Original Article

Assessment of Cardiac Functional Status before and after Treatments in Patients with Covid-19 and Chronic Heart Failure with Pulmonary Hypertension

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Abstract

In this article, the echocardiographic parameters before and after various treatments were compared in patients with Covid-19 and chronic heart failure with pulmonary hypertension. The obtained results revealed that complex treatment with the addition of eplerenone and glucose sodium co-transporter type 2 inhibitors - empagliflozin in patients with chronic heart failure and developed pulmonary hypertension has a positive effect on intracardiac hemodynamics.

Keywords: Covid – 19, Chronic Heart Failure, Pulmonary Hypertension, Eplerenone, Empagliflozin, Echocardiography.

INTRODUCTION

Despite the progress made in research on the pathogenesis and progression of chronic heart failure (CHF) and the widespread use of effective drugs in practice, it is the final stage of the cardiovascular continuum. It remains one of the urgent problems of medicine as a complication with the most common, developing and ending with unpleasant consequences [13, 11].

According to the official epidemiological data, CHF is determined in 1-2.6% of the population in European countries, in 2.2% in the United States of America, and in 7-10% in the Russian Federation. 5% of all hospitalized patients in Europe correspond to this pathology. In the Russian Federation, 16.7% of those hospitalized with cardiovascular disease are patients with CHF. Most of them are re-hospitalized within 6 months after discharge, and 20-25% within 30 days, and this is due to decompensation of the disease in 70% of cases. Therefore, the problem of CHF is very important for the healthcare system. But the presence of comorbid conditions in patients causes the rapid development of CHF, which leads to its early formation among people under the age of 60 [1,2]. Because in a large number of observations, it has been confirmed that the presence of concomitant diseases has a drastic negative effect on the general condition and life expectancy of patients with CHF[3].

Unfortunately, the infection of COVID-19 and its spread in the form of a pandemic in the world are causing a sharp worsening of the general condition of patients as another comorbid condition to CHF, which is considered a serious complication of cardiovascular diseases [12].

A number of other reports have also been made that this infection can be severe and, in many cases, fatal in patients with cardiovascular disease. They found that two-thirds of patients who died from COVID-19 had cardiovascular disease or diabetes [10].

Pulmonary hypertension (PH) is one of the most common complications observed in patients with Covid-19. Currently, PH is detected in 12 - 13% of cases of echocardiography of patients admitted to the hospital after the diagnosis of this disease[9].

However, the changes in the respiratory organs of patients who had Covid-19 and “clinically recovered” were not sufficiently studied. Some of them were carried out in the third or sixth month after the patients were discharged from the hospital, and they revealed a number of changes [4].

It is necessary to take into account the interaction of drugs and prevent possible complications in the treatment of patients with Covid-19 in whom CHF is present[5].

Angiotensin-converting enzyme inhibitor (ACEI), mineralocorticoid receptor antagonists (MRRA), phosphodiesterase-5 inhibitors (PDIE-5) and endothelin antagonists are used in the treatment of PH. Among them, sildenafil belonging to the PDEI-5 group is widely used in practice. However, there is very little data on the effect of sildenafil when used together with different drug groups when PH is observed in patients with CHF.

In recent years, there have been reports of specific direct effects of glucose-sodium co-transporter type 2 inhibitors (GSC2i) on pulmonary arteries [7]. In the EMBRACE–HF randomized trial, there were 65 stable CHF with preserved and reduced left ventricular ejection fraction (LVEF) above 30 mm Hg. empagliflozin has been shown to reduce PH without loop-acting diuretics in patients with high [8].

The above confirms that the GSC2i drug group is effective not only in CHF, but also in the treatment of PH.

From this point of view, it is appropriate to use these groups of drugs in patients who have had Covid-19 and who have suffered from CHF PH. Because it has been shown in several literatures that the virus causes endothelial dysfunction and ultimately causes PH [6].

Therefore, the study of their effect on PH in different combinations is not only of scientific but also of important practical importance.

Purpose of the Study

Coordinating treatment in patients with chronic heart failure II - III FC who have undergone Covid – 19 and have been diagnosed with pulmonary hypertension.

Research Source and Methods

This scientific research work was conducted in 2020 and 2022 in 120 patients who were treated in hospital conditions in the cardiology and cardiorehabilitation departments of the multidisciplinary clinic of the Tashkent Medical Academy, developed PH on the basis of CHF.

