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STUDY OF THE RELATIONSHIP BETWEEN THE DEVELOPMENT OF FIBROSIS PROCESSES AND THE FUNCTIONAL STATE OF THE HEART IN PATIENTS WITH CHRONIC HEART FAILURE

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ABSTRACT: The development of fibrosis processes in patients with chronic heart failure is correlated with the functional state of the heart. This is also confirmed by positive changes in N-pro-natriuretic peptide and aldosterone indicators after treatments in patients involved in the study, as well as reliable positive improvement in cardiac functional status in those who received sacubitril + valsartan and dapagliflozin. It was demonstrated by highly reliable positive changes in end-systolic and diastolic cardiac volumes and left ventricular ejection fraction.

KEYWORDS: Chronic heart failure, N-pro natriuretic peptide, aldosterone, succubitril+valsartan, dapagliflozin.

INTRODUCTION

Chronic heart failure (CHF) is one of the urgent medical and social problems of modern medicine [9, 11]. This is due to its prevalence, severe consequences, and high cost of treatment.

Mortality due to CHF is 4-8 times higher than in the general population, and half of patients die within 5 years of diagnosis. Its IV functional class (FC) has a half-year mortality rate of 44% [1, 8, 13].

According to epidemiological data, in most cases in European countries, CHF develops as a result of arterial hypertension (95%) and ischemic heart disease (IHD) (69.7%) [2]. In our republic, the main cause of this serious complication is often the two diseases listed above.

Due to the increase in the life expectancy of the population, the positive results achieved in the treatment of cardiovascular diseases, and the prevalence of the risk factors that cause the main diseases that cause CHF, IHD and arterial hypertension, this serious complication is more and more common among the world's population [3]. Despite the progress made in recent years, this confirms that CHF still remains a heavy financial burden on the health economy of all countries around the world..

Systemic changes are observed in all organs of CHF and remodeling processes in the heart are of particular importance.

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It is known that a number of testing methods are used to diagnose CHF and evaluate the effectiveness of treatment. Among them, natriuretic hormones are of particular importance as a biological marker. Currently, there are a number of its representatives, among which brain and N-pro brain sodium uretic peptides are widely used in the diagnosis of CHF and evaluation of its course. A.M.Richards was the first to show the use of the concentration of N-pro sodium uretic peptide in the blood to monitor the effect of treatment in patients with CHF. In it, patients diagnosed with CHF II-III FC under hormonal control were monitored by titration of the dose of angiotensin-converting enzyme inhibitors (ACEI) and the feasibility of such an approach was shown. [10.].

In the IMPRESS trial, which included 573 patients receiving lisinopril and omapatrilat, those with CHF and left ventricular ejection fraction less than 40% in a randomized trial reported a reliable neurohormone reduction 1-2 years after initiation of treatment [6.]. Similar data were obtained in experimental observations conducted by S. Tang and co-authors on patients receiving valsartan and benazepril [12].

Also, in a series of observations, a decrease in brain sodium uretic peptide in the blood was found in patients taking β-blockers [5].

A regular increase in the concentration of aldosterone in the blood, which belongs to the group of steroid hormones, affects blood pressure, causes complications in vascular, heart and kidney diseases and causes metabolic changes [4].

Aldosterone activates the sympathetic nervous system and induces apoptosis by increasing the reaction of free radicals. As a result, prolonged hyperadrenosteronism stimulates remodeling processes in the heart and other organs, worsening the course of CHF and the outcome of the disease [15]. It increases collagen synthesis by activating fibroblasts in the heart and causes interstitial fibrosis in the myocardium. It increases the reabsorption of sodium and water in the distal tubules of the kidneys, increases potassium and magnesium excretion, stimulates fibroblasts, increases collagen synthesis and causes mesengial fibrosis. In addition, by affecting vessels, it reduces the production of dilators, increases collagen synthesis, causes proliferation and dysfunction of the endothelium, causing perivascular fibrosis and the formation of blood clots [14, 15].

It should be noted that in recent years, attention has been paid to aldosterone as a special factor in cardiovascular pathologies and kidney damage [7].

