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THE EFFECT OF EMPAGLIFLOZIN ON CARDIAC FUNCTIONAL STATUS IN CHRONIC HEART FAILURE

Hikmatov Azam Asatullayevich
Boboyev Nasimjon Malikovich
Eshonqulov Sardor Sindarovich
National Medical Center, Tashkent, Uzbekistan
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Conclusion

This article presents a comparative study of the effects of various standard treatment regimens on intracardiac hemodynamics and N-terminal pro-B-type natriuretic peptide in patients with chronic heart failure, who were divided into three groups for observation. A highly significant increase in the left ventricular end-diastolic dimension, diastolic volume, and ejection fraction was detected in the third group of patients. This confirms the high cardioprotective effect of sacubitril/valsartan and empagliflozin.

Keywords: chronic heart failure, N-terminal pro-B-type natriuretic peptide, sacubitril/valsartan, empagliflozin.

Introduction. Chronic heart failure (CHF) is considered one of the urgent medical and social problems of modern medicine [19, 12, 15]. This is due to its high prevalence, extremely severe consequences, and the substantial costs associated with treatment [14, 4, 10].

Mortality resulting from CHF is 4-8 times higher than in the general population, and half of the patients die within 5 years of diagnosis. In its functional class (FC) IV, mortality within six months reaches 44% [21, 24, 1, 11, 17, 16].

According to epidemiological data, in the Russian Federation and European countries, chronic heart failure (CHF) develops in the majority of cases as a result of arterial hypertension (95%) and coronary heart disease (CHD) (69.7%). In our republic, the main causes of this severe complication are also often these two aforementioned diseases [18, 2].

Due to increased life expectancy, positive outcomes in treating cardiovascular diseases, and the widespread prevalence of risk factors for CHD and hypertension (HTN) —the primary conditions leading to CHF—this severe complication is becoming increasingly common among the global population [3, 5, 22, 23]. Despite the progress made in recent years, this confirms that CHF continues to be a heavy financial burden on the healthcare economies of all countries worldwide.

In CHF, systemic changes are observed in all organs, with cardiac remodeling processes being of particular importance [20].

It is known that a number of examination methods are used to diagnose CHF and evaluate treatment effectiveness. Among these, natriuretic hormones are of particular importance as biological markers. Currently, several types exist, among which brain natriuretic peptide and N-terminal pro-brain natriuretic peptide are widely used in the diagnosis of CHF and the assessment of its course.

A.M. Richards was the first to demonstrate the use of blood concentrations of N-terminal pro-B-type natriuretic peptide to monitor the effectiveness of treatment in patients with CHF. In his study, patients diagnosed with NYHA functional class II-III CHF were monitored by titrating the dose of angiotensin-converting enzyme inhibitors (ACEIs) under hormone guidance, and the feasibility of such an approach was shown [13].

In the IMPRESS trial, which included 573 patients receiving lisinopril and omapatrilat, a randomized study of patients with CHF and a left ventricular ejection fraction of less than 40% noted a significant decrease in the neurohormone 1-2 years after the start of treatment [8].

Similar data were obtained in experimental observations conducted by S. Tang et al. in patients receiving valsartan and benazepril [16].

Additionally, a number of observations have revealed a decrease in blood levels of B-type natriuretic peptide in patients taking β-blockers [7].

Taking the above into account, we studied the levels of N-terminal pro-B-type natriuretic hormone and cardiac hemodynamics in the patients under our observation before and after various treatment combinations.

Objective of the study. To study the effect of different treatment combinations on serum N-terminal pro-B-type natriuretic hormone and cardiac functional state in patients with chronic heart failure.

