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EFFECT OF DAPAGLIFLOZIN ON CARDIAC FUNCTIONAL STATUS IN CHRONIC HEART FAILURE WITH ANEMIA

Abdigaffar G. Gadaev

Researcher Tashkent Medical Academy, Uzbekistan

Farida I. Khujakulova

Researcher Termiz Branch Of Tashkent Medical Academy, Uzbekistan

Ravshan Q. Qarakhanov

Researcher Termiz Branch Of Tashkent Medical Academy, Uzbekistan

ABSTRACT: We compared the effect of a standard treatment regimen containing the glucose sodium cotransporter type 2 inhibitor dapagliflozin (Forsiga) on intracardiac hemodynamics in anemic patients with chronic heart failure. In the group of patients who received dapagliflozin, the indicators of intracardiac hemodynamics, in particular, left ventricular diastolic and systolic volume, diastolic volume, and ejection fraction increased significantly after treatment, proving the cardioprotective effect of the drug.

KEYWORDS: chronic heart failure, dapagliflozin, intracardiac hemodynamics.

INTRODUCTION

In recent years, the number of patients with chronic heart failure (CHF) has been steadily increasing. On the one hand, this is due to the increase in the average life expectancy of the population in the world, including Uzbekistan, and on the other hand, to the improvement of treatment methods for patients with cardiovascular disease, among which CHF is the leading one. Anemia is one of the most common syndromes in patients with CHF. A large number of clinical studies confirm that 7-79% of anemia occurs in this group of patients [9]. The wide variation in indicators is due to the lack of a uniform approach to the diagnosis of anemia, different causes of the disease and functional classes (FC) of the CHF, demographic conditions and a number of other factors [8]. The Framingham observations were the first to show that anemia is one of the important risk factors of CHF.

In recent years, in patients with chronic heart failure without diabetes and low left ventricular ejection fraction, a number of drugs belonging to the group of glucose-sodium symporter 2 inhibitors have been shown to be effective in anemia. It is known that treatments with Glucose sodium cotransporter type 2 inhibitor (GNKT2i) have diuretic and natriuretic effects. As a result of them, the amount of total water and sodium loss in the body increases [7, 10, 6, 5]. A decrease in circulating serum reduces cardiac preload and left ventricular filling pressure. This, in turn, has a

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positive effect on myocardial activity and reduces interstitial fibrosis [12]. The above shows the cardioprotective effect of the drug. In addition, the drugs of this group normalize the properties caused by glycation, which cause inflammation and endothelial dysfunction, change carbohydrate metabolism in a positive direction, decrease blood pressure and body weight, and cause other positive changes [3,4]. In addition, they block the production of renin by reducing the activity of the intrarenal renin-angiotensin-aldosterone system. As a result of this effect, the cardioprotective effect of the drug is also manifested [11, 1].

In Uzbekistan, a number of scientific studies have been conducted on the diagnosis and treatment of chronic heart failure accompanied by anemia and the impact of this condition on the quality of life of patients [14, 13, 2, 5].

But so far, the effects of drugs belonging to the group of glucose-sodium symporter 2 inhibitors on intracardiac hemodynamics in chronic heart failure with anemia have not been studied. Taking this into account, we set the following goal.

The purpose of the study. Study of the effects of angiotensin-converting enzyme inhibitors and glucose-sodium symporter 2 inhibitor dapagliflozin-forsiga on intracardiac hemodynamics in patients with CHF anemia.

RESEARCH MATERIALS AND METHODS

This scientific research work was conducted in 2021 and 2022 in the cardiology and cardiorehabilitation departments of the multidisciplinary clinic of the Tashkent Medical Academy in patients with CHF developed on the basis of IUD and arterial hypertension. Based on the goals and tasks set before us, the scientific research work was carried out as follows.

120 patients with CHF Ⅱ and Ⅲ FC were included in the follow-up and divided into two groups. The first group was treated with dapagliflozin-forsi, an inhibitor of glucose-sodium cotransporter 2 (gliflozins) as part of complex standard treatment, and the second group was treated with complex standard treatment without iron deficiency anemia. patients who did Both groups of patients were prescribed iron (III) sucrose intravenously.

The first group consisted of 80 patients and their average age was 65.1±1.2 years, 22 (41.5%) men and 31 (58.5%) women. This group, in turn, was divided into two subgroups based on the FC of CHF.

The first subgroup consisted of 40 patients with II FC of CHF, their mean age was 65.2±1.4 years, 24 (60%) men and 16 (40%) women. 26 (65) had myocardial infarction (MI), 11 (27.5) had coronary artery bypass grafting (ACS) or stenting, 8 (20) had obesity, type II diabetes) - 4 (10%) people.