Patients were divided into two groups according to the treatment procedures. The first group consisted of 60 patients, their average age was 65.2±1.2 years, 33 (55%) men and 27 (45%) women. Also, 16 (26.67%) of the patients in this group had CHF II FC, and 44 (73.3%) had III FC of the disease. According to the recommendation of the European Society of Cardiology (2021), they were prescribed an ACE inhibitor (enalapril), a β-adrenoblocker (bisoprolol), a mineralocorticoid receptor antagonist (veroshpiron), according to the instructions, diuretics and sildenafil for the treatment of PH.

The second group consisted of 60 patients, their average age was 63.7±1.2, 37 (61.6%) men and 23 (38.3%) women. Also, 11 (18.3%) of the patients in this group had CHF II FC, and 49 (81.7%) had III FC of the disease. This group of patients received ACE inhibitor (enalapril), β-adrenoblocker (bisoprolol), mineralocorticoid receptor antagonist (eplerenone), GNK2i (empagliflozin - diampa), diuretics according to the instructions, and sildenafil for the treatment of PH.

Clinical and biochemical analyzes of blood, echocardiography examinations were performed in patients who were under prospective observation for 6 months.

MS Excel (2016) package computer program was used for statistical processing of the data obtained in the study. Arithmetic mean and standard deviation (M±m) of indicators presented in all tables were calculated. The reliability of differences between groups was determined using Student's criterion for odd and even differences.

Results

A comparison of patients with CHF II FC PH and Covid-19, involved in the study, was studied before and after complex treatments with different components. Information about them is presented in table 1.

Table 1. Comparative analysis of intracardiac hemodynamic parameters determined by echocardiography before and after procedures in patients with chronic heart failure II FC who underwent Covid-19 and had pulmonary hypertension

№	Indicators	Chronic heart failure II FC standard treatment enalapril + bisoprolol + veroshpiron and sildenafil, n=16		Chronic heart failure II FC standard treatment enalapril + bisoprolol + eplerenone + empagliflozin (diampa) and sildenafil, n=11	
		Before treatment	After treatment	Before treatment	After treatment

1	**Transverse dimension of right lobe (29-46 mm)**	42.8 ±0.7	41.4±0.6	43.32±0.7	41.1±0.6*
2	**Left lobe transverse size (19-40 mm)**	37.2±0.4	36.5±0.5	37.9±0.4	30.4±0.3**
3	**Right ventricular wall thickness, (2-4 mm)**	4.4±0.1	4.25±0.16	4.6±0.1	4.36±0.15
4	**Right ventricular size (7-26 mm)**	31.2±0.34	30.1±0.3*	29.5±0.34	28.1±0.28**
5	**Right ventricular end-diastolic area, 11-28 cm^2**	28.6±0.44	27.8±0.4	27.8±0.44	26.4±0.4*
6	**End systolic area of the right ventricle, 7.5-16 cm^2**	17.6±0.4	16.4±0.3*	19.2±0.32	17.8±0.3**
7	**Fractional change of right ventricular area, 32 – 60 %**	28.6±0.5	30.6±0.54*	29.62±0.5	32.0± 0.6**
8	**Pulmonary artery diameter (11-21 mm)**	24.8±0.4	23.5±0.34*	25.6±0.4	23.8±0.34**
9	**End systolic volume (45-68 ml)**	71.1±2.2	68.2±2.0	72.9±2.21	64.2± 1.9***
10	**End diastolic volume (88-145 ml)**	157.8±2.6	152.4±2.4	162.6±2.6	149.6±2.3***
11	**End systolic size (26-38 mm)**	40.5±1.5	38.2±1.4	42.3±1.5	37.4±1.4*
12	**End diastolic size (44-54 mm)**	52.7±1.6	50.4±1.5	54.24±1.6	49.6±1.4*
13	**Pulmonary artery systolic pressure (25 mm.sim.ust)**	31.2 ±1.1	27.5±1.1*	31.8±1.15	26.2±1.1***
14	**Left ventricular ejection fraction (above 55%)**	53±1.4	54.6±1.5	51.8±1.5	56.8±1.6*
15	**The systolic amplitude of the tricuspid valve neck (TVNSA), the norm > 17 mm**	17.3±0.2	17.7±0.25	17.7±0.26	18.6±0.3*
Note: * - pre-treatment difference reliability: * - p<0,05., ** - p<0,01., *** - p<0,001.					

