IMPORTANCE OF GALECTIN-3 IN THE DEVELOPMENT OF FIBROSIS PROCESSES IN CHRONIC HEART FAILURE DEVELOPED ON THE BASIS OF RHEUMATIC HEART DEFECTS

Gadaev Abdigaffar Gadaevich
Kayumov Laziz Kholmurodovich
Tashkent Medical Academy
Bukhara Medical Institute named after Abu Ali ibn Sina

Summary. *In chronic heart failure developed on the basis of rheumatic heart defects, inflammatory processes are long and hidden. This ultimately leads to the development of fibrotic processes in the interstitial tissue of the heart. The results of correlation and regression analysis showed an increase in galectin-3 indicators in parallel with inflammatory processes in patients.*

Keywords*: inflammatory processes, chronic heart failure, myocardial hypertrophy*

THE URGENCY OF THE PROBLEM

It is known that ischemic heart disease (IHD) and arterial hypertension are the leading causes of chronic heart failure (CHF). At the same time, in the analyzes presented in the literature, it was noted that rheumatic heart defects are of great importance among the non-ischemic causes of the development of CHF. These sources show that rheumatic disease is more common among young children and elderly people. The disease is associated with immune changes against group A streptococci, and primarily mitral and aortic valves are affected [16]. Rheumatism is associated with more mitral valves and prolapse in women, and regurgitation or stenosis of aortic valves in men [8, 7].

According to various sources, the occurrence of CHF in this group of patients ranges from 4% to 14%. In particular, in the observation conducted by J. McMurray and co-authors, a well-known researcher dealing with the problems of CHF in Scotland, 8% of patients had CHF developed on the basis of rheumatic heart defects [8].

Activation of the immune system and systemic inflammatory processes play an important role in the progression and development of the disease in patients with rheumatic heart defects. In CHF, regardless of the etiology of the disease, the amount of pro-inflammatory cytokines in the blood serum was found to be significantly higher than the normal values. Hypoxic processes primarily stimulate the production of hypoxia-inducible factor 1 and α -tumor necrosis factor (α-TNF) in cardiomyocytes, leading to the activation of monocytes and macrophages [3]. Their activation increases the synthesis of a number of inflammatory cytokines, causing further damage to the myocardial cells subjected to ischemia [1]. In a number of scientific studies, it has been proven that galectin-3 in the blood serum of patients

with SUE causes myocardial hypertrophy and has a stimulating effect on fibrosis processes, which are considered important in heart remodeling, and shows the progression of the disease and the development of unpleasant complications [2].

Galectin-3 as a biomarker of fibrotic changes in the myocardium and heart failure is attracting more and more attention of the world's leading researchers. Galectin-3 belongs to the β-galactoside binding protein family and is produced by many cells. Neutrophils, macrophages, fibroblasts and osteoclasts belong to this group of cells [6]. It has chemotoxic properties against macrophages and monocytes, enhances pro-inflammatory signals, increases neutrophil adhesion and release of pro-inflammatory factors from leukocytes, participates in phagocytosis of neutrophils by macrophages [5].

However, the above-mentioned observations were made in advanced cases based on CHF arterial hypertension and UIK. Blood levels of galectin-3 have not been studied in patients with this severe complication resulting from rheumatic heart disease. It is known that the processes observed in the body in rheumatism are somewhat different from arterial hypertension and IUD. From this point of view, the study of galectin-3 in the blood of patients with CHF developed on the basis of rheumatic defects is not only of scientific, but also of practical importance.

MATERIALS AND METHODS

This scientific work was carried out in 2022 and 2023 in- the Bukhara Regional Branch of the Specialized Cardiology Scientific and Applied Medical Center of the Republic of Uzbekistan and in the Bukhara Regional Multidisciplinary Medical Center, patients with advanced CHF on the basis of rheumatic heart defects and ischemic heart diseases. Based on the assigned tasks, the monitoring was carried out as follows. In it, 120 patients with developed CHF on the basis of rheumatic heart disease were recruited as the main group. Their average age was 46.8±1.3, men were 41 (34.2%) and women were 79 (65.8%). The average duration of chronic rheumatic heart disease was 12.84±0.45 years. The main group consisted of 48 (40%) patients who underwent surgery and 72 (60%) patients who did not. 40 patients with advanced CYuE due to ischemic heart disease were included in the control group. Their average age was 64.8±2.3, men were 26 (65%) and women were 14 (35%). The period of illness of the patients with IUD was on average 8.5±0.6 years.

the generally accepted laboratory [general blood analysis and urinalysis, alanine aminotransferase , aspartate aminotransferase , bilirubin, urea, creatinine, C reactive protein, antistreptolysin] and instrumental [electrocardiography, echocardiography, ultrasound examination, X-ray of the lungs] tests in all patients - 6, α-tumor necrosis factor, galectin-3 were detected. Quantitative index of galectin-3 in blood serum was determined by enzyme immunoassay using human Galectin-3 ELISA reagents (Germany). A standard with a molecular weight of 26 kDa was used in the set of reagents used for its determination. Test sensitivity was 0.29 ng/ml. Galectin-3 reference indicator was equal to 8.6[3.7;11.7] ng/ml.