The second subgroup consisted of 40 patients with III FC of CHF. Their average age was 65.1±1.6 years, men were 19 (47.5%) and women were 21 (52.5%). 21 (52.5%) had MI, 9 (22.5%) had coronary artery disease or stenting, 11 (27.5%) were obese, and 6 (15%) had QD II.

The second group consisted of 40 patients, their average age was 66.3±2.0, 20 (50%) men and 20 (50%) women. This group, in turn, was divided into two subgroups based on the FC of CHF.

The first subgroup consisted of 20 patients with II FC of CHF, their average age was 68.4±2.1 years, 10 (50%) men and 10 (50%) women. 11 (55%) had MI, 6 (11.3%) had ACS or stenting, 16 (30.1%) were obese, and 4 (7.5%) had QD II.

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The second subgroup consisted of 20 patients with III FC of CHF. Their average age was 64.4±1.2 years, with 10 (50%) males and 10 (50%) females. There were 17 (85%) who underwent MI, 8 (40%) who underwent ACS or stenting, 16 (30.1%) were obese, and 10 (50%) had QD II.

The diagnosis of CHF and its FC in patients is based on the complaints of observers, the study of medical history, objective examination and laboratory-instrumental examinations in accordance with the "Recommendations for the diagnosis and treatment of acute and chronic heart failure" updated by the European Association of Cardiology in 2021 and the New York Society of Cardiology (New York It was determined according to the criteria of Heart Association, 1964).

In follow-up patients, laboratory-instrumental and functional examinations were performed on 1-3 days after admission to the hospital, and the next examination was carried out after the sixth month of treatment.

ANALYSIS AND DISCUSSION OF RESEARCH RESULTS

After the treatment of patients under our observation, they were followed up dynamically for six months, and all laboratory tests were repeated. Table 1 below shows intracardiac hemodynamic parameters in patients with CHF Ⅱ-Ⅲ FC before and after six months of treatment.

1-Table

Echocardiographic parameters before and six months after treatment in patients with chronic heart failure functional class Ⅱ anemia.

№	Indicators	Main group		Control group	
		Before treatment	After six months	Before treatment	After six months
1	Left ventricular end-diastolic size (44-54 mm), mm	55,2±1,2	48.3±1.4***	56,2±1,3	50.2±1.6**
2	Left ventricular end-diastolic volume (88-145 ml), ml	162.4±3.4	145.4±3.2***	166,7±5,0	146.8±4.4**
3	Left ventricular end-systolic size (26-38 mm), mm	39.8±0.8	36.8±1.1*	41,4±1,4	37.8±1.5
4	Left ventricular end systolic	81.6±1.7	72.8±2.2**	86,2±2,2	72.4±3.4**

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	volume (45-68 ml), ml				
5	Left ventricular ejection fraction, %	48.2±1.2	54.6±1.8**	47.8±1,4	52.1±1.6*
* - differences are significant compared to pre- and post-treatment scores (*-P <0,05, ** - P <0,01, *** - P<0,001)					

In the main group of patients with CHF Ⅱ FC, left ventricular post-diastolic size decreased reliably from 55.2±1.2 mm to 52.6±1.4 mm in the first month of treatment, but after six months of intensive treatment, it was 48.3±1.4 mm (1.14-fold decrease), highly reliable (R<0.001) changes were detected. Significant positive changes in dynamics were also noted in the control group (56.2±1.3 mm before treatment and 50.2±1.6 mm after six months, R<0.01). Left ventricular end-diastolic volume in the main group of patients was 162.4±3.4 ml before treatment and 152.3±3.1 ml after treatment (R<0.05), after six months it was 145.4±3.2 ml and was highly reliable (R<0.001) difference was noted. In the control group, left ventricular end-diastolic volume decreased as reliably as in the main group after the treatments (from 166.7±5.0 ml to 151.4±4.2 ml R<0.05 and 146.8±4.4 ml after six months, respectively) R<0.01). The left ventricular end-systolic size was 39.8±0.8 mm and 36.8±1.1 mm in the main group of patients before and after six months, respectively (R<0.05). In the control group, no reliable difference was detected after six months of treatment (decrease from 41.4±1.4 mm to 37.8±1.5 mm, R>0.05). Left ventricular end-systolic volume changed dynamically after treatment in the main group: 81.6±1.7 ml before treatment, 74.2±1.6 ml after one month, and 72.8±2.2 mm after six months. A reliable (R<0.01) difference was noted in patients when the results were compared. In the control group, left ventricular end-systolic volume was reliably reduced after treatment (from 86.2±2.2 ml to 78.4±2.8 ml and 72.4±3.4 ml after six months, respectively, as in the main group, R<0.01).

Left ventricular ejection fraction in the main group increased 1.13 times to 48.2±1.2% before treatments, 52.3±1.6% after one month (R<0.05) and 54.6±1.8% after six months and was reliable compared to baseline (R <0.01) difference was noted. In the control group, 47.8±1.4% before treatment and 50.9±1.3% after one month, no reliable (R>0.05) difference was observed, while during six months of treatment, the changes were 52.1±1.6%. It was found to be improved by .08 times (R<0.05). But the indicator change was lower compared to the main group.