As shown in the table, in the group of patients who received the standard treatment of CHF, enalapril + bisoprolol + veroshpiron and sildenafil, the transverse dimension of the right lobe was 42.8 ± 0.7 mm before the treatment and 41.4 ± 0.6 mm after the treatment (P>0.05). In patients receiving the standard treatment of chronic heart failure, enalapril + bisoprolol + eplerenone + empagliflozin (diampa) and sildenafil, this indicator decreased from 43.32±0.7 mm to 41.1±0.6 mm after treatment and reliable changes were observed (P<0.05). The transverse dimension of the left lobe was 37.2±0.4 mm and 36.5±0.5 mm before and after the treatment in the first group, respectively, and no reliable changes were noted (P>0.05). In the second group, 37.9±0.4 mm before the treatment and 30.4±0.3 mm after the treatment, highly reliable changes were found (P<0.05). Although the thickness of the right ventricular wall was slightly decreased in both groups of patients, no reliable changes were detected. The mean size of the right ventricle was 31.2±0.34mm before treatment and 30.1±0.3mm after treatment in the first group (P>0.05), and it was 29.5±0.34mm and 28.1±0.28mm in the second group, respectively, highly reliable changes in this group observed (P<0.01). The change in the end-diastolic area of the right ventricle was not reliable after the treatments in the first group (28.6±0.44 cm^2 and 27.8±0.4 cm^2, respectively, P>0.05). In the second group, it decreased from 27.8±0.44 cm^2 to 26.4±0.4 cm^2 before and after treatments, and reliable changes were detected (P<0.05). On the contrary, the change in the end-systolic area of the right ventricle was reliable in the first group (17.6±0.4 cm^2 and 16.4±0.3 cm^2 before and after treatment, respectively, P<0.05), and it was highly reliable in the second group (19.2±0.32 cm^2 and 17.8± 0.3 cm^2, P<0.01).

One of the main indicators of right ventricular dysfunction is the fractional change in its area. In the first group of patients, this indicator decreased from 28.6±0.5% to 30.6±0.54% before and after treatments, and the differences were reliable (P<0.05). In

the second group, highly reliable changes were noted, equal to 29.62±0.5% and 32.0±0.6%, respectively (P<0.01). Pulmonary artery diameter decreased from 24.8±0.4 mm before treatments to 23.5±0.34 mm after treatments in the first group, and a reliable change was noted (P<0.05). In the second group, there were 25.6 ± 0.4 mm and 23.8 ± 0.34 mm, respectively, and highly reliable changes were observed (P < 0.01).

Although changes in left ventricular end-systolic and diastolic volumes were positive after treatments in the first group of patients, the differences were not reliable (P>0.05). In the second group of patients, the end-systolic volume before and after the treatments was 72.9±2.21 ml and 64.2±1.9 ml, respectively, and the end-diastolic volume was equal to 162.6±2.6ml and 149.6±2.3ml, respectively, and high reliable differences were noted in both parameters (P <0.001). The last systolic and diastolic size in the first group was 40.5±1.5 mm and 52.7±1.6 mm before treatment, and 38.2±1.4 mm and 50.4±1.5 mm after treatment (P>0,05). In the second group, the end systolic size before and after treatment decreased from 42.3±1.5 mm to 37.4±1.4 mm, and the end diastolic size decreased from 54.24±1.6 mm to 49.6±1.4 mm (P<0.05). Pulmonary artery systolic pressure in the first group of patients was 31.2 ± 1.1 mmHg before treatment and 27.5±1.1 mmHg after treatment, and the differences were reliable when the values were compared (P<0.05). In the second group of patients, it decreased from 31.8±1.15 mm.sim.ust to 26.2±1.1 mm.sim.ust, and a highly reliable difference was noted (P<0.001). Left ventricular ejection fraction decreased from 53±1.4% to 54.6±1.5% (P>0,05) after treatment in the first group, and from 51.8±1.5% to 56.8±1.6% in the second group (P<0,05). Tricuspid valve neck systolic amplitude (TVNSA) was 17.3±0.2 mm before treatment and 17.7±0.25 mm after treatment in the first group, and no significant difference was detected (P>0.05). changed by mm and recorded a significant difference (P<0.05).

Echocardiographic findings were also compared before and after treatments in patients with CHF III FC undergoing Covid-19. Table 2 below shows the data obtained.

Table 2. Comparative analysis of intracardiac hemodynamic parameters determined by echocardiography before and after treatment in patients with chronic heart failure III FC who underwent Covid-19 and had pulmonary hypertension.

