The State of the Sympatho-Adrenal System and Immune Status in Patients with Coronary Heart Disease

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ABSTRACT

Coronary heart disease (CHD) has acquired not only important medical, but also social significance in recent years due to an increase in morbidity, high mortality, disability of various ages and professions [1].

Recent studies indicate that in order to understand the development of coronary heart disease, further study of blood circulation regulation systems, in particular the sympathetic-adrenal system (SAS), is necessary [2,10]. A change in the activity of SAS is essential in the pathogenesis of coronary heart disease.

Keywords: sympathetic-adrenal system, coronary heart disease, cardiomyocyte, beta-adrenergic receptors, postinfarction cardiosclerosis

At the present stage, attention is drawn to the state of the immune system in CHD, specifically the state of cellular and humoral immunity in CHD – as one of the adaptive mechanisms that regulates the immunogenesis of the body, is responsible for the inflammatory processes of the body, the development and progression of CHD. The mechanism of action of immunogenesis includes a negative inotropic effect, remodeling of the heart, violation of endothelium-dependent dilatation of arterioles, increased apoptosis of cardiomyocytes and peripheral muscle cells [3,5,8,9]. Increased activity of SAS stimulates the production of IL-6, TNF-α. Dopamine and beta-adrenergic receptors are present on the membranes of immunocompetent cells, through which CAC mediators (catecholamines) binding stimulate the immune-inflammatory effect of cytokines, hyperproduction of these cytokines disrupts the contractile function of the myocardium and promotes myocardial hypertrophy and remodeling in patients with CHF [2,4,8].

In response to pathological changes in the myocardium and peripheral tissues, receptor dysfunction occurs, manifested by their overstimulation, which in turn leads to hyperactivation of the SAS, closing a vicious circle [2,6,7].

The purpose of the study: To study violations of the functional state of the CAC and the immune status of patients with coronary heart disease.

Materials and methods of the study: 42 patients aged 30 to 65 years suffering from coronary heart disease with a disease duration of 3 to 15 years were under our supervision. 42 patients were randomized into 3 groups, taking into account the diagnosis. CHD was diagnosed in 20 patients. Stable angina pectoris of tension FC II-III; in 11-x – coronary heart disease. QMI; in the remaining 11 patients with coronary heart disease. Stable angina pectoris of tension FC II-IV. Postinfarction cardiosclerosis. The

control group consisted of 10 relatively healthy individuals aged 20-45 years.

The diagnosis in all examined patients was made on the basis of data from clinical observation, laboratory analysis and functional diagnostics, taking into account risk factors.

As it is known, the most adequate method of assessing the state of CAC is the study of catecholamines (CA) in urine. Determination of adrenaline, norepinephrine, dopamine and DOPA in daily urine was performed by trioxyindole fluorimetric method modified by E.S. Matlina, Z.M. Kiseleva, I.E. Sofieva (1965). A method was used to determine the activity of monoamine oxidase (MAO) in blood serum, consisting in oxidative deamination of synthetic amine - benzylamine in an incubation medium under the action of MAO to benzaldehyde.

To determine immunoglobulins in blood plasma, the method of radial immunodiffusion in gel in the Mancini modification was used.
The concentration of interleukin-6 was determined by a similar method of solid-phase enzyme immunoassay using the test systems of Cytokine LLC (St. Petersburg, Russia) on the Human enzyme immunoassay analyzer (Germany).

The results of the study: The levels of interleukin-6 in patients with angina and PIC did not significantly differ, whereas in patients with myocardial infarction with a Q wave, the index was 118.4±5.9Pkg/ml. In the control group, the IL-6 index was 26.6±1.2Pcg/ml.

The excretion of KA and DOPA in the daily urine of patients with coronary heart disease was also studied in parallel with the immune status. When analyzing the data of daily excretion of KA in urine, the following picture develops: in patients with QMI, a significant statistically significant increase in A and NA is observed at admission. In chronic forms of coronary heart disease (angina pectoris, PICS), there is a decrease in the level of A, NA, and DOPA excretion in the daily urine.

By studying the daily urinary excretion of CA and DOPA in healthy and stable angina, we determined that in patients with coronary heart disease. Stable angina pectoris. FC II-III there is a significant decrease ($p<0.001$) in urinary excretion of free, conjugated, total A and NA.

Thus, the daily excretion of free A in patients with angina compared with healthy individuals decreased by 32.7% ($P<0.001$), conjugated by 19.6% ($P<0.05$) and total by 26.4% ($P<0.001$)

Excretion in daily urine in patients with angina is statistically significantly lower than the control level. The excretion of free NA was reduced by 11.1%, conjugated by 13.3% and total by 12.3% ($P<0.05$) (Table 3.8, Fig. 6). There was a decrease in the daily excretion of all DA fractions compared to healthy ones, free by 43.6%, conjugated by 43.7% was statistically significant ($P<0.001$), a total of 43.7% (Table 3.9, Figure 8). The difference in DOPA excretion was 20.7% ($P<0.05$).