Taking into account the above, we studied N pro brain sodium uretic hormone and aldosterone indicators in our patients before and after treatment with different components.

The scope of the study. Study of the effects of various treatments on serum aldosterone, N pro brain sodium uretic hormone and cardiac functional status in patients with chronic heart failure.

Research materials and methods. This scientific research work was conducted in 2022 and 2023 in 120 patients with developed CHF on the basis of IHD and AG, who were treated at the clinic of the Fergana Public Health Medical Institute. They, in turn, were divided into three groups based on the treatment procedures. Each group consisted of 20 CHF II - III FC 40 patients. The average age of the first group of patients was 66.1±1.8 years, 21 (52.5%) men and 19 (47.5%) women. The 1st

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group of patients under observation was prescribed β-blockers + ACEI or angiotensin receptor antagonists (ARA) + mineralocorticoid receptor antagonists (MRCA)-veroshpiron as a standard treatment of CHF. The average age of the second group of patients was 65.9±1.5, men were 24 (60%) and women were 16 (40%). They received a standard treatment consisting of β-blockers + succubitril-valsartan (yuperio) + MRCA-veroshpirone. The average age of the third group of patients was 64.7±1.3, 21 (52.5%) of them were men and 19 (47.5%) were women. β-blockers + succubitril-valsartan (yuperio) + MRCA-veroshpiron + glucose-sodium co-transporter type 2 inhibitors (dapagliflozin) were recommended to these patients.

All subjects included in the study underwent standard laboratory tests before and after 6 months of treatment, serum N-pro-natriuretic peptide and aldosterone levels were determined, and cardiac functional status was assessed using echocardiography.

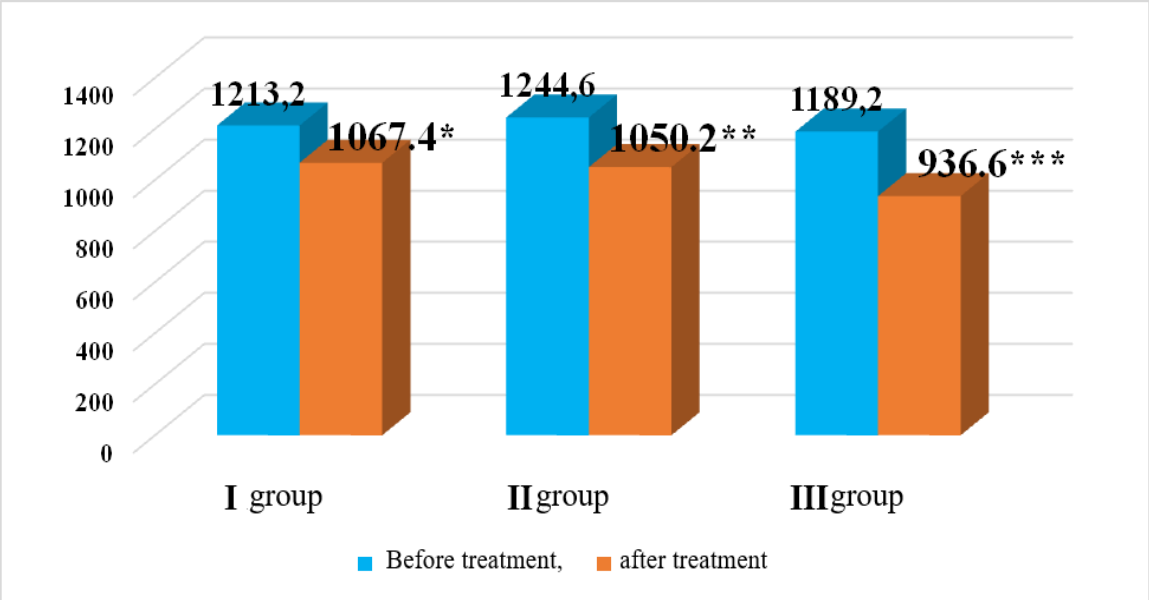
The amount of N-pro-natriuretic peptide in blood serum was determined using immunoenzyme analysis using "Vector-BEST" reagents. The reagent used in the study to determine N-pro natriuretic peptide in blood serum had a detection range of 0-2500 pg/ml and a sensitivity of 20.0 pg/ml.

