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GENDER FEATURES OF THE ANTIOXIDANT SYSTEM IN ISCHEMIC HEART DISEASE

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Introduction. The problem of coronary heart disease has acquired in recent years not only an important medicalcial, but also social significance due to the increase in morbidity, high mortality, and loss of working capacity at different ages [1].Currently, the issue of gender characteristics of the course of cardiovascular diseases (CVD) is being actively discussed in the world, which is relevant for the development of a differentiated approach to the treatment of cardiac pathology in men and women.Research in recent years indicates that further study of the circulatory regulatory systems is necessary to understand the pathogenesis of coronary heart disease.Expert recommendations to date do not contain any differences in approaches to the treatment of CVD in men and women.

Modern measures for the prevention and treatment of CVD in Europe have contributed to a decrease in mortality in men compared to women[2]. Within six months after myocardial infarction (MI), it was 7.8% in men and 22.9% in women.[3].

It is known that in women, especially during menopause, the risk of developing coronary heart disease increases significantly, which is accompanied by oxidative stress (OS) and a decrease in the antioxidant activity (AOA) of the body. In men, coronary heart disease is often diagnosed earlier and is also characterized by disturbances in the lipid peroxidation - antioxidant protection (LPO-AOD) system. Therefore, the study of gender characteristics of the antioxidant status of blood plasma and tissues, its relationship with the clinical course of coronary heart disease, the state of endothelial function, the metabolism of nitric oxide (NO), which has antioxidant properties, the content of homocysteine (HC), which is involved in oxidation processes, seems relevant.

Numerous studies have demonstrated the high efficiency of statins with antioxidant properties in the treatment of coronary heart disease with dyslipoproteinemia (DLP). Gender differences in the tolerability and efficiency of statins have been noted.

Purpose of the study: assessment of gender characteristics of antioxidant status and the possibility of correcting disorders of lipid peroxidation processes and antioxidant protection during treatment with atorvastatin in men and women suffering from stable forms of coronary heart disease with dyslipoproteinemia.

Materials and methods of research:The study included 49 people: 39 patients with coronary heart disease and 10 relatively healthy individuals. The study involved 39 patients with coronary heart disease with stable angina of II-III FC and/or post-infarction cardiosclerosis (PICS) according to the WHO classification, aged 35 to 68 years, average age 58.2±6.4 years, who gave informed consent to participate in the study, divided into 2 groups by gender. Group 1 included 20 men, group 2 - 19 women. Control group 1 consisted of 6 relatively healthy men, control group 2 - 4 relatively healthy women.

The patients received basic therapy (β-blockers, angiotensin-converting enzyme (ACE) inhibitors, calcium antagonists, antiplatelet agents and nitrates). The duration of the study of the effect of atorvastatin as part of cardiac therapy on the parameters of lipid peroxidation-aromatic oxidation, the clinical course of coronary heart disease, and endothelial function was 6 months. Patients in both groups were comparable in age and laboratory parameters, which made it possible to consider them representative for determining the

effectiveness of treatment. The presence of myocardial ischemia according to ECG data, the state of endothelial function, the thickness of the intima-media complex of the common carotid artery (IMCCA), and laboratory parameters were assessed before and after 6 months of treatment.

Research results and discussion:Significant differences in the lipid composition revealed reliable gender differences in the intensity of lipid peroxidation and the activity of tissue and plasma antioxidant enzymes: in men, compared with women, the levels of DK were increased by 9% and TBA-RP by 11%, while AOA AOS CP/TF were decreased ($p<0.05$) by 10%, SOD by 12%, and GP by 19%. This indicates a more pronounced depletion of AOP reserves and lipid peroxidation in the group of men and confirms the available literature data on the role of OS in the pathogenesis of coronary heart disease. The highest SOD/GP in the group of men with coronary heart disease indicates the maximum imbalance towards oxidative stress in the system of tissue antioxidant enzymes, which is necessary to maintain a steady-state concentration of reactive oxygen species (ROS). In our study, ROS occurred in 23% of men and 8% of women with coronary heart disease. Reliable gender differences in homocysteinemia were revealed ($p=0.01$), in men it was 1.5 times higher than in women. The results of the correlation analysis of the Hz level and LPO-AOZ in patients with coronary heart disease show that in coronary heart disease with hypercholesterolemia and hyperlipoperoxidemia there is a reliably higher Hz level compared to that in healthy individuals ($p<0.05$), GHz seems to be one of the factors reducing tissue and plasma AOD. The inverse relationship between age and the Hz level in group 2 indicates the role of GHz in the pathogenesis of coronary heart disease in young women.

A close relationship between NO metabolism and LPO-AOD parameters was revealed, especially in the group of men with coronary artery disease. A significant increase in the level of NO metabolites in a number of women with hyperlipid peroxidemia and hyperhomocysteinemia leads to an imbalance in the relationship between NO and the functioning of the LPO-AOD system. At the same time, NO itself is capable of acting as a prooxidant. In both groups of patients with coronary artery disease, as compared with the control, there were disturbances in endothelium-dependent vasoreactivity, significantly more pronounced in men ($p = 0.001$), and thickening of the CCA IMT - gender differences are insignificant. The number of ischemia episodes, including painless, and the duration of myocardial ischemia according to ECG data were significantly greater in men with coronary artery disease. The state of the endothelium and the clinical course of coronary artery disease in people of both sexes are closely associated with LPO-AOD.

Over 6 months of treatment in both groups of patients with coronary heart disease, the levels of TC and LDL-C became < 4.5 and 2.5 mmol/l; the activity of antioxidant enzymes and NO metabolites significantly increased, and the intensity of lipid peroxidation decreased, approaching that in the control groups.

A more pronounced antioxidant effect of atorvastatin was revealed in the complex therapy of coronary heart disease with DLI in men.

The percentage of changes in the activity of SOD, GP, CP, CP/TF, and NO metabolites as a result of treatment in group 1 was 35, 95, 30.19, and 23%, respectively, and in group 2 - 16, 47, 16, 8, and 12%. In group 1, the content of DK and TBA-RP decreased insignificantly more (by 43 and 37%) than in group 2 (by 35 and 28%). It is possible that the different antioxidant effect of atorvastatin in men and women is explained by gender differences in the activity of key enzyme systems of NO synthetases, NAD(P)H oxidases, differences in the balance of ROS and NO synthesis by them, as well as a more pronounced decrease in the blood plasma of women of ubiquinone Qio, the most effective LDL antioxidant synthesized in the side chain of cholesterol synthesis.

Reduction of OS and restoration of NO biological activity are the key mechanisms of the beneficial effects of statins on endothelial dysfunction. Over 6 months of treatment, endothelial function and the clinical course of coronary heart disease significantly improved in both groups. Cardiac therapy, including atorvastatin, contributed to a more pronounced increase in EDVD in group 1 by 34%, in group 2 - by 21% ($p < 0.05$) and had a significantly more pronounced effect on the duration of myocardial ischemia in men ($p = 0.04$), reducing it in group 1 by 88%, in group 2 - by 81%.

Conclusion. Thus, based on the conducted studies in stable forms of coronary heart disease, gender differences in the content of LPO products, HCV, NO metabolites and the activity of tissue and plasma antioxidant systems were revealed. A reliable relationship between LPO-AOD, endothelial function,

atherosclerotic lesions of the coronary arteries, and the clinical course of the disease was proven. More pronounced non-lipid effects of atorvastatin in men were shown, in particular, its effect on the activity of antioxidant enzymes, endothelial function and the duration of myocardial ischemia, which emphasizes the need for a gender approach to the correction of antioxidant status disorders in coronary heart disease with DLP.

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