In the study of QMI patients (11 people) on the first day of admission to the hospital, a significant increase in daily urinary excretion of CA and DOPA was found.

There was a statistically significant increase in the excretion of free A compared to healthy ones by 1.7 times ($P<0.001$). Compared with the control, the excretion of conjugated A was 3.1 times greater, and compared with patients with coronary heart disease. Stable angina by 3.9 times ($P<0.001$). Accordingly, the coefficient of increase in the content of total A in the daily urine in relation to the control value was 2.6 ($P <0.001$), in relation to the indicator of the group of patients with coronary heart disease. Stable angina pectoris. FC II-III – 3.3 ($P<0.001$).

The excretion of free, conjugated and total DA in patients remained relatively lower than in healthy patients and was statistically unreliable. The excretion of free, conjugated and total dopamine in healthy subjects was respectively 141.4 7.6 mcg/day; 141.4 7.6 mcg/day; 282.8 10 mcg/day (see Table 1). The level of DOPA excretion in QMI patients on the 1st-2nd day of the disease was significantly lower ($P<0.001$) than in healthy subjects and amounted to 23.9 1.9 mcg/day, and in healthy people, the excretion of DOPA was 47.9 2 mcg/day.

In the metabolism of biogenic amines, the oxidative deamination reaction catalyzed by MAO is of key importance. In the studied groups of patients with coronary heart disease, the activity of MAO was manifested as follows. Thus, in the group of patients with coronary artery disease with stable angina pectoris, MAO activity decreased and amounted to 0.05±0.001 units/ex, which is 28.6% lower than the control indicators (p1<0.001) (Table 2). In the group of ischemic heart disease PEAKS, MAO activity decreases even more, amounting to 0.04±0.001 units/ex, which is 42.9% below the control indicators (p2 0.001). In the group of patients with IHD QMI, MAO activity was maximally reduced, amounting to 0.03±0.0009 units /ex, which is 57.2% lower than the control (p4<0.001).

Discussion of the results: Biological effects of interleukin-6 involvement in the development of inflammatory and immune reactions, as well as in the regulation of intersystem interactions. Provides the relationship between the autonomic and immune systems [9,11]. Studies have shown that an increase in the blood content of IL-6 in patients with coronary heart disease is correlated with the severity of clinical manifestations and the activity of SAS.

KA, being released in excess in the acute period of MI, as biochemically active substances, can have a significant impact on the further development of the disease, its outcome [4,11].

When analyzing the data of daily excretion of KA in urine, the following picture develops: in patients with QMI, a significant statistically significant increase in A and NA is observed at admission, especially with QMI. In chronic forms of coronary heart disease (angina pectoris, PICS), there is a decrease in the level of A, NA, and DOPA excretion in the daily urine.

As already noted in patients with acute coronary heart disease, an increase in the excretion of A and NA in the first days of MI was accompanied by a significant decrease in the content of DA and DOPA in the daily urine. The low content of KA precursors in the daily urine in the first days of observation is apparently due to their accelerated transition to NA and A, as well as reflex inhibition of their formation due to excessive A and NA content. According to literature sources, it should be noted that subsequently, for a long time after the onset of the disease, the level of excretion and DOPA remains significantly below normal. Low excretion of DA and DOPA with a parallel decrease in excretion of A and NA in the dynamics of the disease indicates the depletion of the reserve capabilities of SAS in patients with MI.

Conclusion. Thus, the "immunocytokine" model of IHD pathogenesis does not contradict the neurohumoral theory, but complements our ideas about the mechanisms of IHD development. The participation of immune inflammation mediators in the disease scheme expands the "base of therapeutic intervention" and opens up new prospects for improving the effectiveness of treatment. The ways of influencing the cytokine link are already being seriously discussed. And it is possible that soon anti-cytokine drugs will become as common a means of treating patients with coronary artery disease as antianginal pills, cardiac glycosides and i-ACE.

A comprehensive study of the sympathetic-adrenal system and the metabolism of biogenic amines in patients with coronary heart disease showed that in acute myocardial infarction there is a pronounced violation of the biosynthesis of catecholamines, which is expressed by increased urinary excretion of free and conjugated forms of adrenaline and norepinephrine. With stable angina pectoris and PICS, inhibition of the functions of CAC is observed, as evidenced by a general decrease and violation of urinary excretion of catecholamines and their conjugated forms, as well as their metabolic precursor DOPA.

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