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PROGNOSTIC ESSENCE OF BASIC BIOMARKERS IN THE POST-COVID PERIOD IN CHRONIC HEART FAILURE

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Resume

The activity of galectin - 3 (G-3) in patients with chronic heart failure (CHF) in the blood serum is interdependent with myocardial hypertrophy. All this stimulates the migration of macrophages, the proliferation of fibroblasts, as well as fibrosis during remodeling heart. The importance of G 3 has recently been important for assessing the prognosis of disease progression, as well as the development of its adverse complications. An increase in the concentration of Galectin-3 in the blood of patients of the main group in relation to the control group by 3.5 times and 0.22 times to the comparative group indicates the negative consequences of a long post-COVID period (p<0.01).

Key words: chronic heart failure, galectin - 3, post-COVID period, hemodynamic parameters

ПРОГНОСТИЧЕСКАЯ ВАЖНОСТЬ ОСНОВНОГО БИОМАРКЕРА В ПОСТКОВИДНОМ ПЕРИОДЕ ПРИ ХРОНИЧЕСКОЙ СЕРДЕЧНОЙ НЕДОСТАТОЧНОСТИ

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Резюме

Активность галектина - 3 (Г-3) у пациентов с хронической сердечной недостаточностью (ХСН) в сыворотке крови взаимозависима с гипертрофией миокарда. Все это стимулирует миграцию макрофагов, пролиферацию фибробластов, а также фиброз при ремоделировании сердца. Важность Г-3 в последнее время имеет значение для оценки прогноза прогрессирования заболевания, а также развития его неблагоприятных осложнений. Повышение концентрации Галектина-3 в крови больных основной группы по отношению к контрольной в 3,5 раза и 0,22 раза к сравнительной группе указывает на негативные последствия длительного постковидного периода (p<0,01).

Ключевые слова: хроническая сердечная недостаточность, галектин-3, посковидный период, гемодинамические параметры

SURUNKALI YURAK YETISHMOVCHILIGIDA KOVIDDAN KEYINGI DAVRDA ASOSIY BIOMARKERNING PROGNOSTIK MOHIYATI

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Rezyume

Surunkali yurak yetishmovchiligi (SYY) bo'lgan bemorlarda qon zardobida galektin - 3 (Gal-3) faolligi miokard gipertrofiyasi bilan o'zaro bog'liq. Bularning barchasi makrofaglarning migratsiyasini, fibroblastlarning ko'payishini, shuningdek, remodelyatsiya paytida fibrozni rag'batlantiradi. G 3 ning ahamiyati yaqinda kasallikning rivojlanishining prognozini, shuningdek, uning rivojlanishini baholash uchun salbiy asoratlar muhim ahamiyatga ega. Asosiy guruhdagi bemorlarning qonida Galektin-3 kontsentratsiyasining nazorat guruhiga nisbatan 3,5 baravar va qiyosiy guruhga nisbatan 0,22 baravar oshishi COVIDdan keyingi uzoq davrning salbiy oqibatlaridan dalolat beradi (p<0,01) .

Kaliy so'zlari: Surunkali yurak yetishmovchiligi, galektin - 3, COVIDdan keyingi davr, gemodinamik parametrlar

Relevance

Nowadays, several targeted scientific studies are being conducted all over the world to study the pathophysiological mechanisms of the development of pulmonary and cardiovascular complications associated with COVID-19, and evaluate the role of the activation of mediators of inflammatory, proliferative and fibrotic processes. Patients with ischemic heart disease (IHD) may be at risk of developing and exacerbating severe chronic heart failure (CHF) after infection with the coronavirus. Understanding the mechanisms of interrelated effects between COVID-19 and cardiovascular diseases (CVDs) will provide an opportunity to improve the efficiency of early diagnosis and prediction of exacerbations of patients with CVDs, especially CVDs, in the post-COVID-19 period.