The amount of aldosterone in the blood serum was determined by means of an immunoenzymatic analysis using "DBC Aldosterone ELISA" (Canada) reagents. The reagent used to determine serum aldosterone in the study had a detection range of 9.0 - 2000 pg/ml, a sensitivity of 9.1 pg/ml, and a reference value of 55.4 pg/ml.

Analysis and discussion of research results. We studied N-pro cerebral sodium uretic peptide indicators in blood serum in all groups of patients under our observation before and after treatments. Figure 1 below shows a comparative analysis of pre- and post-treatment serum levels of N-pro brain natriuretic peptide.

Fig 1.

Comparative analysis of N-pro brain sodium uretic peptide indicators before and after treatments (pg/ml) in patients with chronic heart failure.



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Note: * - the reliability of the difference between indicators before and after treatment: * - r<0.05., ** - r<0.01, ***r<0.001.

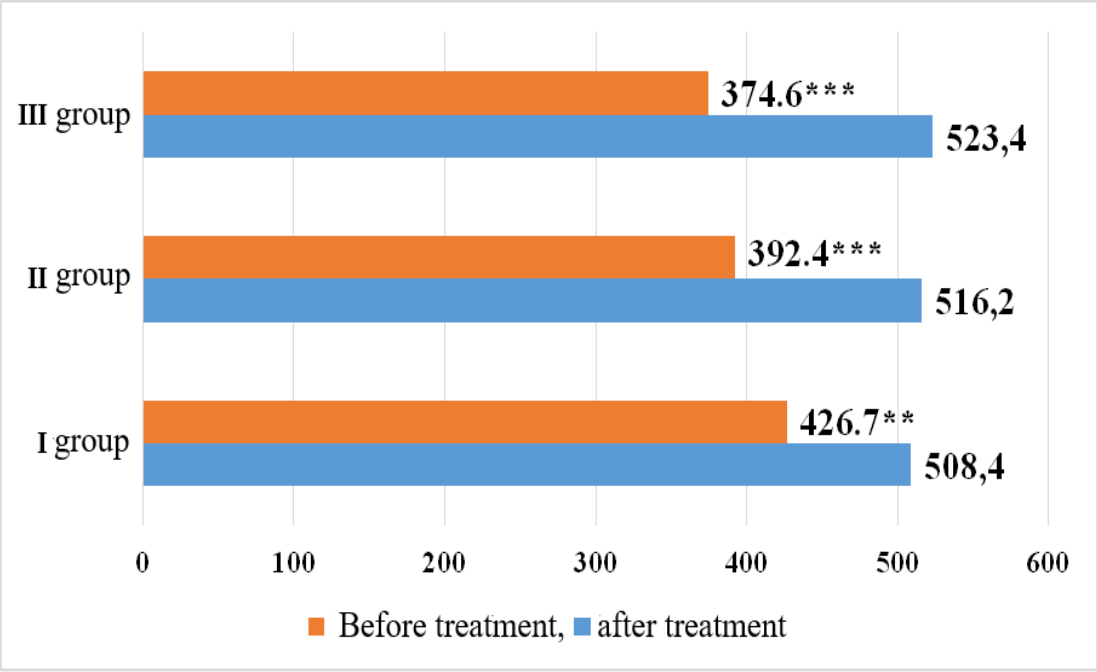
No reliable differences (R>0.05) were observed between the groups when N-pro brain sodium uretic peptide indicator was compared before treatments.

