main parenchymal organs. Increased circulatory levels of fractalkin and decreased clusterin content in patients with postinfarction cardiosclerosis with concomitant type 2 diabetes mellitus and obesity is accompanied by an increase in the functional class of chronic heart failure. Fractalkin and clusterin play a significant role in the progression of chronic heart failure in patients with postinfarction cardiosclerosis with concomitant type 2 diabetes and obesity, so they can be used as biomarkers of the severity of heart failure.

Keywords: chronic heart failure, obesity, postinfarction cardiosclerosis, type 2 diabetes, biomarkers of inflammation.