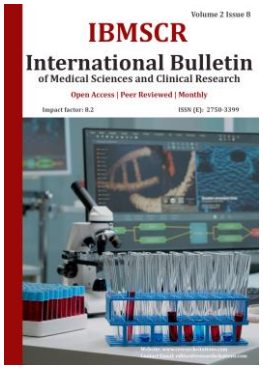

INFLUENCEOF MODIFIED COMPLEX THERAPY WITH THE ADDITION OF COLCHICINE AND PENTAXOPHYLIN TO THE STANDARD TREATMENTON THE DYNAMICS OF C-REACTIVE PROTEIN AND PRO-INFLAMMATORY CYTOKINESIN PATIENTS WITH POST-INFARCTION CHF, DEPENDING ON THE FEATURES OF LV MYOCARDIAL DYSFUNCTION

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At present, the pathogenesis of CHF should be considered in the light of modern concepts in the field of cardiology, endocrinology, immunology, and molecular medicine. One of the latest achievements of modern cardiology is the establishment of the role of activation of the cytokine system in the pathogenesis of CHF [23,49].

The concept of the formation of pathophysiological mechanisms of CHF remains not fully understood. At present, the pathogenesis of CHF should be considered in the light of modern concepts in the field of cardiology, endocrinology, immunology, and molecular medicine. One of the latest achievements of modern cardiology is the establishment of the role of activation of the cytokine system in the pathogenesis of CHF [59, 65, 66]. One of the latest achievements of modern cardiology is the establishment of the role of activation of the cytokine system in the pathogenesis of CHF [56].

This mechanism is based on the concept of nonspecific activation of macrophages and monocytes in the interstitial fluid as an inducer of the synthesis of pro-inflammatory cytokines that determine the evolution of left ventricular (LV) dysfunction of the heart [61,130,147].

The most important class of biologically active substances that have an immunoinflammatory effect are pro-inflammatory cytokines. Among them, only a few are related to the formation and progression of CHF, affecting the cardiovascular system through various mechanisms. They have a negative inotropic effect, stimulate protein synthesis, increase capillary permeability, promote the progression of myocardial hypertrophy and participate in left ventricular remodeling processes [1,44,50].

Purpose of the study: to study the effect of modified complex therapy with the addition of colchicine and pentaxophiline to standard treatment on the dynamics of patients with postinfarction CHF

Material and methods: All patients who carried out a modified anti-inflammatory and immunocorrective therapy with the addition of colchicine and pentaxophylline to the standard therapy were divided into 2 groups depending on the severity of LV remodeling according to echocardiography data, LV myocardial diastolic dysfunction and mixed LV myocardial dysfunction, according to OSSN criteria (2010). Group 1 included 36 (62.1%) patients with LV diastolic dysfunction (stages I–IIA), group 2 included 22 (37.9%) patients with mixed systo-diastolic LV myocardial dysfunction (stage IIB). During the observation period, 4 (6.9%) adverse cardiovascular events occurred. 1 patient of group 1 and 3 patients

of group 2 died. The cause of death of one patient from group 1 was complex arrhythmias. In group 2, the cause of death was progressive heart failure.

Research results showed that patients with mixed LV myocardial dysfunction had significantly more severe manifestations of CHF: a higher FC of circulatory failure and a more significant decrease in exercise tolerance. It was also noted that the development of CHF is accompanied primarily by a change in the geometry of the LV and an increase in the mass of the LV myocardium.

As CHF progressed, an increase in the linear dimensions of the LV cavity was observed. In patients with the development of mixed LV myocardial dysfunction, as a result of remodeling, there was a decrease in the relative LV wall thickness index, which indicates the development of eccentric LV hypertrophy and the progression of mixed LV myocardial dysfunction, the severity of which increases with the increase in CHF FC. In patients with diastolic LV dysfunction, concentric LV hypertrophy prevailed (77%), and in 23% of cases in this group of patients, the development of eccentric LV hypertrophy was noted.