In this regard, it is desirable to determine the immunoblot-chemical basis of the formation of the fibrotic process in myocardial and lung tissue in patients with COVID-19 who infected with IHD. Therefore, measures to eliminate fibrosis, improve the clinical and functional condition of patients and increase the quality of life by early detection and forecasting of the activation of fibrotic processes leading to the development of CHF and the development of its severe complications are the priorities of modern medicine. Admittedly, none of the existing biological markers can fully reflect the occurrence, development, stage of disease, and possibility of negative clinical consequences. In this regard, the most promising approach is the comprehensive evaluation of data based on laboratory cardio markers, along with clinical and instrumental studies, which significantly increase the overall accuracy of diagnosis and prognosis. One of them, Galectin-3 (G-3), is expressed by many cells, including neutrophils, macrophages, mast cells, fibroblasts, and osteoclasts; it is found in the lungs, stomach, intestines, uterus, and ovaries [1]. In the complex diagnosis of IHD, determining the amount of G-3 in the blood can be expressed as an additional criterion confirming the presence of myocardial fibrosis, and it has an additional predicting value. [2,3]. According to some studies, there is an increase in the quantitative level of (G-3) in the blood plasma of COVID-19 patients, which in turn confirms the prognostic value of (G-3) as a highly sensitive biomarker in the severe course of COVID-19 by triggering the "cytokine storm" process. It is proved that, COVID-19 patients have significantly elevated circulating G-3 levels on admission to the hospital compared to pre-pandemic age-matched healthy individuals (28.77 ng/mL [17.52–42.04] vs. 65 ng/mL [8.27–14.71], p < 0.0001) [4].

Taking into account the above, the aim of our scientific research is to predict inflammatory and proliferative processes based on the analysis of blood (G-3) levels in the post-covid period.

Materials and methods.

70 patients of both genders, with an average age of 58.6±1.26 years, suffering from ischemic heart disease (IHD), angina pectoris, complicated by chronic heart failure II-III functional class according to NYHA. Patients were divided into two groups: the main group - 36 patients with chronic heart failure who underwent COVID-19 (infected with a moderate severity of coronavirus infection during the last 6 months) and, for comparison, the second group - 34 patients who were not infected with coronavirus disease.

To assess the clinical and functional state of patients with CHF was carried out six-minute walk test (6-MWT) and clinical condition severity rating scale (ShOKS, modified by Mareev V.Yu., 2000). The level of fibromarker (G-3) in blood serum was evaluated by ELISA-linked immunosorbent assay method. Quantitative indicator of G-3 in the blood serum of the patients under our observation was determined using the

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Cobas - 6000 (Roshe, Germany) device using the enzyme immunoassay method in the case where human Galectin-3 ELISA reagent (Germany) was used. In the study, the reference index of G-3 in blood serum was 8.6 [3].

The analysis of the process was carried out as follows:

- 3 ml of blood with heparin was taken from the wrist veins of the patient in the morning. The obtained blood sample was centrifuged and blood serum was separated. The analysis was carried out within 24 hours at 2 - 8 ° C, when checked after 24 hours, it was stored in a refrigerator at - 20 ° C;

- blood serum sample and standard solutions of Gal-3 were poured into microplate wells in the set. The microplate was covered with a film and incubated for 60 minutes at a temperature of 37°C;

special biotin-bound antibodies were added to the wells and incubated for 60 minutes at 37°C. The unbound part of biotin was washed away with phosphate-saline buffer solution;

- avidin-biotin-peroxidase (ABP) was added to the wells and incubated for 30 minutes at 37°C. The part of ABP that did not form a complex was washed away with phosphorus-saline buffer solution;

