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Changes in the Production of Certain Proinflammatory Cytokines in Patients with Various Variants of Coronary Heart Disease

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Abstract: To date, it is the inflammatory process that is considered as one of the main links in the pathogenesis, clinic and prognosis of coronary heart disease. He also plays a significant role in the occurrence and subsequent development of acute myocardial infarction and the outcome of the disease, namely in the formation of atherothrombosis, alteration, necrosis and repair with further remodeling of the myocardium of the heart. Given that the prognosis of myocardial infarction is determined by both the degree of myocardial damage and complications arising during various periods of the disease, primarily cardiovascular insufficiency, studies aimed at identifying indicators that can be used in practice to predict and prevent the development of complications of myocardial infarction, determining the tactics of their treatment, are of particular relevance.

Keywords: cytokines, coronary heart disease, myocardial infarction, atherosclerosis.

Introduction

The evidence of the pathogenetic role of cytokines in atherogenesis is growing. The results of our study showed that the levels of IL-10, IL-6 were significantly higher in the group of patients with acute myocardial infarction compared with similar data in the group of patients with stable angina pectoris. The levels of IL-2, IL-8 and TNF-a in the group of patients with acute myocardial infarction were significantly lower than in the group of patients with stable angina. In the group of patients with progressive angina, the level of IL-8 was significantly lower than in the group with stable angina. An increase in the degree of atherosclerotic damage to the coronary bed was associated with an increase in IL-1P, IL-6, IL-8, TNF-a levels and a decrease in IL-2 levels. Thus, the data obtained indicate an abnormal cytokine profile in large patients with coronary disease. The use of the definition of the main proinflammatory cytokines makes it possible to expand the range of diagnostic methods for predicting the clinical course and treatment results of patients with various forms of coronary heart disease. The data obtained provide grounds for further clinical studies in this direction

The purpose of the research:

Evaluation of the effect of certain cytokines (IL-1ß, IL-2, IL-6, IL-8, TNF-α) during the atherosclerotic process in patients with various forms of coronary heart disease: myocardial infarction, stable and progressive angina pectoris.

Materials and methods of the research:

70 patients (65 men and 5 women) aged 40-68 years (on average 50+6 years) who were treated at the Samarkand branch of the Republican Scientific Center of Emergency Medical Care for coronary heart disease were examined. The duration of the disease ranged from 2 months to 15 years (on average 6 + 4.2 years). Of these, 50 patients (group 1) had angina pectoris of grades 1-4 (according to the classification of the Canadian Association of Cardiologists), 10 people (group 2) had progressive angina pectoris, 10 people (group 3) had acute myocardial infarction.

Among the patients of the first group, angina pectoris of functional class 1 (FC) was detected in 5 patients, 2 FC - in 20 patients, 3 FC - in 20 patients, 4 FC - in 5 patients. Large-focal postinfarction

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cardiosclerosis was in 20 patients. In 28 cases, there was a combination of coronary heart disease with hypertension; in 7 patients, the phenomena of circulatory insufficiency of stage 2 were detected.

In the second group of patients diagnosed with progressive angina pectoris, signs of coronary blood flow disorders were recorded earlier (2 patients had stable angina pectoris of 2 FC, 4 patients - FC, 4 patients - 4 FC), postinfarction cardiosclerosis was detected in 5 cases, hypertension was accompanied by coronary artery disease in 3 patients.

In the third group, 7 patients had a large-focal myocardial infarction, and 3 had a small-focal myocardial infarction, 2 to 10 hours old from the onset of the first signs of the disease. Coronary atherosclerosis anamnestic was detected in all patients of this group, in 4 cases myocardial infarction was repeated. The course of acute infarction was complicated in 8 patients (3 cases of cardiogenic shock, 2 cases of recurrent ventricular tachycardia, 1 case of supraventricular tachycardia paroxysm, 6 cases of stage 2 circulatory insufficiency). Hypertension was combined with coronary heart disease in 4 patients.

Results and discussions.

The study of the content of cytokines IL-2, IL-8 and TNF-α in patients with coronary heart disease revealed an inverse relationship: lower cytokine values were recorded in myocardial infarction, and high values in stable angina. The level of IL-2 in the first group was 9.1+1.6 pg/ml, and in the group of patients with myocardial infarction - 0.81+0.57 pg/ml ($p<0.01$); the level of IL-8 in the group of patients with stable angina was 94.2+27.6 pg/ml, and in the groups of patients with progressive angina and myocardial infarction- 20.03+7.4 ($p<0.01$) and 22.47+4.8 pg/ml ($p<0.05$), respectively. TNF-α values were almost three times higher in the group of patients with stable angina (0.23+0.06 pg/ml) compared with its level in patients with myocardial infarction - 0.08+0.03 pg/ml ($p<0.05$).

A repeated study of the cytokine content, performed two weeks later on the background of treatment, revealed a tendency to decrease the level of IL-1ß from 0.45+0.08 to 0.24+0.07 pg/ml and a significant decrease. During the treatment period, there was an increase in IL-8 content in patients with myocardial infarction from 22.5+4.8 to 69.8+18.8 pg/ml ($p<0.01$).

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It seemed important to find out whether there is a relationship between the severity of the course of stable angina (depending on the functional class) and the content of cytokines in the blood.

Table 1
Cytokine content in the blood of patients (pg/ml) with stable angina pectoris

Functional class of angina pectoris	IL-1P	IL-2	IL-6	IL-8	TNF-a
I-II	0,34+0,12	11,56+2,6	2,20+0,6	87+31	0,14+0,04
III-IV	0,39+0,07	8,3+2,0	2,3+0,31	83,1+36,7	0,41+0,14

The data presented in Table 1 indicate the absence of a clear relationship between the severity of stable angina pectoris and the blood content of the studied cytokines, at the same time, there was a tendency to increase the TNF-α content in patients with severe angina - 0.14+0.04 pg/ml (I-II f.c.) and 0.41+0.14 pg/ml (III-IV f.c.), and the tendency to decrease the level of IL-2 in patients with severe coronary pathology - 11.56+2.6 pg/ml (I-II f.c.) and 8.3+2.0 pg/ml (III-IV f.c.).

Depending on the degree of violation of coronary blood flow, patients were divided into 2 groups: the first included patients without hemodynamically significant stenoses, the second included patients with severe coronary insufficiency (2-3 vascular lesions with stenoses of 50% or more pa).

The dependence between the IL-2 content and the state of coronary blood flow was revealed: in patients without coronary obstruction, the cytokine level was 18.1+3.6 ng/ml, in patients with coronary sclerosis - 8.3+2.1 pg/ml ($p<0.05$).

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Cytokines IL-lß, IL-6, IL-8, had the opposite tendency, i.e. higher values were detected in patients with coronary obstruction, compared with the group of patients without coronary insufficiency.

Conclusions

Summarizing the data obtained, it can be assumed that cytokines are actively involved in the pathogenesis of coronary atherosclerosis. The content of cytokines such as IL-lß and IL-6 in the blood increases already in the first hours of myocardial infarction, and IL-8 gradually, reaching maximum values by the end of 2 weeks. Cytokines IL-2 and TNF-α practically do not react to the development of acute coronary syndrome, their values remained stably low during the acute phase of myocardial infarction.

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