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ASSESSMENT OF IMMUNOREACTIVITY DISORDER IN CHRONIC HEART FAILURE OF VARIOUS ETIOLOGIES

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Abstract:
Despite the development of special recommendations for the treatment of patients with CHF, the total number of hospitalizations and the frequency of early readmissions in this condition has not decreased, but tends to increase. All this leads to the search for new methods of diagnosis and therapy of CHF. According to a number of researchers [Mustafina D.M., 2001, El Sherif W.T., El Tooney L.F., Meki A.R., Abdel Moneim A., 2005] immune changes can play a key role in the pathogenesis of CHF. But in order to understand the contribution of immune mechanisms to the development of complications in coronary heart disease, it is necessary to compare this nosology with each other, where immune disorders play a key role.
The available data suggest that cytokines play an important role in the pathogenesis of inflammation in CHF of ischemic and non-ischemic etiology. However, the mechanisms of inflammation development involving cytokines have not been disclosed, and the features of the relationship of inflammatory mediators with other parts of the immune system in CHF of various etiologies have not been established.

Keywords: antimyocardial autoantibodies, alatate aminotransferase, angiotensin II receptor antagonists, aspartate aminotransferase, dilated cardiomyopathy, endothelial dysfunction.

Introduction

Chronic heart failure (CHF) is the outcome of many cardiovascular diseases of both inflammatory and non-inflammatory nature, a serious cause of disability and shortening of life expectancy of the population of developed countries.
Statistics show that over the past 20 years, the prevalence of CHF in developed countries has increased significantly, reaching epidemic levels in some of them [Cowie M.R. et

al., 1997; Kannel W.B., 1991; Brophy J.M., 1992; Messner T. et al., 1996; Connel J.B. et al.., 1994; Smith W., 1985; Vasan R.S. et al., 1995; Czuriga I., 2005]. In the USA, more than 5 million people suffer from heart failure, of which 1.5 million have its high (III-IV) functional class according to the NYHA classification [American Heart Association, 1998]. In 2002, there were 8.1 million people in the Russian Federation with clear signs of CHF, of which 3.4 million had terminal III-III FC diseases [Ageev F.T. et al., 2004].

Recent studies indicate the involvement of the immune system, namely proinflammatory cytokines in the development of CHF [Olbinskaya L.I. et al., 2001; Parission J.T.et al., 2005; Conraads V. et al., 2006; von Haehling S.et al., 2006]. The effect of elevated IL-18 levels on the severe clinical course of the disease (increased functional class (FC) of CHF) and decompensation in CHF of ischemic etiology has been proven [Yamaoka-Tojo M et al., 2002]. An increase in CHF FC was observed [Munger M.A. et al., 1996; Torre-Amione G et al., 1996; El SherifWT et al, 2005] and impaired diastolic heart function [El Sherif WT et al., 2005] with increased levels of IL-1, sIL-2R, TNF-a, IL-6, and high levels of TNF-a were combined with the progression of CHF [Mann D.L et al., 2001] and deterioration of the quality of life [Mustafina D.M., 2003]. A high concentration of IL-6 was found to be associated with a deterioration in the contractile function of the heart in CHF [Kell R et al., 2002]. Cytokines IL-1 and TNF-a have been found to enhance the production of the MCP-1 protein, which causes the migration of monocytes into the intima of blood vessels [Libby P et al., 1995], and thereby contribute to the development of atherosclerosis. It was proved that high levels of IL-12, IL-18, and IFN-y in experimental animals contributed to the development of atherosclerosis, and the blockade of these cytokines reduced the severity of atherosclerosis by 15-69% [Kleemann R et al., 2008]. A number of authors have investigated inflammatory factors involved in the pathogenesis of dilated cardiomyopathy (DCM). Thus, the study of endomyocardial biopsies revealed an increase in the production of CRP mRNA by cardiomyocytes and an increase in the expression of TNF-a mRNA in the myocardium, which correlated with the expansion of cavities and an increase in heart volume [Satoh M et al., 2005; Chang HJ et al., 2003]. The authors showed that high levels of IL-6 are associated with left ventricular dysfunction and high mortality [Kanda T et., 2004], and increased levels of TNF-a, IL-6 were combined with impaired interstitial myocardial collagen metabolism [Timonen P et al., 2008]. It was revealed that high levels of cytokines TNF-a and IFN-a [Paleev F.N. et al., 2004] correspond to the malignant course of myocarditis and the progression of circulatory insufficiency.