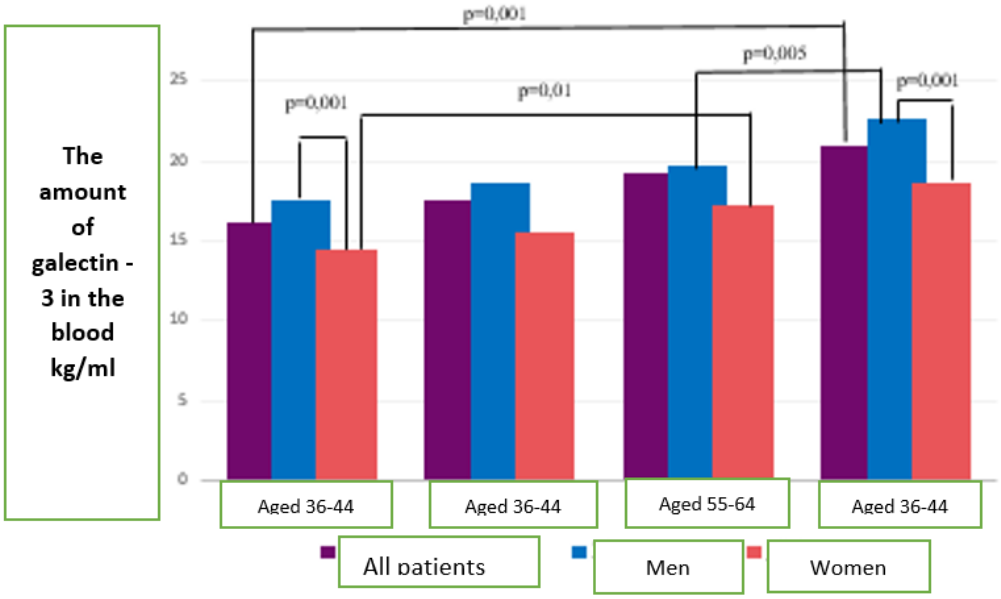
- in order to clearly see the resulting reaction, the peroxidase solution was poured, a blue colored solution was formed as a result of the enzymatic reaction;

- then 100 µl of "stop solution" was added to the resulting solution. The optical density of the resulting solution was checked in the IFA analyzer at a wavelength of 450 nm, and the quantitative index of G-3 was determined.

Statistical data processing was carried out using the statistical software package "Statistics 8.0". Spearman's rank correlation coefficient was calculated to statistically describe the relationship between different parameters. The significance of differences between the two groups was tested using Student's t-test. The level of statistical significance was considered to be $r < 0.05$.

Result and discussion.

In order to identify biochemical markers of the development of fibrotic processes in the body, a quantitative evaluation of Gal-3, a disorder of collagen metabolism due to the previous coronavirus, was carried out in IHD patients complicated by CHF. ELISA analysis of Gal-3 concentration in blood was performed in 88 subjects, including 70 patients with CHF complicated IHD and arterial hypertension, as well as 18 healthy people. Age and gender differences were found in the mean level of Gal-3 in the blood during the quantification of the fibrosis biomarker (Figure 1). It was found that the average values of Gal-3 in the blood were 1.3 times higher in elderly people than in middle-aged people, with an average of 20.4 ± 0.13 ng / ml and 16.1 ± 0.07 ng / ml. respectively ($r < 0.05$).



According to the obtained data, the average concentration of Gal-3 in blood in men was 19.6 ± 0.11 ng/ml, the average value of Gal-3 in women was 16.5 ± 0.09 ng/ml, so in men this indicator 3.1

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ng/ml increased (r < 0.05). Thus, elderly men often have high levels of Gal-3 in the blood, which indicates the influence of youth and male gender on the activation of fibrotic and proliferative processes in the body.

Comparative analysis of the average concentration of Gal-3 in blood plasma revealed statistically significant differences between the studied groups (Fig. 2). Thus, in the main group of patients with ischemic heart disease, in the post-covid period, the average value of Galectin-3 was 20.0±0.84 ng/ml. The average value of Galectin-3 in patients without COVID-19 in the comparison group was 16.2±0.85 ng/ml was (r<0.01). The observed differences between the groups indicate a tendency for the development of myocardial fibrosis and increased production of Gal-3 in patients with CHF in the post-covid period.