RESEARCH RESULTS AND DISCUSSION

It is known that fibrotic processes in the heart muscle are one of the leading causes of its remodeling. Therefore, the study of fibrosis markers plays an important role in predicting the course of the disease and choosing a monad treatment plan. In a number of scientific studies, it has been proven that galectin-3 in the blood serum of patients with SUE causes myocardial hypertrophy and has a stimulating effect on fibrosis processes, which are considered important in heart remodeling, and shows the progression of the disease and the development of unpleasant complications [4]. Taking into account the above, we studied the level of galectin-3 in the blood serum of the patients involved in our study, as well as the level of correlation with a number of other indicators.

In our study, we compared the correlation of galectin-3 with inflammatory cytokines and hemodynamic indicators of the heart in patients with CHF developed on the basis of rheumatic defects. Between interleukin (IL)-6 and galectin-3 (r=0.542, p < 001), *α-O'NO* (r=0.543, p < 001), moderately strong S-reactive protein (r=0.259, p < 0.004) and a weak positive correlation was noted with antistreptolysin-O (r=0.256, p < *0.004). A weak negative* correlation (r=-0.287, p < *0.002) was found* between left ventricular ejection fraction and IL-6 . Between galectin-3 and S-reactive protein (r=0.577, p < 001) and *α-O'NO* (r=0.501, p < 001), moderately strong, left ventricular myocardial mass (r=0.409, p < 0.001) and A weak positive correlation was noted between the age of patients (r=0.375, p < *0.001). A weak negative (r=-0.301, p* < 0.001) correlation was observed with the left ventricular ejection fraction . *A weak positive* (r=0.238, p < 009) and a weak negative (r=-0.243, p < *0.01*) correlation between left ventricular ejection fraction and S-reactive protein (r=0.238, p < 0.009) were found. A weak negative correlation was observed between left ventricular myocardial mass and ejection fraction (r=-0.231, p < 0.05) , and a weak positive correlation with patients' age (r=0.351, p < 001) .

The conducted correlational analysis confirms that long-term inflammation and fibrosis processes in patients with CHF developed on the basis of rheumatic defects have a negative effect on the functional state of the heart, independently of hemodynamic disturbances.

Also, in our study, we evaluated the effects of galectin-3, which is considered as a fibrosis marker, on other indicators using regression analysis. Table 1 below shows the results obtained.

Table 1 .

Study of a number of factors affecting galectin-3 in chronic heart failure developed on the basis of rheumatic heart defects using regression analysis .

Indicators	B-coefficient	Standard Error (SE)	X^2	R	Relative Odds (OR)	95% Confidence Interval (II)	
						Low	High
C reactive protein	0.332	0.117	8,099	0.004	1,394	1,109	1,752
Antistreptolysin-O	-0.002	0.003	0.364	0.546	0.998	0.994	1,003
α-tumor necrosis factor	0.073	0.037	3,782	0.052	1,075	0.999	1,157
Interleukin-6	0.303	0.128	5,632	0.018	1,354	1,054	1,739
End diastolic size	1,707	3,448	0.245	0.621	5,514	0.006	475.93
End systolic size	0.660	2,503	0.070	0.792	1,936	0.014	261,240
Right ventricular size	-0.003	0.057	0.003	0.955	0.997	0.892	1,114
Right slice size	0.008	0.023	0.115	0.735	1,008	0.963	1,054
End diastolic volume	-0.014	0.048	0.079	0.779	0.987	0.897	1,085
End cytologic volume	-0.047	0.042	1,228	0.268	0.954	0.879	1,036
Left ventricular myocardial mass	0.001	0.003	0.034	0.854	1,001	0.994	1,007
Left ventricular ejection fraction	-0.073	0.034	4,583	0.032	0.930	0.870	0.994

Left slice size	-0.001	0.019	0.006	0.939	0.999	0.962	1,037

G- alectin-3 and several laboratory and heart functional indicators ranged from -0.003 (right ventricle) to 1.707 (end diastolic size). The standard error ranged from 0.003 (antistreptolysin-O) to 3.448 (end diastolic measurement).