It has been proven that the serum of patients with DCMP has a high chemotactic ability, which was associated with an increased level of MCP-1 [Sigusch NN et ai., 2006]. In DCMP, chemokines (MCP-1, IL-8) and chemokine receptors (CXCR 4) were localized in large numbers in the myocardium, which proves the participation of these factors in the development and progression of this disease [Seino Y et al., 1995; Damas JK et al., 2000].

The purpose of the work. To study the role of humoral factors of inflammation and endothelial dysfunction in the development of chronic heart failure of various etiologies

Materials and methods of research. A screening examination of 50 patients was conducted. As a result of the screening, 27 patients with CHF-IV FC (NYHA), which complicated the course of coronary heart disease and DCMP, were included in the study. Markers of endothelial and left ventricular dysfunction and immune activation were studied in 23 patients with CHD stage I-IIB and I-IV FC according to NYHA. Of these, 21 (95%) men and 2 (5%) women aged 23-64 years. The average age is 48±8 years. FC I had 10 (23%) people, FC II - 10 (23%), FC III - 11 (26%), FC IV - 12 (28%).
The study also included 44 patients with DCMP stages I-IIB and I-I FC CHF. Among them, 42 men (95%) and 2 women (5%) aged 22 to 61 years old. The average age is 43±10 years. There were 10 (23%) people with FC I, 9 (20%) with FC II, 13 (30%) with FC III, 12 (27%) with FC IV. General clinical examination of patients with coronary heart disease+PIX and CHD+AH with heart failure FKI-IV (NYHA)
Determination of markers of immune inflammation of proinflammatory cytokines-IL-6, TNF α and anti-inflammatory cytokine IL-10 in blood serum by solid-phase enzyme immunoassay in patients with coronary heart disease+PEAKS and CHD+AH complicated by heart failure FC I-IV (NYHA) A comparative analysis of the relationship of inflammatory markers in patients with CHF of various etiologies (CHD + PIC, CHD + AH).
Investigation of the dynamics of humoral inflammatory and autoimmune factors in patients with coronary heart disease+PEAKS and CHD+AH complicated by heart failure FC I-IV (NYHA) on the background of standard therapy and on the background of statin treatment. Statistical processing of the received material.

The results of the study. As can be seen from the table data, during statin treatment in the CHD group, there was a statistically significant decrease in the levels of NT-proBNP, CRP, IFN-Y, IL-8, sIL-2R, endothelin, and nitric oxide metabolites. Increased levels of IL-6 and IgG were detected during statin therapy, which indicates that statins do not fully control all aspects of the inflammatory process.
Against the background of statin treatment, there is a decrease in the number of patients in the III, IV FC CHF (NYHA). Initially, there were the following number of patients in FC CHF: FC I - 10 (23%) people, FC II - 10 (23%), FC III – 11 (26%), FC IV - 12 (28%).After statin treatment: I FC CHF - 16 (40%) people, II FC CHF - 9 (22.5%) people, III FC CHF- 9 people (22.5%), IV FC CHF - 6 people (15%). Thus, against the background of statins, CHF decreased in 16 (37%) patients with FC, and in 24 (56%) patients, FC remained unchanged. In this group, 3 (7%) patients died, the cause was sudden death.
Against the background of statin therapy, despite a decrease in the content of inflammatory markers, pronounced correlations between proinflammatory factors

remain, which indicates that statin therapy does not fully control all links of the inflammatory process in patients with CHF with coronary heart disease.

As can be seen from the table, against the background of statin therapy in patients with CHF with coronary heart disease, the level of NT-proBNP was statistically significantly correlated with the content of CRP (p=0.45), with IL-6 (p=0.48). IL-8 content was negatively correlated with PV (p=-0.58). IFN-y concentration was negatively correlated with diastolic heart function IVRT (p=-0.82).

Elevated IL-10 levels negatively correlated with IgG (p=-0.48) and IgA (p=-0.44) concentrations. CRP value correlated with IL-6 levels (p=0.46), with endothelin content (p=0.42), with systolic heart function: CSR (p=0.46), with CSR (p=0.46), with CDR (p=0.43), with CDR (p=0.42), with PV (p=-0.35). The content of IL-6 was directly correlated with the level of endothelin (p=0.49).

