THE LEVEL OF SYSTEMIC INFLAMMATION AND THE STATE OF CENTRAL HEMODYNAMICS IN PATIENTS WITH CORONARY HEART DISEASE

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Introduction. Cardiovascular disease, and coronary heart disease (CHD) first and foremost, is one of the leading causes of mortality in developed countries of the world [1]. The prognosis for patients with coronary heart disease depends, predominantly, on the progression of coronary atherosclerosis (CA). The pathogenetic basis of CA is chronic systemic inflammation (CSI) [2]. CSI in CA is supported by induction of cytokine-associated pathways of intracellular signaling. The central component of CSI is the nuclear factor kappa B (NF-kB), the main activators of which are proinflammatory cytokines (CK), especially interleukin 1 (IL-1) and tumor necrosis factor α (TNFα) [3, 4]. The effector unit of the CSI is CK Th1 of the immune response type, involved in the formation and destabilization of the atheromatous plaque [5].

Due to structural and functional remodeling, activation of neuro-humoral systems and reactions involving inflammatory molecules in patients with coronary artery disease, the disruption of systolic function of the left ventricle (LV) is formed. The biomechanical reorganization of the heart causes changes in the expression of genes that mediate CSI, apoptotic reactions, etc. [6].

Therefore, it is expedient to study in detail the molecular mechanisms of atherogenesis in order to find new targets for pharmacological effects in CA and CHD.

The aim of our research was to examine the relationship between the level of CSI and central hemodynamic disorders in patients with coronary heart disease.

Materials and methods. An open clinical trial was conducted. 230 patients with CHD were examined: stable angina pectoris, II FC, CH 0-I (119 men and 111 women aged 57 $\pm$ 8.3 years) and 30 healthy subjects (control group). The criteria for inclusion in the study were the age of men and women (40-75 years), the presence of CHD: exertional angina of II FC in the absence of destabilization of the course for at least two months, the informed consent of the patient to participate in the study. The exclusion criteria were the presence of chronic heart failure higher than stage I, high blood pressure, complications of cardiac rhythm and conduction disorders, rheumatism, cancer, anemia, diabetes mellitus, renal and hepatic insufficiency.

To achieve the aim of the research, patients' blood was tested for levels of IL-1β and TNFα by the immune enzyme method; fibrinogen (FG) plasma levels – by weight method and echocardiography (echo) [7]. The global contractile ability of LV was estimated by the stroke volume (SV), the ejection fraction (EF), and the velocity of the blood flow (v) in the external path (EP) of the LV. The diastolic function of LV was investigated by recording the transmitral blood flow rates by the ratio of the velocities of the early (E) and late (L) diastolic filling of the LV (E / A), the delay time of early diastolic filling of the LV (DT) and the time of isovolumic LV relaxation (IVRT) [7].

Results. In patients with coronary heart disease, an increase in the concentration of pro-inflammatory CK was found in the blood: the TNFα level was 8.48 + 2.15 pg / ml, and the level of IL-1β was 9.34 + 2.80 pg / ml. In 37.4% of patients with coronary heart disease, high levels of FG in the blood plasma were observed.

In patients with coronary heart disease, EF of LV, SV and *v* of EP of LV were significantly lower in comparison with the group of healthy individuals ($p < 0.05$). The ratio of transmitral blood flow phases in patients with coronary heart disease was disrupted – E / A <1, the DT value was increased ($p < 0.05$), IVRT was delayed ($p < 0.05$). The clinical evaluation of echo results showed that LV diastolic dysfunction was detected in 99% of patients with CHD by the type of relaxation disturbances, 1.6% – by the type of pseudonormalization.

The study of the ratio in the indices of central hemodynamics and CSI markers revealed the reverse correlation between EF of LV and TNFα ($r = -0.340$, $p < 0.05$), EF of LV and FG ($r = -0.3369$, $p < 0.01$), the E / A value and IL-1β ($r = 0.333$, $p < 0.05$).

Conclusion. The obtained results demonstrate the negative effect of CSI on the systolic and diastolic function of LV in patients with coronary heart disease.

Prospects for further research. Further study of the levels of pro-inflammatory CK and other markers of inflammation in patients with CA and CHD can be the basis for constructing a diagnostic algorithm to determine the predictors of destabilization of the course and progression of the specified pathology and the development of optimal pathogenetically substantiated therapies.

Recommendations. It is expedient to use the levels of CK and FG in the blood as diagnostic and prognostic markers for assessing the course of coronary heart disease, the progression of CA and the effectiveness of therapeutic measures.

Key words: coronary heart disease, chronic systemic inflammation, cytokines, central hemodynamics.

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