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THE ROLE OF ALDOSTERONE AND GALECTIN-3 INDICATORS IN THE DEVELOPMENT OF FIBROSIS PROCESSES IN CARDIORENAL SYNDROME

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Abstract. The role of aldosterone and galectin-3 in the development of fibrotic processes in the heart and kidneys in cardiorenal syndrome that developed against the background of chronic heart failure (CHF). In all three groups of patients under observation, a statistically significant increase ($r<0.05$) was found, compared with the reference values of the concentration of galectin -3. Along with this, a statistically significant increase in aldosterone concentration was found in patients of the main group compared to the control group ($r<0.001$). Also, there was a significant increase in its concentration in patients with low and intermediate ejection fraction of CHF. Thus, in patients with CHF with intermediate and low ejection fraction of the left ventricle, significantly increased concentrations of galecten-3 and aldosterone, indicating the processes of myocardial fibrosis, and their correlation with the severity of the disease, were established.
Keywords: *chronic heart failure, cardiorenal syndrome, galectin-3, aldosterone.*

Introduction

Activation of the renin-angiotensin-aldosterone system (RAAS) and its components in chronic heart failure (CHF) and the related cardiorenal syndrome also causes the slowing of aldosterone clearance in the liver. As a result, the half-life of aldosterone in the plasma increases significantly, that is, from 30-35 minutes to 70-100 minutes, and the amount of the hormone in the blood serum increases 3-4 times [4]. In patients with CHF, hyperaldosteronism affects the proliferation of fibroblasts, collagen synthesis and degradation, tissue growth factor, matrix metalloproteinase and its tissue inhibitor enzyme system, which further increases the development of organic (fibrous) changes in the cardiovascular system, liver and kidney [7].

CHF parallel to the changes in the heart, fibrotic processes also develop in the kidney under the influence of hypoxia, hemodynamics and a number of other factors.

As mentioned above, it has been proved by reliable evidence that the components of RAAS are synthesized in various organs, including kidney tissues. Even if their activity is low in the general blood system, the damage to the target organs, including the kidney, is explained by this reason. Limited activation of RAAS in the kidney has a damaging effect on podocytes and leads to its dysfunction. AT II production by podocytes activates profibrotic transforming growth factor-β1 (TGF-β1), reactive oxygen radicals, and mechanical stretching [10].

Although the limited activation of RAAS components in the kidney is important in the development of nephropathy, the involvement of AT II in the processes has been more thoroughly studied. But there is not enough information about the effect of its component aldosterone [1].

Activation of CHF neurohumoral factors, in particular RAAS and its component aldosterone, leads to the parallel development of fibrotic processes in the heart and kidney, as a result, cardiorenal syndrome increases.

Biopsy is the most reliable way to detect fibrotic processes in internal organs. But because it is invasive and traumatic, it causes a number of complications during the life of patients. Therefore, it is appropriate to use its markers in the detection of fibrotic processes in organs, including the heart and kidney.

In recent years, it has been noted that galectin-3 in blood serum plays an important role in the development of connective tissue damage and fibrosis processes in cardiovascular diseases, and it is recommended to use it in practice as a biological marker representing the collagen system, myocardial fibrosis, and heart remodeling [2, 11].

Purpose of the research

Assessment of the role of aldosterone and galectin-3 in the development of fibrosis processes in advanced cardiorenal syndrome based on CHF.

Materials and Methods

As a research source, 60 chronic heart failure patients with advanced cardiorenal syndrome on the basis of II-III FS according to NYHA, who were treated in the cardioreanimation, cardiology and cardiorehabilitation departments of the multidisciplinary clinic of the Tashkent Medical Academy. They were divided into groups with preserved intermediate and decreased left ventricular ejection fraction and consisted of 30 patients, respectively. The first group consisted of 30 people (average age 58.3±1.2 years, 21 men and 9 women) with low left ventricular ejection fraction (LVEF) (< 40%), the second group consisted of 30 people (average age 57.4±1.1 , 12 men and 18 women) LVEF (41 - 49%) intermediate, the third group consisted of 30 people (on average 56.7±0.8 years, 14 men and 16 women) LVEF (>50%) preserved chronic heart failure developed cardiorenal syndrome established existing patients. The clinical description of the patients included in the study is presented in Table 1.