Materials and Methods. This scientific research was conducted on 120 patients with chronic heart failure (CHF) secondary to ischemic heart disease (IHD) and arterial hypertension (AH) , who were treated at the National Medical Center in 2024 and 2025. The patients were divided into three groups based on the treatment they received. Each group consisted of 40 patients, comprising 20 patients with CHF Functional Class (FC) II and 20 with FC III. The mean age of patients in the first group was 66.1±1.8 years; the group included 21 men (52.5%) and 19 women (47.5%). In the first group of observed patients, 28 (70%) had a history of myocardial infarction (MI), 11 (27.5%) had undergone coronary artery bypass grafting (CABG) or stenting, 12 (30%) had documented rhythm disturbances and blockades, 31 (77.5%) had AH, 17 (42.5%) were diagnosed with varying degrees of obesity, and 21 (52.5%) had anemia. This group was prescribed standard CHF therapy consisting of β-blockers, ACE inhibitors or angiotensin receptor blockers (ARBs), and the mineralocorticoid receptor antagonist (MRA) spironolactone. The mean age of patients in the second group was 65.9±1.5 years, with 24 men (60%) and 16 women (40%). In this group, 25 (62.5%) had a history of MI, 13 (32.5%) had undergone CABG or stenting, 15 (37.5%) had documented rhythm disturbances and blockades, 27 (67.5%) had AH, 16 (40%) were diagnosed with varying degrees of obesity, and 19 (47.5%) had anemia. They received standard therapy comprising β-blockers, sacubitril/valsartan (Yuperio), and the MRA spironolactone. The mean age of patients in the third group was 64.7±1.3 years, of whom 21 (52.5%) were men and 19 (47.5%) were women. In this group, 27 (67.5%) had a history of MI, 16 (40%) had undergone CABG or stenting, 17 (42.5%) had documented rhythm disturbances and blockades, 25 (62.5%) had AH, 15 (37.5%) were diagnosed with varying degrees of obesity, and 19 (47.5%) had anemia. These patients were prescribed a combination of β-blockers, sacubitril/valsartan (Yuperio), the MRA spironolactone, and a sodium-glucose cotransporter-2 (SGLT2) inhibitor (empagliflozin).

Special attention was paid to ensuring an equal number of patients with FC II and III in each group and their representativeness.

In all subjects included in the study, serum N-terminal pro-B-type natriuretic peptide levels were determined, and the functional state of the heart was assessed using echocardiography, along with standard laboratory tests, before the start of treatment and 6 months after it.

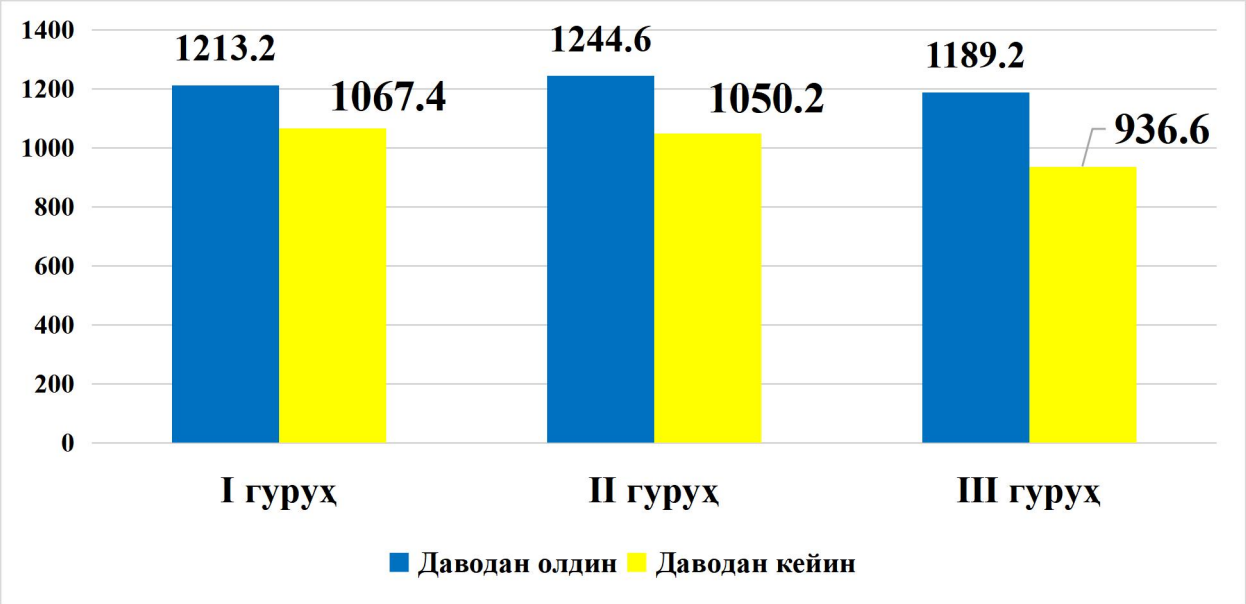
The serum N-terminal pro-B-type natriuretic peptide level was determined by enzyme-linked immunosorbent assay (ELISA) using "Vector-BEST" (Russia) reagent kits. The detection range of the reagent used in the study to determine serum N-terminal pro-B-type natriuretic peptide was 0–2500 pg/ml, with a sensitivity of 20.0 pg/ml.

