THE RELATIONSHIP BETWEEN THE ACTIVITY OF THE SYMPATHETIC-ADRENALINE SYSTEM AND IMMUNE STATUS IN PATIENTS WITH MYOCARDIAL INFARCTION

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Abstract: Ischemic heart disease (IHD), especially the acute form of myocardial infarction (MI), has acquired in recent years not only important medical but also social significance due to the increase in morbidity, high mortality, and loss of working capacity at various ages and professions [1]. Literary sources of recent years indicate that in order to understand the development of coronary heart disease, it is necessary to further study the systems of blood circulation regulation, in particular the sympathetic-adrenal system (SAS) [2,10]. Changes in the activity of the SAS are of significant importance in the pathogenesis of coronary heart disease.

Keywords: humoral link, overstimulation, clinical observation, heart disease.

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

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

Purpose of the study:

Study of disorders of the functional state of the cardiovascular system and the immune status of patients with coronary heart disease.

Materials and methods of the study: we observed 42 patients aged 30 to 65 years suffering from ischemic heart disease with a disease duration of 3 to 15 years. 42 patients were randomized into 3 groups based on the diagnosis. 20 patients were diagnosed with coronary heart disease. Stable angina of FC II - III ; 11 patients had coronary heart disease. QMI ; the remaining 11 patients had coronary heart disease. Stable angina of 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 clinical observation data, laboratory analysis and functional diagnostics, taking into account risk factors.

As is known, the most adequate method for assessing the state of the SAS is the study of catecholamines (CA) in urine. Determination of adrenaline, noradrenaline, dopamine and DOPA in daily urine was performed by trioxyindole fluorimetric method as modified by E.Sh. Matlina , Z.M. Kiseleva, I.E. Sofieva (1965). The method used for determining the activity of monoamine oxidase (MAO) in blood serum consists of oxidative deamination of a synthetic amine - benzylamine in an incubation medium under the action of MAO to benzaldehyde .

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To determine immunoglobulins in blood plasma, the radial immunodiffusion method in gel modified by Mancini was used .

The concentration of interleukin-6 was determined by a similar method of solid-phase enzyme-linked immunosorbent assay using test systems from Cytokine LLC (St. Petersburg, Russia) on a Human enzyme-linked immunosorbent analyzer (Germany).

Research results :

The levels of interleukin-6 in patients with angina and PICS did not differ significantly, whereas in patients with myocardial infarction with Q wave the indicator was 118.4±5.9 Pg/ml. In the control group, the IL-6 indicator was 26.6±1.2 Pg/ml (Fig. 1).

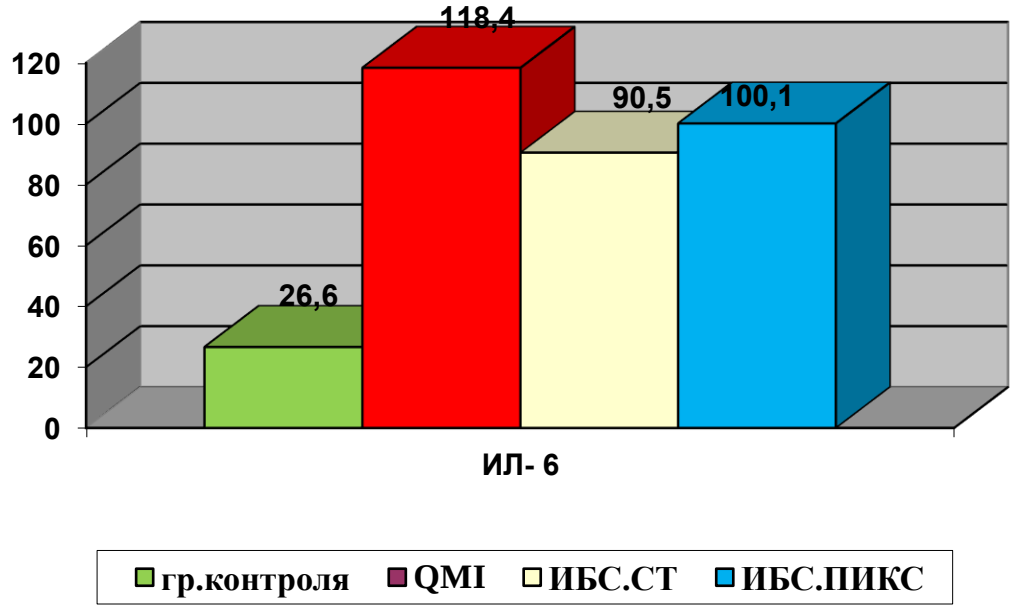

Fig. 1. Interleukin-6 levels in patients with coronary heart disease.

In parallel with the immune status, the excretion of CA and DOPA in the daily urine of patients with coronary heart disease was also studied. When analyzing the data on the daily excretion of CA in urine, the following picture is formed: in patients with QMI, a significant statistically reliable increase in A and NA is observed upon admission . In chronic forms of coronary heart disease (angina pectoris, PICS), a decrease in the level of excretion of A , NA, DA and DOPA in daily urine is noted.