According to the results of logistic regression analysis, galectin-3 indicators and S-reactive protein (x^2 =8.09, OR=1.394.95 % II 1.109-1.752, p=0.004) in patients with CHF developed on the basis of rheumatic heart defects, α-tumor necrosis factor (x^2 =3.78, OR=1.075.95 % II 0.999-1.157, p=0.052), interleukin-6 (x^2 =5.632, OR=1.354.95 % II 1.054-1.739, p=0.018) and left ventricular ejection fraction (x^2 =4.583, OR=0.930,95 % II 0.870-0.994, p=0.032) were statistically reliable.

In the course of our study, we performed a linear regression analysis between galectin-3 and laboratory-instrumental indicators in order to predict the course of the disease in patients with CHF developed on the basis of rheumatic defects. Figure 1 shows the linear regression analysis between α-tumor necrosis factor and galectin-3.

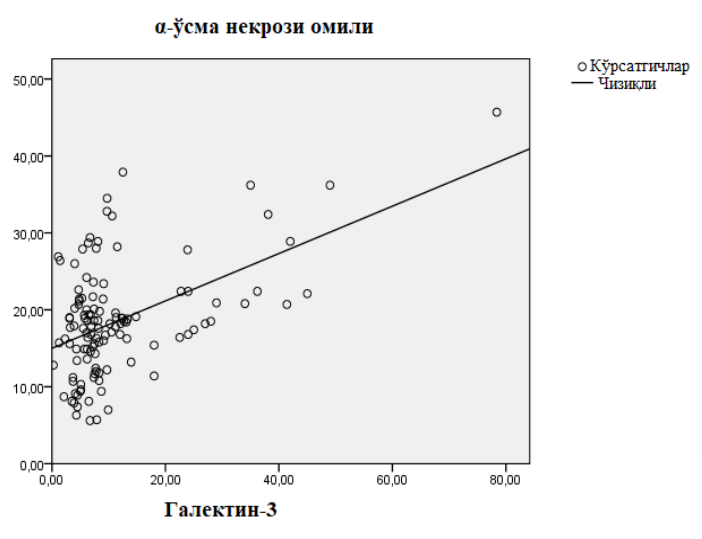

Figure 1. Linear regression relationship of galectin-3 and α-tumor necrosis factor in patients with chronic heart failure developed on the basis of rheumatic heart defects.

This figure shows a linear regression relationship between galectin-3 and α-tumor necrosis factor in patients with CHF developed on the basis of rheumatic heart defects. The obtained results confirmed that the high level of α-tumor necrosis factor in the body causes an increase in galectin-3 indicators (beta coefficient-0.492, t=6.137, p<0.001). Consequently, this leads to the exacerbation of fibrosis processes.

Our next linear regression analysis was devoted to the study of the relationship between galectin-3 and interleukin-6 (Figure 2).

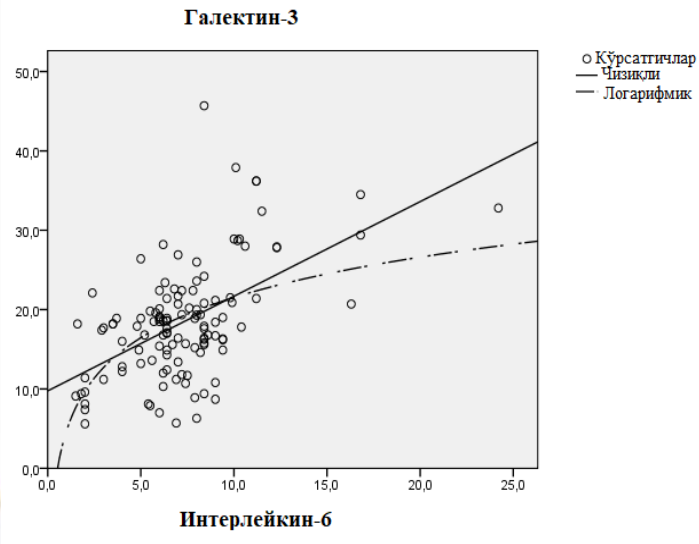

Figure 2. Linear regression relationship of galectin-3 and

interleukin-6 in patients with chronic heart failure developed on the basis of rheumatic defects.

The figure shows a linear regression relationship between galectin-3 and interleukin-6 in patients with CHF developed on the basis of rheumatic heart defects. The obtained result is the basis for saying that the increase of galectin-3 in blood serum is caused by the increase of interleukin-6, which is one of the main inflammatory markers, over the standard level (beta coefficient-0.542, t=6.981, p<0.001). Consequently, this leads to the exacerbation of fibrosis processes.

SUMMARY

It was found that the hemodynamic changes observed in SUE developed on the basis of rheumatic heart defects have negative deviations in a number of indicators from the changes in heart failure caused by SCI. This can be attributed to the long and hidden course of inflammatory processes in our patients.

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