Table 1

Clinical description of patients with cardiorenal syndrome

Indicators	Total, n=90	Group 1 LVEF lo n=30	2-group LVE interval n=30	3rd group LVEF kept n=30
Age, year	57,9±1,3	56,3±1,2	59,6±1,1	57,8±0,9
Gender, male/female	47/43	21/9	12/18	14/16
Body mass index, kg/m^2	31,5±0,8	31,6±0,4	32,3±0,3	30,7±0,2
CHF duration, ye	3,7±1,6	3,8±1,8	3,6±1,4	3,7±1,4
Left ventricular ejectio fraction, %	46,1±0,3	35,1±0,2	44,3 ±0,3	59,0 ±0,2
Ball filtration rate (BFI ml/min/1.73m^2)	53,3±1,2	48,2±1,2	57,2±1,4	54,4±1,1
Comorbid diseases				
Diabetes	21 (23,3 %)	7(23,3 %)	8 (26,7 %)	6 (20 %)
Obesity	22 (24,4%)	11 (36,7 %)	9 (30 %)	6 (20 %)
Anemia	12 (13,3%)	5 (16,7 %)	4 (13,3 %)	3 (10 %)

Biological markers G-3 and aldosterone, which represent fibrosis processes in the body, were determined by the immunoenzyme analysis method, central hemodynamic parameters and

myocardial remodeling were determined by the EchoCG method, and the obtained results were compared with the parameters of a control group consisting of 20 healthy volunteers.

Results

In all three groups of patients under observation, the quantitative index of neuro hormone G-3, which is directly involved in the balance of collagen metabolism in the body, was found to be statistically significantly higher than the reference values (Figure 1).

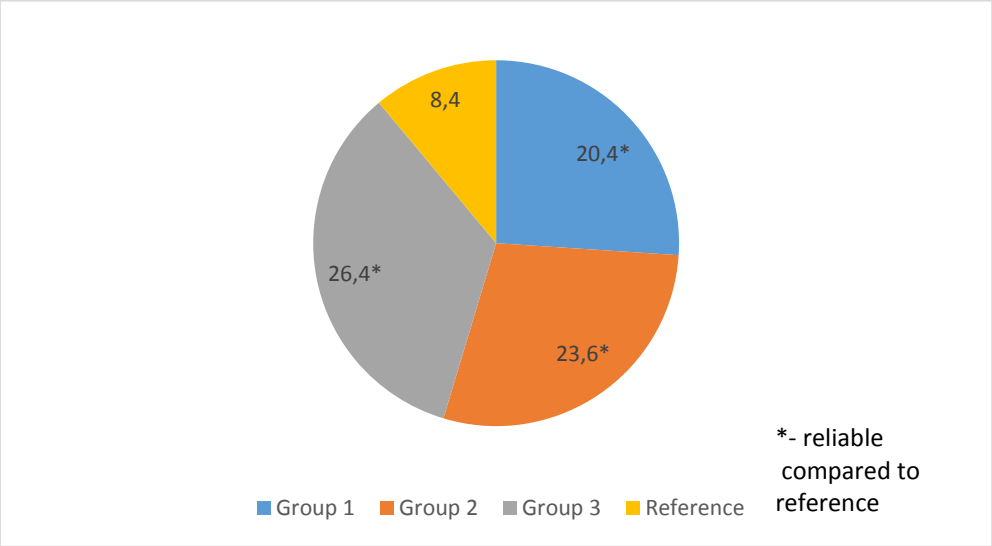

Figure 1. Comparative analysis of galacten-3 quantification between groups.

As can be seen from Figure 1, serum G-3 levels were higher in all three groups compared to reference values. The amount of G-3 in blood serum in patients of group 1, respectively, was 20.4 ng/ml (2.4 times higher than the reference value) ($r < 0.001$). G-3 increased by 2.8 times (23.6 ng/ml) ($r<0.001$) in patients in group 2, respectively. In group 3 patients, this biological marker indicating the activity of fibrosis processes increased by 3.1 times (26.4 ng/ml) from the reference value ($r<0.001$).