Studying the daily urinary excretion of CA and DOPA in healthy individuals and individuals with stable angina, we have determined that in patients with coronary heart disease. Stable angina. 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 pectoris compared to healthy individuals was reduced by 32.7% ($P < 0.001$), conjugated by 19.6% ($P < 0.05$) and total by 26.4 % ($P < 0.001$)

Daily urinary excretion of NA patients with angina pectoris 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). A decrease in the daily excretion of all DA fractions was noted compared to healthy individuals: free by 43.6%, conjugated by 43.7%, which was statistically significant ($P <0.001$), and total by 43.7% (Table 3.9, Fig. 8) . The difference in DOPA excretion was 20.7% ($P <0.05$).

In a study of QMI patients (11 people), a significant increase in the daily excretion of CA and DOPA in the urine was found on the first day of admission to hospital (Table 1).

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A statistically significant increase in the excretion of free A was noted compared to healthy individuals 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 pectoris by 3.9 times (P < 0.001). Accordingly, the coefficient of increase in the content of total A in 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) (Table 1).

Excretion of free, conjugated and total DA in patients remained relatively lower than that of healthy subjects and was statistically insignificant. Excretion of free, conjugated and total dopamine in healthy subjects was 141.4 ±± 7.6 μg/ day ; 141.4 ±± 7.6 μg/ day ; 282.8 ±± 10 μg/ day, respectively (see Table 1). The level of DOPA excretion in QMI patients on days 1–2 of the disease was significantly lower (P < 0.001) than that of healthy subjects and was 23.9 ±± 1.9 μg/ day , while in healthy subjects the excretion of DOPA was 47.9 ±± 2 μg/ day (Table 1).

Table 1.

Content of catecholamines in daily urine in healthy people, patients with coronary heart disease. Stable angina pectoris FC II - III , QMI and PICS (mcg/ day)

No.	Groups	Catecholamines			
		A sum . (mcg/ day)	ON sum . (mcg/ day)	YES summary (μg/ milk)	**DOFA** (μg/ milk)
1	Healthy	7.3 ±0.2	16.4 ±0.3	282.8 ±6.2	47.9 ±1.0
2	IBS. Stab . angina pectoris	5.4 ±0.2	14.4 ±0.9	159.4 ±6.3	36.1 ±3.2
3	**QMI**	17.6 ±1.1	36,0±2,4	256,6±32,4	23,9±5,1
4	**ПИКС**	2,6±0,3	9,3±0,5	89,5±27,4	33,6±2,3
P_{1-2}		**P<0,001**	**P<0,05**	P<0,001	P<0,05
P_{1-3}		**P<0,001**	**P<0,001**	P>0,05	P<0,001
P_{1-4}		**P>0,05**	**P<0,001**	P<0,05	P<0,01

IN **In the metabolism of biogenic amines, the reaction of oxidative** deamination catalyzed by MAO is of key importance . In the studied groups of patients with coronary artery disease, MAO activity was manifested as follows. Thus, in the group of patients with coronary artery disease with stable angina, MAO activity decreased and amounted to 0.05±0.001 units / ex, which is 28.6% lower than the control values (p_1 <0.001) (Table 2). In the group of coronary artery disease with stable angina, MAO activity decreased even more, amounting to 0.04±0.001 units / ex, which is 42.9% lower than the control values (p_2 <0.001) (Table 2) .

In the group of patients with coronary heart disease, QMI MAO activity was maximally reduced, amounting to 0.03 ± 0.0009 units /ex, which is 57.2% lower than the control (p_4< 0.001) (Table 2).

Table 2. Monoamine oxidase activity indices in patients with coronary heart disease (M±t , units /ex.)

No.	**Groups**	**MAO**
	Control	0.07±0.002

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I	Patients with coronary heart disease, stable angina	0.05±0.001
II	Patients with coronary heart disease. QMI	0.03±0.0009
III	Patients with coronary heart disease PICS	0.04±0.001
	R_{1-2}	<0.001
	R_{1-3}	<0.001

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

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

When analyzing the data on daily excretion of CA in urine, the following picture emerges: in patients with QMI, a significant statistically reliable increase in A and NA is observed upon admission, especially with QMI . In chronic forms of coronary heart disease (angina, PICS), a decrease in the level of excretion of A , NA, DA and DOPA in daily urine is noted.

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 reliable decrease in the content of DA and DOPA in daily urine. The low content of CA precursors in 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 the excess content of A and NA. According to literary sources, it should be noted that subsequently, for a long time from the onset of the disease, the level of excretion of DA and DOPA remains significantly below the norm. Low excretion of DA and DOPA with a parallel decrease in the excretion of A and NA in the dynamics of the disease indicates depletion of the reserve capacity of the SAS in patients with MI.

Conclusion

Thus, the " immunocytokine " model of the pathogenesis of coronary heart disease does not contradict the neurohumoral theory, but complements our understanding of the mechanisms of development of coronary heart disease. The participation of immune inflammation mediators in the disease scheme expands the "base of therapeutic intervention" and opens up new prospects for increasing the effectiveness of treatment. 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 heart disease as antianginal tablets, cardiac glycosides and ACE inhibitors.

A comprehensive study of the sympathetic-adrenal system and metabolism of biogenic amines in patients with coronary heart disease showed that acute myocardial infarction is characterized by a marked impairment of catecholamine biosynthesis, which is expressed by increased urinary excretion of free and conjugated forms of adrenaline and noradrenaline. Stable angina and PICS are characterized by inhibition of the SAS functions, as evidenced by a general decrease and impairment

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of urinary excretion of catecholamines and their conjugated forms, as well as their metabolic precursor DOPA.

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