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Indicators of Cytokine Status in Acute Myocardial Infarction in Women

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Abstract The problem of acute myocardial infarction is still relevant today, as mortality from it remains consistently high. The predictor for prediction in this process can be considered immunological markers that change in the early stages of the ischemic process. This article is devoted to this problem. To determine indicators of cytokine status in acute myocardial infarction in women. The study included 190 patients with coronary heart disease (CHD) aged 25 to 93 years. Of these, the 1st group consisted of 125 patients with coronary heart disease. Comparative assessment of the content of the studied cytokines in women with S-T segment elevation in coronary artery disease and obesity against the background of obesity showed. Thus, the cytokine status in women with coronary heart disease transitioning to MI, depending on the state of the S-T segment in syntropy with obesity, has features of the synthesis of pro-inflammatory cytokines (IL-17A, TNF-α) and INF-γ.

Keywords Ischemic heart disease (IHD), Cardiovascular diseases (CVD), Biomarkers

1. Introduction

In the modern world, the search for and study of new biomarkers capable of assisting in the early diagnosis of cardiovascular diseases (CVD), serving as a tool for assessing the effectiveness of therapy, being a prognostic marker of possible clinical outcomes, and a significant indicator in risk stratification remains relevant [1,3,7,10,14]. In clinical practice, the problem of multiple combined diseases has long been identified. Up to 80% of the healthcare budget in developed countries is spent on patients with four or more diseases. The most common term for this phenomenon is comorbidity [2,4,6,11]. However, only the part of combined diseases that has a common genetic basis and similar pathogenesis belongs to syntropia, diseases of "attraction," "mutual attraction" [5,8,9,12,13]. Many clinically proven syntropic diseases are known: immunocomprAMIsed diseases (allergic and autoimmune); endocrine diseases, including combined.

Purpose of the study. To determine indicators of cytokine status in acute myocardial infarction in women.

2. Materials and Methods of Research

The study included 190 patients with coronary heart disease (CHD) aged 25 to 93 years. Of these, the 1st group consisted of 125 patients with coronary heart disease, where women were somewhat more numerous - 65 (52%), with an average age of 63.2±8.7 years. The number of men was 60 (48%), their average age was 62.1 ± 11.1 years; The 2nd group consisted of 65 patients with obesity, including 30 women (average age 62.6±7.8 years) and 35 men (average age 62.8±10.3 years). The verification of coronary heart disease was carried out according to the requirements of the World Health Organization (WHO), classified according to the International Classification of Diseases (ICD-10). Exclusion criteria for the study were patients with acute coronavirus infection (positive PCR test and presence of IgM class antibodies on ELISA), cardiomyopathies and myocarditis, acute infectious and systemic diseases. Inclusion criteria were patients with a diagnosis of coronary heart disease, clinically confirmed by changes in the electrocardiogram and/or the dynamics of cardiospecific enzymes, hospitalized for OCS. The onset of symptoms was no more than 24 hours before hospitalization. Symptoms that make suspicion of OCS (anginal pain at rest ≥ 20 min, first-time occurrence of angina of at least III functional class (FC), increase of angina class to III FC) and presence of OCS signs with ST elevation on ECG (or absence of changes on ECG).

3. Research Results

To study the immunological aspects of S-T segment instability in AMI in patients with obesity, analyses were conducted to study cytokines IL-17A, TNF-α, and INF-γ. For statistical processing of patients with coronary artery disease against the background of obesity and transition to

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MI, we distributed the S-T segment condition.

The 1st group consisted of 35 women with S-T segment elevation and obesity.

The 2nd group consisted of 35 women with obesity without S-T segment elevation.

The 3rd comparison group consisted of 30 patients with coronary artery disease with stable angina against a background of obesity;

Pro- and anti-inflammatory cytokines are considered important mediators of intercellular interactions in the immune system, as well as primary mediators of neuroimmune interactions. The study of cytokines in AMI showed statistically significant shifts in the studied parameters in women depending on the state of the S-T segment against a background of obesity. A statistically significant increase in the level of IL-17A in women, regardless of the state of the S-T segment, is noted in AMI by 2.2 times (up to 210.3±13.2 pg/ml in patients of the 1st group, up to 219.6±26.0 pg/ml in patients of the 2nd group), compared to the data of women in the comparison group (98.1±12.3 pg/ml) (Table 1).

Table 1. Cytokines in women with AMI

References	1-st group n=35	2-nd group n=35	3-rd group, n=30
IL-17A, pg/ml	210,3 ±13,2*	219,6±18,4*	98,1±12,3
TNF-α, pg/ml	87,5±19,7	105,1±16,2*	57,2±7,6
INF-γ, pg/ml	34,5 ±6,7*	34,4±6,8*	70,9± 9,7

Note: * Significance is significant compared to the 3rd comparison group (*P<0.05);

It is known that IL-17A is a pro-inflammatory cytokine, mediating the connection between T-cells and the hematopoietic system. T-cell-derived IL-17A induces fibroblasts, which, as a result, produce IL-6, -8, ICAM-1 and G-CSF, presumably through an NF-κB-mediated mechanism. IL-17 enhances the proliferation of partially activated T-cells and increases the production of nitric oxide (NO) in the cartilage, which also allows it to be considered a cytokine of bone resorption.