Changes in intracardiac hemodynamics after treatment in patients with CHF ⅡI FC anemia are presented in Table 2 below..

2-Table

Echocardiographic parameters before and six months after treatment in patients with functional class Ⅲ chronic heart failure anemia.

N⁹	Indicators	Main group	Control group

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		Before treatment	After six months	Before treatment	After six months
1	Left ventricular end-diastolic size (44-54 mm), mm	60.2±1.4	54.1±1.5**	60.4±1.2	55.6±1.4*
2	Left ventricular end-diastolic volume (88-145 ml), ml	192.4±5.2	166.5±4.6***	190.4±4.8	168.6±5.4**
3	Left ventricular end-systolic size (26-38 mm), mm	45.5±1.6	41.2±1.3*	46.2±1.4	42.2±1.2*
4	Left ventricular end systolic volume (45-68 ml), ml	106.6±2.7	86.5±2.7***	107.4±3.2	89.6±4.2**
5	Left ventricular ejection fraction, %	42.6±0.9	50.5±1.8***	42.1±1.3	47.2±1.6*
* - differences are significant compared to pre- and post-treatment scores (*-P <0,05, ** - P <0,01, *** - P<0,001)					

As shown in the table, the left ventricular post-diastolic size in the main group of patients with CHF ⅡI FC anemia decreased by 1.12 times from 60.2±1.4 mm to 55.8±1.3 mm (R<0.05) in the first month of treatment and to 54.1±1.5 mm in the sixth month, and higher a reliable (R<0.01) difference was found. In the control group, reliable changes were observed in the first month of treatment (decreased from 60.4±1.2 mm to 56.2±1.1 mm, R<0.05), and after six months of treatment, the changes further improved to 55.6±1.4 mm in left ventricular end-diastolic size 1.08 times. decreased (R<0.05). Left ventricular end-diastolic volume decreased by 1.07 (R<0.05) and 1.16 times in the first and sixth months of treatment in the main group, respectively, and a reliable difference (R<0.001) was found. In the control group, it decreased from 190.4±4.8 ml to 176.8±4.2 ml (R<0.05) in the first month of treatment, and after the sixth month, the left ventricular end-diastolic volume was 168.6±5.4 ml. The left ventricular end-systolic size was 45.5±1.6 mm and 43.2±1.2 mm in the main group before and one month after the treatment, respectively, and no reliable difference was detected (R>0,05). In the control group, it was equal to 46.2±1.4 mm and 43.9±1.5 mm (R>0,05). After six months of treatment, reliable changes were observed in both groups of patients (41.2±1.3 mm and 42.2±1.2 mm, respectively, R<0.05). The left ventricular end-systolic volume improved from 106.6±2.7 ml to 88.4±2.2 ml after one month in the main group and decreased by 1.23 times compared to the initial value after six months, a highly reliable (R<0.001)

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difference was noted in both cases. In the control group, a reliable (R<0.05) difference decreased from 107.4 ± 3.2 ml to 93.6 ± 4.2 ml after one month of treatment, and after six months, the left ventricular post-systolic volume was further improved and a highly reliable difference was observed (89.6 ± 4.2 ml, R<0.01).

In the group that received the main, that is, the standard treatment of CHF containing dapagliflozin (Forsiga), the left ventricular ejection fraction was 42.6±0.9% before the treatments, 46.7±1.6% after one month, and 50.5±1.8% after six months, which was equal to 7.9%. increased and a highly reliable (R<0.001) difference was noted. In the control, i.e. those who received the standard treatment of CHF, during the treatment, during the first month, from 42.2±1.3% to 45.5±1.5% unreliable (R>0.05), it increased by 5% to 47.2±1.6% in the sixth month, reliable (R<0, 05) difference was observed.

The analysis confirmed that intracardiac hemodynamics in the main group, in particular, systolic and diastolic volumes and dimensions, were significantly increased in almost all indicators compared to the control group. Left ventricular ejection fraction also changed to a high confidence positive with a 7.9% increase in the baseline group. The obtained results showed that the use of dapagliflozin (forsiga) in combination with iron Ⅲ sucrose drugs as part of the standard treatment was more effective compared to the control group without the last drug in the complex treatment. This confirms the positive effect of drugs belonging to the group of inhibitors of glucose sodium cotransporter type 2 on the recovery of the functional state of the heart. Our results are consistent with those obtained in recent years and reported in the literature below.

CONCLUSION

It was found that the use of glucose sodium cotransporter type 2 inhibitor dapagliflozin (forsiga) as part of standard treatment in patients with chronic heart failure with anemia has a positive effect on intracardiac hemodynamics, having a cardioprotective effect.

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