In a number of studies, an increase in the amount of aldosterone, a component of the RAA system in the blood serum, which is directly involved in the progression of myocardial remodeling and fibrosis processes, was noted in patients with CHF [8], and in our study, the amount of this hormone was statistically significantly higher in all patients than in the control group. was determined ($r<0.001$) (Fig. 2).

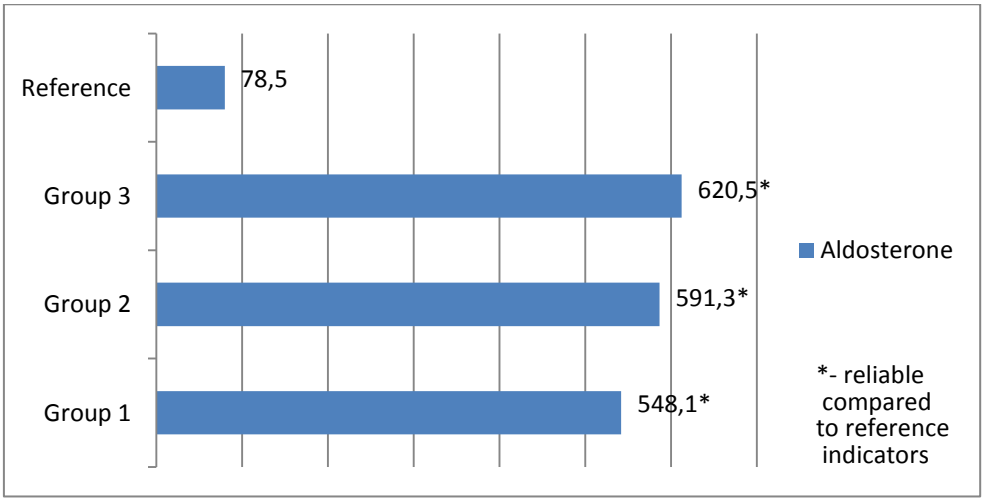

Figure 2. Comparative analysis of serum aldosterone levels between groups

Aldosterone was 7 times (548.1 pg/ml) of the reference value in group 1 patients, 7.5 times (591.3 pg/ml) of the reference value in group 2 patients, and 7.9 times the reference value in group 3 patients. it was noted that it increased by 620.5 pg/ml.

Discussion

G-3 is directly involved in the proliferation of fibroblasts and the production of type I collagen in the body [3, 5]. This process has been proven in a number of studies, where it was observed that G-3 synthesis increased due to aldosterone's effect on mineralocorticoid receptors in vascular smooth muscle cells. This means that G-3 is involved in the process as an intermediate link in the development of aldosterone-induced fibrosis in the myocardium [6, 9]. At the same time, G-3 is superior to other biological markers in terms of resistance to hemodynamic stress, myocardial fibrosis, ventricular remodeling, and early harbinger of renal dysfunction [4,12]. Therefore, G-3 is currently recognized as a biological marker of myocardial fibrosis and cardiac remodeling, and it is recommended that it can be used in the selection of risk factors of the disease in patients with CHF, determining its course and outcome, and evaluating the effectiveness of treatment [3, 5].

In our study, patients with cardiorenal syndrome showed a higher level of serum G-3 than the reference values, consistent with a decrease in the CHF ejection fraction. In particular, the amount of G-3 was 2.4 times higher than that of the control group in patients of the 1st group of LVEF with low CHF, and 2.8 and 3.1 times higher in the 2nd and 3rd groups of patients with intermediate and preserved CHF of LVEF, respectively. Also, the aldosterone index was 7.0 between the groups compared to the control group; 7.5 and 7.9 times higher, and in the severe stages of the disease, fibrosis processes are accelerated. This indicator means that the patients of the first group have more chronic systemic hypoxia and slow inflammation and endothelial dysfunction in the body, and the fibrosis processes are clearly developed in the patients of the 2-3 groups, and it corresponds to the conclusions of previous studies [9].

Conclusion

In patients with cardiorenal syndrome, G-3 and aldosterone indicators, which represent fibrosis processes, were clearly increased in groups 1 and 2 and correlated with the severity of the disease, and are important in predicting the course of the disease and the development of unconscious complications.

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