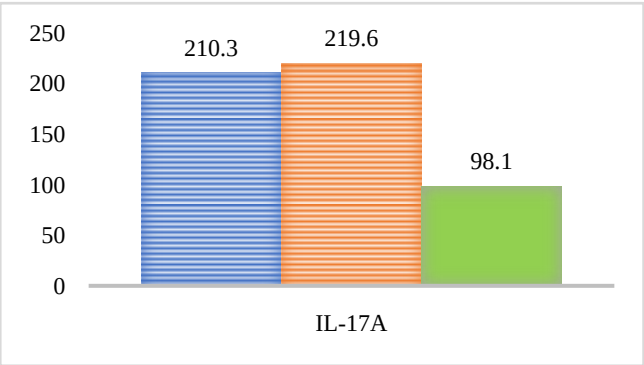

Figure 1. Interleukin-17A content in women with cardiovascular pathology

The study established an increase in the level of IL-17A in AMI in women with obesity indicates an activation of the cytokine synthesis system in response to a disruption of microcirculation in the myocardium. A higher increase in its level is observed in women with S-T segment elevation (2nd group - 219.6±18.4 pg/ml), compared to the indicators of the comparison group - 98.1±12.3 pg/ml, which is 2.3 times higher.

At the same time, the peak concentration of IL-17A >118.0 pg/ml in AMI with S-T segment elevation, IL-17A>162.0 pg/ml in AMI without S-T segment elevation, acts as an informative indicator of the severity and outcome of AMI in women with obesity.

It is important to consider the content of TNF-α and INF-γ in AMI. In our studies, the content of TNF-α in women differed in a comparative aspect, which indicates a dependence of tumor necrosis factor synthesis on the state of metabolism in the body, in particular, the S-T segment in obesity-induced AMI.

TNF-α in women of the 1st group tended to increase to 87.5±19.7 pg/ml, and in the group of women of the 2nd group it increased 1.84 times (to 105.1±16.2 pg/ml) compared to the data of the comparison group 57.2±7.6 pg/ml (p<0.05).

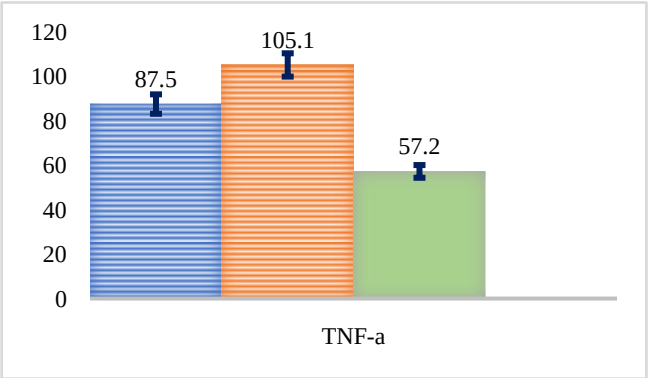

Figure 2. The content of tumor necrosis factor alpha in cardiovascular pathology in women

Consequently, obesity and the absence of S-T segment elevation in women is a critical risk factor for the development of MI.

Currently, it has been proven that IFN-γ is a playootropic cytokine, possessing a wide spectrum of antiviral, antiparasitic, and antitumor effects; it has numerous immunomodulatory effects, including stimulation of tissue compatibility antigen expression of classes I and II.

The study of the state of IFN-γ synthesis showed a 2.0-fold decrease in its level both in women of the 1st group - 34.5±6.7 ng/ml, and in women of the 2nd group - 34.4±6.8 ng/ml, versus the values of the comparison group - 70.9±9.7 ng/ml (p<0.05).

Taking into account the established fact that INF-γ has an irreversible cytotoxic effect on transformed cells, while its cytostatic effect on normal cells is reversible; it enhances cytotoxic reactions mediated by T-lymphocytes and NK-cells; at the same time, it selectively increases the resistance of normal cells to the cytopathic effects of NK-cells, the obtained information on a decrease in its level in cardiovascular diseases in women regardless of the state of the S-T segment in the syntropy of coronary heart disease with obesity allows us to conclude that in women in the postmenopausal period, a decrease in the protective properties of the body occurs,

the resistance of normal cells to the cytopathic effects of NK-cells decreases, and as a result of the decrease in the cytotoxic effect of gamma interferon on transformed cells, conditions are created for the transformation of cardiomyocytes with the development of MI.

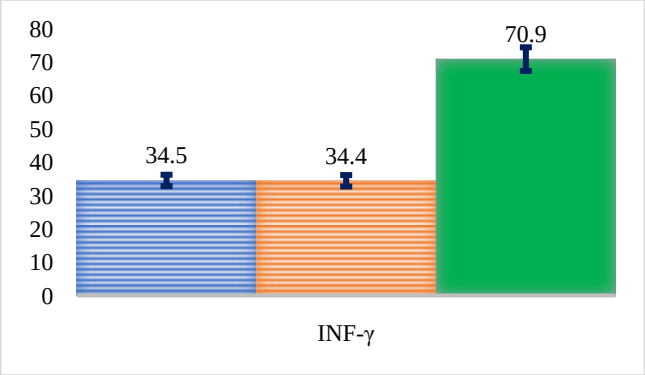

Figure 3. Interferon alpha content in women with cardiovascular pathology

Comparative assessment of the content of the studied cytokines in women with S-T segment elevation in coronary artery disease and obesity against the background of obesity showed.

Consequently, all the obtained analysis results indicate the activation of pro-inflammatory cytokine synthesis with cardiomyocyte breakdown due to a decrease in INF-γ synthesis in the development of obesity in women with coronary artery disease. At the same time, the simultaneous increase in the levels of IL-17A and TNF-α in women without an increase in the S-T segment in coronary artery disease against the background of obesity shows a higher risk of developing ischemia and cardiac tissue necrosis.

4. Conclusions

Thus, the cytokine status in women with coronary heart disease transitioning to MI, depending on the state of the S-T segment in syntropy with obesity, has features of the synthesis of pro-inflammatory cytokines (IL-17A, TNF-α) and INF-γ.

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