Analysis and Discussion of Study Results. We studied the serum N-terminal pro-B-type natriuretic peptide levels in all groups of patients under our observation before and after treatment. Figure 1 below presents a comparative analysis of serum N-terminal pro-B-type natriuretic peptide levels before and after treatment.

Figure 1.

Comparative analysis of N-terminal pro-B-type natriuretic peptide levels in patients with chronic heart failure before and after treatment (pg/ml).

Note: * - significance of the difference between pre- and post-treatment indicators: * - p<0.05, ** - p<0.01,
- p<0.001.



Гуруҳлар ўртасида муолажалардан олдин N–про мия натрий уретик пептид кўрсатгичи ўзаро солиштирма ўрганилганда ишончли фарқлар (P>0.05) кузатилмади.

In the first group of patients, the serum level of N-terminal pro-brain natriuretic peptide decreased 1.14-fold from 1213.2±40.2 pg/ml to 1067.4±36.4 pg/ml before and after treatment, and a statistically significant difference was recorded (p<0.05). In the second group, its level was 1244.6±47.2 pg/ml before treatment and 1050.2±39.8 pg/ml after treatment, decreasing 1.2-fold, and a highly significant difference was identified (p<0.01). In Group III, which received standard therapy consisting of β-blockers + sacubitril-valsartan (Yuperio) + MRA + sodium-glucose cotransporter-2 inhibitors (empagliflozin), the N-terminal pro-brain natriuretic peptide level decreased 1.3-fold from 1189.2±32.5 pg/ml to 936.6±29.3 pg/ml, and a highly significant difference was observed (p<0.001).

During a six-month prospective follow-up of patients after treatment, their cardiac functional status was also studied, and the results obtained were comparatively evaluated against pre-treatment indicators. The following Table 1 presents a comparative analysis of cardiac functional status indicators between the groups of patients with CHF included in the study, before and after treatment procedures.

Table 1

Comparative analysis of cardiac functional status indicators in patients with chronic heart failure after standard treatment procedures with various compositions.

No.	Indicators	Group I (n=40)		Group II (n=40)		Group III (n=40)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
1	Left atrial dimension (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 dimension (2.6–3.8 cm), cm	4.6±0.16	4.1±0.14*	4.7± 0.15	4.2±0.13*	Left ventricular end-diastolic dimension (4.4-5.4 cm), cm	5.8±0.13
5.5±0.12	6.1±0.2	5.8±0.13	5.2±0.2	4	Left ventricular end-diastolic volume (88-145 ml), ml	186.6±5.8	5.2±0.2***
4	150.2±5.8	5	Left ventricular end-systolic volume (45-68 ml), ml	90.4±5.2	76.5±5.6	92.6±5.8	150.2±5.8***
5	Left ventricular ejection fraction, %	40.6±1.8	76.5±5.6	92.6±5.8	51.5±1.4	7	Left ventricular myocardial mass, g
204.2±10	186.5±9.8	205.6±10.7	182.5±11.3	202.6±9.9	176.2±10.4	Note: Statistical significance of the difference between pre- and post-	51.5±1.4***

.2						treatment indicators: * - p<0.05; ** - p<0.01;	
7	Чап қоринча миокард вазни, г	204.2±10,2	186.5±9.8	205,6±10,7	182.5±11.3	202,6±9,9	176.2±10.4
Изоҳ: * - даводан олдинги ҳамда кейинги кўрсатгичлар фарқи ишончлилиги: * - p<0,05., ** - p<0,01, ***p<0,001.							

