THE INFLUENCE OF BETARGIN AND QUERCETIN ON THE INDICATORS OF CHRONIC SYSTEMIC INFLAMMATION IN PATIENTS WITH CORONARY HEART DISEASE CONCURRENT WITH NON-ALCOHOLIC FATTY LIVER DISEASE

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Introduction. Comorbidity is one of the major issues of modern medicine, characterized by masking of pathological conditions, aggravated course and unfavorable prognosis [1].

Recently, there is a significant increase in the incidence of coronary heart disease (CHD) and non-alcoholic fatty liver disease (NAFLD) all over the world [2]. The formation of both CHD and NAFLD is associated with the intensity of chronic systemic inflammation (CSI), dyslipidemia, endothelial dysfunction, and oxidative stress [3, 4]. The detection of the leading role of low-intensity CSI in the pathogenesis of both pathological conditions underlies the scientific searches for effective and well-founded therapeutic approaches under conditions of comorbidity [5].

The aim of our research was to study the indicators of chronic systemic inflammation in patients with stable ischemic heart disease concurrent with non-alcoholic fatty liver disease and the effect of comprehensive therapy with the addition of betaine, arginine and quercetin on the detected disorders.

Materials and methods. The study included 75 patients of both sexes, aged from 40 to 69, with the diagnosis of coronary heart disease: stable exertional angina, FC II, HF 0-I, NAFLD. Patients were divided by random sampling into 2 groups – the study group (27 patients) and the comparison group (48 patients). Patients were examined to determine the levels of cytokines (CK) – tumor necrosis factor alpha (TNFα), interleukin-6 (IL-6) and interleukin-10 (IL-10) in the serum by immunoenzymatic method, fibrinogen content (FG) in the blood plasma by weight method, and the expression level of mRNA gene of inhibitor kappa B alpha (IKBα) of nuclear factor-kappa B (NF-kB) in mononuclear cells by PCR in real-time mode [6, 7].

All patients are prescribed standard therapy for stable coronary heart disease (β-blockers, statins, aspirin), as well as silymarin (90 mg per day) and lecithin (1200 mg per day) for NAFLD correction. Patients in the study group were additionally prescribed betargin at a dose of 2 g of arginine citrate and 2 g of betaine daily per os, as well as quercetin at a dose of 120 mg daily per os. In 2 months, patients were re-examined to the aforementioned extent of studies.

Results. All patients with coronary heart disease had elevated blood levels of TNFα (10.56±3.74 pg / ml). The levels of proinflammatory CK IL-6 and anti-inflammatory CK IL-10 were within the physiological norm and amounted to 4.69±1.21 pg / ml and 11.43±2.12 pg / ml, respectively; the FG content in the blood plasma was moderately elevated (4.65±1.04 g / l).

We studied the expression level of mRNA gene of IkBα in mononuclear cells, reflecting the level of transcriptional activity of NF-kB, and, accordingly, the severity of systemic inflammation in patients with stable coronary heart disease concurrent with NAFLD, which was 0.215±0.015 c.u.

Two months after initiation of treatment, a reliable decrease in TNFα levels was observed in the study group by 55.6% ($p<0.001$), in the comparison group – by 34.5% ($p<0.01$). The level of IL-6 was reliably decreased only in the study group ($p>0.05$). The level of anti-inflammatory CK IL-10 under the influence of therapy was significantly increased only in the comparison group ($p<0.001$).

The content of acute phase reactant and FG coagulation factor in the blood after the treatment in both groups was not statistically different from the baseline data.

The level of expression of mRNA gene of IkBα in mononuclear cells was significantly decreased in the study group and amounted to -0.496 (-0.591 – +0.665) ($p=0.048$), whereas in the comparison group it increased (0.424 (-0.589 – +1.817)), but not statistically reliably ($p=0.296$).

Conclusion. In patients with stable coronary heart disease concurrent with NAFLD, activation of low-intensity CSI has been detected. The use of combination of betaine, arginine and quercetin in the comprehensive therapy of patients contributes to lowering the level of CSI by inhibiting the signal transduction via the NF-kB pathway, which may be due to the anti-inflammatory properties of these components of integrated therapy with an effect on certain targets of the pro-inflammatory cascade.

Prospects for further research. The obtained results substantiate the importance of identifying the low intensity CSI markers for assessing the course and progression of CHD concurrent with NAFLD. Detection of anti-inflammatory effect rendered by the combination of betaine, arginine and quercetin in these patients demonstrates the need for further studies of the molecular mechanisms of action and clinical efficacy of these components of integrated therapy with the aim of developing new therapeutic approaches.

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

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