In the first group of patients, the level of N-pro brain sodium uretic peptide in the blood serum decreased by 1.14 times from 1213.2±40.2 pg/ml to 1067.4±36.4 pg/ml before and after treatments, and a reliable difference was noted (r<0.05). . In the second group, its amount before treatment was 1244.6±47.2 pg/ml and after it was 1.2 times decreased to 1050.2±39.8 pg/ml, and a highly reliable (r<0.01) difference was found. N-pro brain sodium uretic peptide indicator increased from 1189.2±32.5 pg/ml to 936.6±29 in group III receiving standard treatment containing β-blockers + sacubitril-valsartan (yuperio) + MRCA + glucose-sodium co-transporter type 2 inhibitors (dapagliflozin). .3 pg/ml decreased by 1.3 times and a highly reliable (r<0.001) difference was observed.

Figure 2 below shows a comparative analysis of serum aldosterone levels before and after treatments.

Fig 2.

Comparative analysis of pre- and post-treatment aldosterone levels (pg/ml) in patients with chronic heart failure.



Note: * - the reliability of the difference between indicators before and after treatment: * - r<0.05., ** - r<0.01, ***r<0.001.

A reliable difference (R>0.05) was not revealed between the groups under our observation when the aldosterone indicators were compared before the treatments.

Aldosterone indicators decreased by 16% reliably (r<0.01) from 508.4±20.52 pg/ml to 426.7±15.2 pg/ml in the first group of patients after the treatments. In the second group of patients, a highly reliable (r<0,001) decrease in aldosterone level by 23.9% was noted, which was 516.2±25.8 pg/ml

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before treatment and 392.4±16.5 pg/ml after treatment. After the treatments, it was observed that the aldosterone level in blood serum improved by the highest 28.3% in the third group of patients (from 523.4±17.6 pg/ml to 374.6±14.2 pg/ml, r<0.001).

During the six-month prospective follow-up of the patients after the treatment, the functional state of the heart was also studied and the obtained results were evaluated in comparison with the indicators before the treatments. Table 1 below presents a comparative analysis between groups of pre- and post-treatment cardiac functional status indicators in patients with CHF enrolled in the study.

Table 1

Comparative analysis of heart functional status indicators after standard medical treatments with different content in patients with chronic heart failure.

№	Indicators	Ⅰ group (n=40)		Ⅱ group (n=40)		Ⅲ group (n=40)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
1	Left lobe size (19-40 mm)	42.2±1.4	39.5±1.5	42.6±1.5	38.1±1.2*	41.8±1.4	36.2±1.3**
2	Left ventricular end-systolic size (2.6-3.8 cm), cm	4.6± 0.16	4.1±0.14*	4.7± 0.15	4.2±0.13*	4.8±0,15	3.9±0.2**
3	Left ventricular end-diastolic size (4.4-5.4 cm)	5.8±0.13	5.5±0.12	6.1±0.2	5.5±0.15*	6.3±0,16	5.2±0.2***
4	Left ventricular end-diastolic volume (88-145 ml), ml	186,6±5.8	161.4±6.3**	188.2±6.4	158.8±6.6**	190,5±6,5	150.2±5.8***
5	Left ventricular end systolic	90.4±5.2	76.5±5.6	92.6±5.8	73.5±5.5*	89,4±5,6	68.2±5.2**

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	volume (45-68 ml), ml						
6	Left ventricular ejection fraction, %	40,6 ±1.8	47.8±2.0*	39.6 ±1.8	48.2±2.2**	38.2±1,6	51.5±1.4***
7	Left ventricular myocardial weight, g	204.2±10,2	186.5±9.8	205,6±10,7	182.5±11.3	202,6±9,9	176.2±10.4
Note: * - the reliability of the difference between indicators before and after treatment: * - r<0.05., ** - r<0.01, ***r<0.001.							

