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THE EFFECT OF BETARGIN ON THE INDICATORS OF CHRONIC SYSTEMIC INFLAMMATION, ENDOTHELIAL DYSFUNCTION AND ANTIOXIDANT DEFENSE IN PATIENTS WITH CORONARY HEART DISEASE CONCURRENT WITH NON-ALCOHOLIC FATTY LIVER DISEASE

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Introduction. At present, the increased incidence of coronary heart disease (CHD) concurrent with non-alcoholic fatty liver disease (NAFLD) is observed on a global basis, which leads to aggravation of the course of diseases and unfavorable prognosis [1,2,6]. Pathogenetically, the main role in the formation of both CHD and NAFLD belongs to chronic systemic inflammation (CSI), dyslipidemia, endothelial dysfunction and oxidative stress, which justifies the search for effective and scientifically substantiated therapeutic measures in the conditions of comorbidity.

The aim of our study was to determine the effect of comprehensive therapy with the addition of betaine [3] and arginine [5] on the indicators of chronic systemic inflammation of low intensity, endothelial dysfunction, antioxidant defense and indicators of blood flow velocity in the portal and hepatic veins in patients with stable coronary heart disease concurrent with nonalcoholic fatty liver disease [4].

Materials and methods. We conducted an open, randomized, controlled clinical trial. The study included 82 persons of both sexes aged 40-69 with the diagnosis of coronary heart disease, stable exertional angina, FC II, HF 0-I, in the absence of destabilization of the course for two months, and the presence of concomitant NAFLD (steatohepatosis). By random selection, patients were divided into 2 groups – the study group (35 patients) and the comparison group (48 patients). We examined patients in terms of the level of cytokine (CK), the factor of tumor necrosis alpha (TNFa) in the serum by the immune enzyme method, the fibrinogen content (FG) in the blood plasma by weight, the level of expression of the mRNA kappa inhibitor alpha (IKBa) of nuclear kappa transcription factor B (NF-kB) in mononuclear cells by polymerase chain reaction in real-time mode (Real-time PCR), the number of circulating endothelial microparticles (CEM) in the peripheral blood with expression of CD32 and CD40 antigens by flow cytometry using monoclonal antibodies, the indicator of antioxidant system – ceruloplasmin (CP) in the serum according to biochemical Ravin method. Ultrasound examination of the liver was conducted according to the standard method for determining the velocity of blood flow in the portal and hepatic veins.

All patients are prescribed standard therapy for stable coronary heart disease (β-blockers, statins, aspirin). Patients in the study group were additionally prescribed betargin at a dose of 2 grams of arginine citrate and 2 grams of betaine daily per os. In 2 months, patients were re-examined to the aforementioned extent of studies.

Results. In patients with stable CHD concurrent with NAFLD, an increase in the blood levels of TNFa (10.56+3.74 pg / ml) was found, and the FG content in the blood plasma was moderately elevated (4.65+1.04 g / l).

The study of the expression of the mRNA gene of IkBa in mononuclear cells in patients with stable coronary heart disease concurrent with NAFLD was 0.215±0.015 c.u.

In patients with comorbidity, we found an increase in the marker of endothelial dysfunction (CEM) CD32 CD40 – 2.69 x 107 / l at the normal rate of 1.3 (1.05-2.11) x 107/ l.

Furthermore, increased velocity of blood flow in the portal and hepatic veins was found: 0.38±0.10 m / s and 0.21±0.06 m / s, respectively. The level of CP as the indicator of antioxidant defense was within the limits of the physiological norm and amounted

to 259.8±52.8 mg / l. Re-examination after 2 months of treatment showed a reliable decrease in TNFa level by 69% (p <0.001) in the study group and by 65% in the comparison group (p <0.01). The content of acute phase reactant and FG coagulation factor after treatment in the study group decreased by 8% and in the comparison group – by 3%. The level of expression of the mRNA gene of IkBa in mononuclear cells was significantly lower in the study group and was -0.576 (-0.497 – -0.759) (p = 0.048), and increased in the comparison group (0.424 (-0.589 – +1.817)), but not statistically reliable (p = 0.296). Study of the amount of CEM CD32 and CD40 after treatment showed a reliable decrease in the study group by 30.4% (p <0.05), while in the comparison group there was an increase by 24% (p> 0.05), statistically unreliable. The applied therapy has led to a significant decrease in the blood flow in the portal vein in the study group by 15% (p = 0.021), and in the comparison group – by 5.5% (p = 0.02). The study of the blood flow velocity in the hepatic veins showed a reliable decrease in the index in the study group by 9.6% (p = 0.002), whereas in the comparison group, an unreliable decrease by 5% was detected (p = 0.099). The level of CP has increased significantly within the normal range in the study group by 16.6% (p <0.05), whereas in the comparison group, an unreliable decrease by 12% (p> 0.05) was detected.

Conclusion. In patients with stable CHD concurrent with NAFLD, the presence of low-intensity CSI and endothelial dysfunction has been detected. The addition of betaine and arginine to standard therapy in patients contributes to lowering the level of CSI by inhibiting the signal transduction of NF-kB, indicating the anti-inflammatory effect of these components of therapy. Furthermore, decreased marker of endothelial dysfunction and restoration of normal venous blood flow in the liver were observed, indicating the endothelial-protective properties. We also detected an increased activity of antioxidant defense, indicating the antioxidant effect. Prospects for further research. The obtained results substantiate the importance of identifying the markers of low intensity CSI, endothelial dysfunction and antioxidant defense to assess the course and progression of CHD concurrent with NAFLD. Detection of anti-inflammatory, endothelial-protective and antioxidant properties of the combination of betaine and arginine in patients with comorbid pathology justifies the expediency of further research on the clinical efficacy of these components of therapy in order to improve therapeutic approaches.

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Key words: *coronary heart disease, chronic systemic inflammation, endothelial dysfunction, non-alcoholic fatty liver disease, betargin.*