Changes in the levels of the studied cytokines in the blood serum and the concentration of CRP in patients with CHF were characterized by their significant increase with the progression of CHF (Table 1).

The maximum level of cytokines - TNF-α (191.9±19.7pg/ml),IL-1β (193.4±54pg/ml),IL-6 (199.1±35.1pg/ml)was found in patients with mixed LV dysfunction. In patients with LV diastolic dysfunction, there was also an increase in the level of TNF-α (137.9±31.6pg/ml)blood serum, the level of serum CRP before treatment was increased both in group 1 and in group 2, and amounted to 5.4±0.41 and 9.7±0.23 mg/l, respectively, which is significantly higher than normal values.

Table 1.

Dynamics of inflammation markers and laboratory parameters before and after treatment in the group receiving modified therapy with the addition of colchicine and pentaxophiline to standard therapy in sick with diastolic and mixed LV dysfunction

Indicators	Group ILV diastolic dysfunction (n=20)		Group IIMixed LV dysfunction (n=16)	
	Before treatment	After 3 months	Before treatment	After 3 months
CRP, mg/l	5.4±0.41	3.4±0.65	9.7±0.23	4.7±0.31
IL-1β, pg/ml	158.4±37.1	68.1±45.4	193.4±54	93.4±19.4
IL-6, pg/ml	149.3±32.4	88.9±12.2	199.1±35.1	139.3±18.9
TNF-α, pg/ml	137.9±31.6	82.9±14.6	191.9±19.7	107.9±21.6

* Significant difference (p< 0.05) from pre-treatment scores; ** significant difference(R< 0.05) from that of group 1.

We have established a relationship between the levels of pro-inflammatory cytokines in the blood serum and the morphofunctional parameters of the left ventricle. In the group of patients with mixed LV dysfunction, maladaptive remodeling showed a correlation between TNF-α and myocardial mass (r = 0.65; p < 0.05); MS (r = 0.63; p < 0.05); with the state of diastolic function: peak E and E/A (r = 0.72; p < 0.05, r = 0.58; p < 0.05). There was no

connection with EF, but there was a correlation with the EF/MS index, which characterizes the specific contractility of the myocardium ($r = 0.46$; $p < 0.05$). In patients with LV diastolic dysfunction, IL-6 correlated with MS ($r = 0.39$; $p < 0.05$) and LV wall thickness ($r = 0.75$; $p < 0.05$), while TNF-α correlated with LDL ($r = 0.41$; $p < 0.05$) and TAG ($r = 0.38$; $p < 0.05$).

Therefore, the results of this study demonstrated that serum levels of pro-inflammatory cytokines in patients with CHF are associated with the development and severity of clinical manifestations of CHF. An increase in serum pro-inflammatory cytokines was found in patients with mixed left ventricular dysfunction.

In our study, the level of CRP significantly decreased during treatment with colchicine and pentaxophylline in both groups, which indicates a decrease in inflammation and is associated with a decrease in cardiac decompensation and, accordingly, the risk of an unfavorable course. This is consistent with the results of a number of studies, which also noted a correlation between the level of pro-inflammatory cytokines and the severity of clinical manifestations of CHF, a decrease in life expectancy, and a decrease in their concentration during treatment is associated with clinical improvement [2].

Conclusions: Summarizing, it can be noted that the development of mixed LV myocardial dysfunction is accompanied by a significant increase in the level of pro-inflammatory cytokines and CRP in the blood serum. The use of modified complex therapy with colchicine and pentaxophylline in patients with postinfarction CHF is accompanied by a decrease in the level of pro-inflammatory cytokines (TNF-α,IL-1β, IL-6), CRP of blood serum and improvement of the structural and functional state of the left ventricle in CHF in patients with AMI

Thus, after 12 weeks, most patients achieved a significant decrease in the level of pro-inflammatory cytokines and CRP, which contributed to the prevention and inhibition of the progression of remodeling and myocardial dysfunction. The results achieved expand the range of therapeutic effects and indicate the emergence of new and modern aspects of assessing the effectiveness of therapy in this category of patients.

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