As shown in the table, the size of the left lobe in the first group after the treatment was 42.2±1.4 mm before and after the treatment. from 39.5±1.5mm. decreased to , but no reliable difference was detected (r>0.05). 42.6±1.5 mm after treatment in the second group. from 38.1±1.2 mm. reliable (r<0.05) and 41.8±1.4mm in the third group. from 36.2±1.3mm. highly reliable (r<0.01) decrease. Left ventricular end-systolic size before treatment was 4.6±0.16 and 4.7±0.15 cm in the first and second groups, respectively. was equal to 4.1 ± 0.14 and 4.2 ± 0.13 cm after the treatments, and a reliable (r<0.05) difference was noted. In the third group, it improved by 1.23 times to 4.8±0.15 cm before treatment and 3.9±0.2 cm after treatment, and a highly reliable difference was observed (r<0.01). In the first group of patients who received β-blockers + ACEI or ARA + MRCA, the left ventricular end-diastolic size decreased from 5.8±0.13 cm to 5.5±0.12 cm, and no reliable difference was noted (r>0.05). In patients receiving the second β-blockers + sacubitril-valsartan (yuperio) + MRCA, its size improved by 10% from 6.1±0.2 cm to 5.5±0.15 cm and a reliable difference was found (r<0.05). In the third group of patients who were prescribed β-blockers + sacubitril-valsartan (yuperio) + MRCA + glucose-sodium co-transporter type 2 inhibitors (dapagliflozin), the left ventricular end-diastolic size changed positively by 18% after the treatments and a highly reliable difference was noted. (from 6.3±0.16 to 5.2±0.2 cm, r<0.001).

Left ventricular end-diastolic volume improved from 186.6±5.8ml to 161.4±6.3ml and from 188.2±6.4ml to 158.8±6.6ml before and after treatment in the first and second groups, respectively. Differences in both groups were reliable (r<0.01). In the third group, a highly reliable difference (r<0.001) was found, decreasing by 1.27 times to 190.5±6.5ml before treatment and 150.2±5.8ml after treatment.

Left ventricular end-systolic volume improved by 15% from 90.4±5.2ml to 76.5±5.6ml in the first group before and after treatment, but no significant difference was noted (r>0.05). In the second group, a reliable difference of 20.5% was found, from 92.6±5.8 ml to 73.5±5.5 ml. In the third group, left ventricular end systolic volume changed from 89.4±5.6 ml to 68.2±5.2 ml by 23.7% and a reliable difference was observed (p<0.01). After treatment, the left ventricular ejection fraction increased from 40.6±1.8% to 47.8±2.0% in the first group (r<0.05), from 39.6±1.8% to 48.2±2.2% in the second group (r<0.01) and in the third group, a highly reliable (r<0.001) increase was noted

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from 38.2±1.6% to 51.5±1.4%. Left ventricular myocardium weight before and after treatment in the first group increased from 204.2±10.2 to 186.5±9.8 g, from 205.6±10.7 g to 182.5±11.3 g in the second group, and from 202.6±9.9 g in the third group. Although there was a significant decrease of 176.2±10.4 g, the changes in all groups were not reliable (r> 0.05).

In the analysis, intra-cardiac hemodynamics, in particular, systolic and diastolic volume and left ventricular ejection fraction, showed highly reliable positive changes in the third group compared to the other two groups. The obtained results showed that the combined use of sacubitril-valsartan (yuperio) and glucose-sodium co-transporter type 2 inhibitors (dapagliflozin) as part of the standard treatment in patients with CHF is highly effective. This proves that drugs belonging to the group of inhibitors of glucose sodium cotransporter type 2 also have a positive effect on the recovery of the functional state of the heart.

CONCLUSION

After treatments, positive changes in N-pro natriuretic peptide and aldosterone indicators were observed in all groups of patients. The highly reliable changes in indicators in those who received sacubitril + valsartan and dapagliflozin confirm the effective effect on the functional state of the heart. It was demonstrated by highly reliable positive changes in end-systolic and diastolic cardiac volumes and left ventricular ejection fraction.