In the CHD group, an increase in the number of patients with detectable IL-10 levels was observed: before statin treatment, 3 (7%) people had detectable IL-10 levels (0.62 pg/ml, 11.36 pg/ml, 1.57 pg/ml). After the therapy with atorvastatin, the detectable level of IL-10 was in 21 people (49%) (3.60 (2.40; 6.90) pg/ml).

Thus, statins in coronary heart disease have a multidirectional effect on the level of inflammatory markers, which indicates that statins do not completely correct all links of the inflammatory process. The preservation of pronounced correlations between proinflammatory factors against the background of statin therapy, despite a decrease in their content, apparently indicates that statin therapy does not allow controlling all aspects of the inflammatory process in patients with CHF with coronary heart disease.

In our study, 23 (52%) patients had a sinus rhythm of the heart, and 21 (48%) patients with DCMP had a cardiac arrhythmia type disorder. The following CRP levels were found in patients with sinus rhythm - 1.19 (0.86; 2.22) g/l, IFN-y -22.33 (19.87; 34.22) pg/ml. Atrial fibrillation, an increase in CRP levels was detected - 3.24 (1.50; 6.27) g/l, IFN-y - 34.22 (32.17; 117.07) pg/ml. The analysis of the studied parameters in the groups with sinus rhythm and atrial fibrillation showed that patients with atrial fibrillation had a higher content of IFN-y and CRP (p=0.006, p=0.026, respectively), which indicates the key role of inflammation in the occurrence of complications of the disease - rhythm disturbances of the type of atrial fibrillation.

In the study, the value of CRP <3 g/l was taken as normal. Our studies have shown that patients with normal CRP (<3 g/l) and elevated CRP (>3 g/l) differ in the concentration of sIL-2R and metabolites of nitric oxide (N0) (Table 13). CRP was increased in 17 (38.6%) patients and amounted to 6.27 (3.78; 7.76) g/l. And also, as a result of the correlation analysis, a statistically significant direct relationship was revealed between the content of CRP and the severity of heart failure according to CHF FC (p=0.41), with the level of NO metabolites (p=0.46). A statistically significant association of IL-8 with CRP was revealed in patients with elevated NT-

proBNP (NT-proBNP >1382 pg/ml) p=0.47. No such association was found in the group of patients with NT-proBNP <1382 pg/ml. A correlation was established between the elevated level of IL-8 and NT-proBNP (p=0.40), with sIL-2R (p=0.41). And the relationship between the levels of IL-6 and IL-10 (p=0.95) (p=0.051) was also revealed, and the detectable level of IL-10 was noted in 7 (16%) patients.

As can be seen from the table, with an increase in FC CHF (NYHA), there is an increase in the level of CRP, NT-proBNP and a decrease in PV. A correlation was established between the severity of heart failure with the concentration of CRP (p=0.41), with NT-proBNP (p=0.65), with endothelin content (p=0.41), with the level of nitric oxide metabolites (p=0.36), with PV (p=-0.37) and with diastolic heart function: Peak A vel (rate of transmittal flow into the late diastole) (p=-0.64), IVRT (p=-0.56), Decel time (p=-0.74), E/A (p=0.58). The level of IFN-y was inversely correlated with the diastolic function of the Decel time heart (p= - 0.59). In patients with DCMP with detectable IL-6 levels, the E/A ratio is statistically significantly higher (p=0.040) than in the group where IL-6 was not detected (2.2 (1.6; 2.4) vs. 1.4 (0.7; 1.8)).

These autoantibodies were found in 15 patients with DCMP, of which 6 had a titer of 1:80, 4 had a titer of 1:160, and 5 had a titer of 1:20 (see Figure 4). We have identified certain correlations between inflammatory mediators in the absence and presence of AMAT. In patients with DCMP in the presence of AMAT, elevated IL-8 levels directly correlated with the content of endothelin (p=0.58) and nitric oxide metabolites (p=0.54), negatively with PV (p=-0.56). The content of CRP correlated with the level of nitric oxide metabolites (p=0.61) and IL-6 (p=0.83). The level of IL-6 was directly correlated with the level of IL-18 (p=0.94), with the level of nitric oxide metabolites (p=0.83). IFN-y was negatively correlated with PV (p=-0.55), with the diastolic function of the heart Decel time (p=-0.89), which indicates the involvement of inflammatory mediators in the development of endothelial dysfunction and disorders of systolic and diastolic heart function. Correlations between NT-proBNP and IL-8 (p=0.57)1 were revealed in DCMP with the presence of AMAT, indicating a link between the inflammatory process and the severity of heart failure.