As shown in the table, following the prescribed treatments, the left atrial dimension in the first group decreased from 42.2±1.4 mm before treatment to 39.5±1.5 mm after treatment, but no statistically significant difference was found (p>0.05). In the second group, the dimension significantly decreased after treatment from 42.6±1.5 mm to 38.1±1.2 mm (p<0.05), and in the third group, it decreased from 41.8±1.4 mm to 36.2±1.3 mm with high statistical significance (p<0.01). The left ventricular end-systolic dimension, which was 4.6±0.16 cm and 4.7±0.15 cm in the first and second groups, respectively, before treatment, became 4.1±0.14 cm and 4.2±0.13 cm, respectively, after treatment, with a statistically significant difference noted (p<0.05). In the third group, it improved 1.23-fold from 4.8±0.15 cm before treatment to 3.9±0.2 cm after, and a highly significant difference was observed (p<0.01). In the first group of patients receiving β-blockers + ACE inhibitors or ARBs + MRAs, the left ventricular end-diastolic dimension decreased from 5.8±0.13 cm to 5.5±0.12 cm, and no significant difference was noted (p>0.05). In the second group of patients, who received β-blockers + sacubitril-valsartan (Yuperio) + MRAs, its dimension improved by 10%, decreasing from 6.1±0.2 cm to 5.5±0.15 cm, and a significant difference was identified (p<0.05). In the third group of patients, who were prescribed β-blockers + sacubitril-valsartan (Yuperio) + MRAs + sodium-glucose co-transporter 2 inhibitors (empagliflozin), the left ventricular end-diastolic dimension showed a positive change of 18% after treatment, and a highly significant difference was recorded (from 6.3±0.16 to 5.2±0.2 cm, p<0.001).

In the first and second groups, the left ventricular end-diastolic volume improved from 186.6±5.8 ml to 161.4±6.3 ml and from 188.2±6.4 ml to 158.8±6.6 ml, respectively, before and after treatment. The differences in both groups were statistically significant (p<0.01). In the third group, this volume decreased from 190.5±6.5 ml before treatment to 150.2±5.8 ml after treatment, a 1.27-fold reduction, which was a highly significant difference (p<0.001).

In the first group, the left ventricular end-systolic volume improved by 15%, decreasing from 90.4±5.2 ml before treatment to 76.5±5.6 ml after treatment; however, the difference was not statistically significant (p>0.05). In the second group, a statistically significant difference was found, with the volume decreasing by 20.5% from 92.6±5.8 ml to 73.5±5.5 ml. In the third group, the left ventricular end-systolic volume changed positively by 23.7%, from 89.4±5.6 ml to 68.2±5.2 ml, and a statistically significant difference was observed (p<0.01). Following treatment, the left ventricular ejection fraction was noted to have increased significantly in the first group from 40.6±1.8% to 47.8±2.0% (p<0.05), in the second group from 39.6±1.8% to 48.2±2.2% (p<0.01), and with high significance in the third group from 38.2±1.6% to 51.5±1.4% (p<0.001). Although the left ventricular myocardial mass decreased in the first group from 204.2±10.2 g to 186.5±9.8 g, in the second group from 205.6±10.7 g to 182.5±11.3 g, and in the third group from 202.6±9.9 g to 176.2±10.4 g before and after treatment, the changes were not statistically significant in any of the groups (p>0.05).

The correlation between the N-terminal pro-B-type natriuretic peptide and the left ventricular ejection fraction in patients enrolled in the study was analyzed, and the results are presented in Figure 2 below.

Figure 2

The correlation between N-terminal pro-B-type natriuretic peptide and left ventricular ejection fraction in patients with chronic heart failure.

As shown in the figure, a moderately strong negative correlation ($r = -0.434$, $p<0.01$) was identified between the left ventricular ejection fraction and N-terminal pro-B-type natriuretic peptide. This indicates that as the level of the studied peptide increases, the left ventricular ejection fraction decreases.

The analysis revealed that the third group, compared to the other two groups, showed highly significant positive changes in intracardiac hemodynamic indicators, particularly in end-systolic and diastolic volumes, as well as the left ventricular ejection fraction. The results obtained demonstrated that the combined use of sacubitril-valsartan (Yuperio) and sodium-glucose cotransporter-2 (SGLT2) inhibitors (empagliflozin) as part of standard therapy is highly effective in patients with CHF. This also indicates that drugs belonging to the SGLT2 inhibitor group have a positive effect on the restoration of the heart's functional state.

Conclusion. Following treatment, positive changes in N-pro natriuretic peptide levels were observed in all patient groups. However, the highly significant changes in these levels within the third group confirm that the combination of sacubitril+valsartan and empagliflozin had a more effective impact on cardiac functional status compared to the first two groups. Furthermore, the highly significant positive changes in end-systolic volume, end-diastolic volume, and left ventricular ejection fraction were observed in the group receiving a sodium-glucose co-transporter 2 (SGLT2) inhibitor (empagliflozin), indicating its crucial role in stabilizing cardiac hemodynamics.

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