REFERENCES

1. Alzahrani, S., Alosaimi, M., Malibarey, W. M., Alhumaidi, A. A.,Alhawaj, A. H., Alsulami, N. J., Alsharari, A. S., Alyami,A. A., Alkhateeb, Z. A., Alqarni, S. M. et al. (2019). Saudi Family Physicians' Knowledge of Secondary Prevention of Heart Disease: A National Assessment Survey. Archieves of Pharmacy Practice, 10(4), 54-60.
2. Anavekar NS, McMurray JJ, Velazquez EJ et al. Relation between renal dysfunction and cardiovascular outcomes after myocardial infarction. N Engl J Med 2004; 351:1285-1295.
3. Bhatt A.S., Ambrosy A.P., Dunning A., DeVore A.D., Butler J., Reed S., Voors A., Starling R., Armstrong P.W., Ezekowitz J.A., Metra M., Hernandez A.F., O'Connor C.M., Mentz R.J. The burden of non-cardiac comorbidities and association with clinical outcomes in an acute heart failure trial - insights from ASCEND-HF. Eur J Heart Fail. 2020 Jun;22(6):1022-1031.
4. Calvier L. Miana M., Reboul P. et al. Galectin-3 mediates aldosterone-induced vascular fibrosis // Atheroscler. Thromb. Vasc. Biol. — 2013. — Vol. 33 — P. 67–75.
5. Davis M.E., Richards A.M., Nicholls M.G., Yandle T.G., Frampton C.M., Troughton R.W. Introduction of metoprolol increases plasma B-type cardiac natriuretic peptides in mild, stable heart failure. Circulation 2006; 113(7): 977–985.
6. Eisenstein E.L., Nelson C.L., Simon T.A., Smitten A.L., Lapuerta P., Mark D.B. Vasopeptidase inhibitor reduces inhospital costs for patients with congestive heart failure: results from the IMPRESS trial. Inhibition of Metallo Protease by BMS-186716 in a Randomized Exercise and Symptoms Study in Subjects with Heart Failure. Am Heart J 2002; 143(6): 1112–1117.

Published: January 30, 2024 | Pages: 107-1114

7. Esayan A.M., Nimgirova A.N. Mineralokortikoid receptor antagonists new extended roles in cardio-and nephroprotection // Медицинский совет № 5. 2018.
8. Groenewegen, A., Rutten, F. H., Mosterd, A., & Hoes, A. W. (2020). Epidemiology of heart failure. European Journal of Heart Failure, 22(8), 1342-1356;, Permadi, A. W., Hartono, S., Wahjuni, E. S., & Lestari, N. K. D. (2020). The Combination of Physical Exercise Programs in Patients with Heart Failure. International Journal of Pharmaceutical and Phytopharmacological Research, 10(1), 22-28.
9. Reibis R., Jannowitz C., Halle M., Pittrow D., Gitt A., Völler H. Management and outcomes of patients with reduced ejection fraction after acute myocardial infarction in cardiac rehabilitation centers. Curr Med Res Opin 2015; 31(2): 211–219.,
10. Richards A.M. Variability of NT-proBNP levels in heart failure: implications for clinical application. Heart 2007; 93(8): 899–900.
11. Shiba N, Shimokawa H. Chronic kidney disease and heart failure--Bidirectional close link and common therapeutic goal. J Cardiol. 2011 Jan;57(1):8-17.
12. Tang S., Peng D., Hu Y., Chen J. Protective effects of valsartan and benazepril combined with atorvastatin on cardiorenal syndrome in rats. Eur Rev Med Pharmacol Sci 2015; 19(5): 759–766.
13. Virani, S. S., Alonso, A., Aparicio, H. J., Benjamin, E. J., Bittencourt, M. S., Callaway, C. W., Carson, A. P., Chamberlain, A. M., Cheng, S., Delling, F. N. et al. (2021). Heart Disease and Stroke Statistics-2021 Update: A Report from the American Heart Association. Circulation. 143(8):e254-e743.
14. Гуревич М.А., Кузьменко Н.А. Блокада альдостерона в лечении артериальной гипертензии (аспекты применения эплеренона). Кардиология. РМЖ «Медицинское обозрение» №11 от 31.05.2017 стр. 776-779.
15. Евдокимова А.Г., Коваленко Е.В., Евдокимов В.В., Ющук Е.Н., Стрюк Р.И. Антагонисты минералкортикоидных рецепторов: преимущества применения эплеренона (Иплерон) у больных хронической сердечной недостаточностью. журнал Поликлиника № X(X) 2019. С.1-6.