In patients with DCMP and high AMAT titers (1:80 and 1:160), the following correlations were revealed: NT-proBNP negatively correlated with PV (p=-0.71), directly correlated with IL-8 (p=0.68) and sIL-2R (p=0.67). High levels IL-8 was directly correlated with sIL-2R (p=0.66), with CRP (p=0.64), and with nitric oxide metabolites (p=0.68). The content of CRP was directly correlated with the level of IL-8 (p=0.64), IL-6 (p=0.90), and nitric oxide metabolites (p=0.64). The IgA level was directly correlated with the DAC (p=0.67).

Conclusions

In chronic heart failure, patients with ischemic heart disease and dilated cardiomyopathy have impaired endothelial function. At the same time, the data in patients with ischemic heart disease and dilated cardiomyopathy do not significantly differ (in ischemic heart disease, the indicators of flow-dependent vasodilation were 4.27 (2.50; 6.65)%, in dilated cardiomyopathy -4.71 (3.57; 6.81)%)

In CHD, an association of inflammatory mediators with the severity of heart failure was revealed (in CHD - CRP, IL-6 with NT-proBNP; in DCM - IL-8 with NT-proBNP) indicating the involvement of inflammatory mechanisms in the pathogenesis of heart failure in this category of patients

In CHD and DCMP, an association of rhythm disturbances by the type of atrial fibrillation with an increase in the level of proinflammatory factors was revealed. In patients with coronary heart disease and arrhythmia, an increase in the content of proinflammatory mediators (IL-18, SIL-2R, CRP) was found. In the group of patients with DCMP with cardiac arrhythmia, an increase in the level of IFN-y, CRP was detected, which is probably associated with the Th-I type of inflammatory reaction.

References

1. Belenkov Yu.N., Ageev F.T. et al. Epidemiology and prognosis of chronic heart failure (Epidemiology and Prognosis of chronic heart failure) [in Russian]. Russian Medical Journal. 1999; 2:51-56.
2. Belenkov Yu.N., Mareev V.Yu., Ageev F.T. Medicinal ways to improve prognosis in patients with heart failure. M.; "Insight". 1997:77.
3. G.I.Kodirov, I.M.Tashtemirov, N.R.Uzbekov, G.Yuldashev noninvasive method of diagnosis of heart failure. Eurasian Journal of Cardiology, 267
4. Kobn J.N. Treatment of chronic heart failure. N. English J-Med.1996; 335: 490-8.
5. Deranged cardiac metabolism and the pathogenesis of heart failure. Card Fail Rev 2016; 2: 8-13.
6. S.A. Kityan, M.A. Khujamberdiev, N.R. Uzbekova, N.M. Badalbaeva Significant Pathogenetic Factors in the Development of Chronic Heart Failure with Preserved Ejection Fraction JournalNX 7 (03), 67-72
7. Blumink G.S., Knetsch A.M., Sturkenbum M.K., Strauss S.M., Hoffman A., Dekers J., Witteman J.Sm., Stricker B.K. Quantitative assessment of the heart failure epidemic: prevalence, incidence, lifetime risk and prognosis of heart failure Rotterdam To study. EurHeartJ England. 2004;25: 1614-1619.
8. G.I. Kodirova, M.A. Khuzhamberdiev, I.M. Toshtemirov, B.M. Vakhabov Violation of the processes of peroxidation and the immune system in patients with myocardial infarction Eurasian Journal of Cardiology, 212
9. SOLVD researchers studied the effect of enalapril on mortality and development of heart failure in asymptomatic patients with reduced left ventricular ejection fraction.

N English J Med. 1992; 327:685-691.

10. Redfade M. et al. The burden of systolic and diastolic ventricular dysfunction in a community assessing the magnitude of the heart failure epidemic. JAMA. 2003; 289, 194-202.
11. Vanrietis, Hawes O.V., Limburg A., K.Silva., Landman May, Van der Hoeven H., Rutten F.H. Prevalence of unrecognized heart failure in elderly people with shortness of breath during exercise. Eur J Heart failure. 2014; 16:772-777.
12. Filippatos G., Parissis J.T. Diagnosis and prognosis of heart failure in the elderly: proof of the usefulness of pudding lies in its consumption. Eur J Heart failure. 2011; 1:467-471.