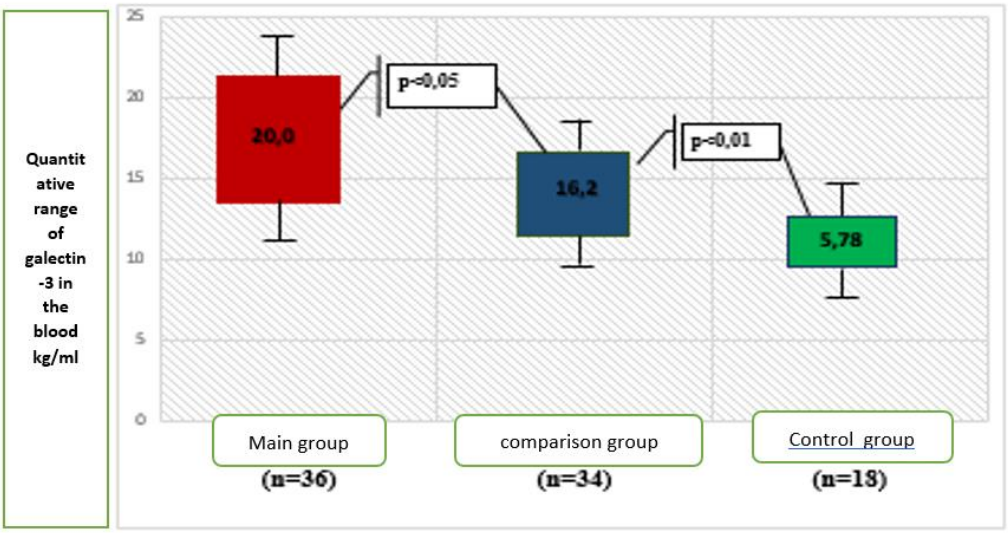

Figure 2. Quantitative analysis of Galectin-3 in blood in study groups

The increase in the concentration of Galectin-3 in the blood of patients in the main group compared to the control group and 3.5 times and 0.22 times to the comparison group indicates the negative consequences of the long post-covid period (p<0.01). Based on these data, it can be assumed that the expression of the Galectin-3 biomarker is a connecting pathogenetic link in the development and progression of complex CHF and coronavirus disease. Thus, Gal-3, the main mediator of fibrotic and proliferative processes, may serve as a predictor not only for further complications, but also for the development and progression of CHF with preserved systolic function.

Clinical studies confirm a high diagnostic potential for Gal-3 levels exceeding 19-25 ng/ml, which divide patients into a high-risk group of adverse clinical outcomes. Circulating Galectin-3 levels above 19 pg/ml are associated with increased risk of newly diagnosed diastolic heart failure and mortality [5].

Gal-3 is produced by activated macrophages, which leads to the proliferation of fibroblasts, the excessive production of myocardial collagen, the development of interstitial fibrosis, the activation of growth factor and, as a result, the development of left ventricular dysfunction. Thus, Gal-3 plays a leading role in shaping the response to injury and inflammation – in the processes of left ventricular remodeling [6]. When analyzing the correlation between G3 levels and central hemodynamic parameters in patients without a previous covid infection, it was found that in patients with II-III FC CHF, there was an unreliable weak positive correlation between G3 and left ventricular posterior wall thickness (LVPWT) and a significantly strong negative correlation between G3 and left ventricular ejection fraction (LVEF) (respectively, p<0.001 and p<0.001). This situation is explained by a sharp decrease in myocardial contractility due to chronic systemic hypoxia, slow-acting inflammatory and fibrotic processes in the body, where maladaptive remodeling is clearly developing [3].

In the correlation analysis in patients with CHF, a correlation was established between the level of Gal-3 and the severity of CHF FC, regardless of the infectious process carried out - correlation coefficient r=0.48 (r=0.001). Thus, the

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average level with 2nd FC was 17.6±0.86 ng/ml, with 3rd FC - 21.1±0.71 ng/ml (p=0.01). The study showed that the level of Gal-3 in patients with CHF was directly related to the level of systolic (r=0.36; r=0.05) and diastolic blood pressure (r=0.35; r=0.05).

Correlational analysis of the relationship between the level of the fibromarker Galectin-3 and the high level of the clinical condition on the COPD scale, as well as the dependence on training on the COPD, revealed the following correlations: the level of positive correlation between the concentration Gal-3 in the blood and COPD intervals (r = 0.53; r = 0 ,05) and 6-MWT inverse correlation between average force and distance parameters (r = 0.38; p = 0.01). The results obtained during the study show a negative effect of the Gal-3 biomarker level on the clinical-functional status and hemodynamic parameters of patients with coronary artery disease against the background of COVID-19, this negative effect persists in the post-covid period.

Conclusions

1. It can be assumed that galectin-3 has a predictive value not only for post-covid complications, but also for the development and progression of CHF with preserved systolic function due to IHD. Gal-3 biomarker expression is a linking pathogenetic link in the development and progression of CHF and COVID-19 complicated coronary artery disease.

2. G-3, which is the main mediator of fibrotic and proliferative processes, can serve as a specific biomarker for the early diagnosis of severe CHF and the development of cardiovascular complications in patients with IHD who underwent COVID-19 in the post-covid period.

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