№	Indicators	Chronic heart failure III FC standard treatment enalapril + bisoprolol + veroshpiron and sildenafil, n=44		Chronic heart failure III FS standard treatment enalapril + bisoprolol + eplerenone + empagliflozin (diampa) and sildenafil, n=49	
		Before treatment	After treatment	Before treatment	After treatment
1	Transverse dimension of right lobe (29-46 mm)	51.4±0.7	49.6±0.6	53.8±0.7	51.4±0.6*
2	Left lobe transverse size (19-40 mm)	40.8±0.5	39.4±0.35*	41.6±0.4	39.8±0.3**
3	Right ventricular wall thickness, (2-4 mm)	6.8±0.1	6.4±0.12*	6.4±0.1	5.8±0.12**
4	Right ventricular size (7-26 mm)	33.58±0.34	32.4±0.3*	35.2±0.34	33.6±0.3**
5	Right ventricular end-diastolic area, 11-28 cm ^{2}	33.7±0.43	32.1±0.4*	35.9±0.44	34±0.4**
6	End systolic area of the right ventricle, 7.5-16 cm ^{2}	24.2±0.28	23.4±0.3	25±0.28	23.8±0.25**
7	Fractional change in right ventricular area, 32–60%	28.3±0.5	30±0.4*	27.92±0.5	30±0.4***
8	Pulmonary artery diameter (11-21 mm)	27±0.3	25.8±0.4*	26.8±0.3	26±0.2*
9	End systolic volume (45-68 ml)	80.3±2.04	76.4±2.1	79.24±2.04	72±2.1*
10	End diastolic volume (88-145 ml)	166.8±2.53	159.7±2.4	172.8±2.53	164.2±2.45*
11	End systolic size (26-38 mm)	43.4±1.45	40.1±1.5	45.54±1.45	40.3±1.4*
12	End diastolic size (44-54 mm)	61.8±1.36	56.6±1.4*	63.6±1.36	58.8±1.3*
13	Pulmonary artery systolic pressure (25 mm.sim.ust)	37.9±1.3	33.8±1.2*	39.7±1.4	33.5±1.3**
14	Left ventricular ejection fraction (greater than 55%)	38.5 ± 1.1	42.5±1.2*	36.3±1.1	41±1.04**
15	The systolic amplitude of the tricuspid valve neck (TVNSA), the norm > 17 mm	16.7± 0.15	17.2±0.2	15.8±0.18	16.5±0.21**
Note: * - pre-treatment difference reliability: *- p<0,05., ** - p<0,01., *** - p<0,001.					

Significant positive changes in a number of indicators were found after the treatment of various components of CHF III FC patients with existing pulmonary hypertension who performed Covid-19. The transverse dimension of the right lobe in the first group of patients was 51.4±0.7mm and 49.6±0.6mm before and after the treatments, respectively ($p>0.05$). In the second group of patients, it reliably decreased from 53.8±0.7 mm to 51.4±0.6 mm after treatment ($p<0.05$). The transverse dimension of the left lobe changed from 40.8±0.5mm to 39.4±0.35mm in the first group ($p<0.05$), from 41.6±0.4mm to 39.8±0.3mm in the second group, and the differences were reliable ($p<0.01$). The thickness of the right ventricular wall was 6.8±0.1mm and 6.4±0.12mm ($p<0.05$) in patients who received CHF standard treatment enalapril + bisoprolol + veroshpiron and sildenafil before and after treatments, CHF standard treatment enalapril + bisoprolol + eplerenone + empagliflozin (Diampa) and 6.4±0.1mm and 5.8±0.12mm in sildenafil patients, respectively ($p<0.01$). The size of the right ventricle before and after treatment in the first group was 33.58±0.34mm and 32.4±0.3mm, respectively, and the differences were reliable ($p<0.05$). In the second group of patients, this indicator reliably decreased from 35.2±0.34mm to 33.6±0.3mm ($r<0.01$). Right ventricular end-diastolic area reliably changed after treatments in both groups of patients. The end-systolic area of the right ventricle decreased from 24.2±0.28 cm^2 to 23.4±0.3 cm^2 before and after treatment in the group of patients, but no significant difference was detected ($r>0.05$). In the second group of patients, after treatment, it was 25±0.28 cm2 and 23.8±0.25 cm^2, respectively, and a reliable difference was noted ($p<0.01$). Fractional changes in right ventricular area were observed in patients with CHF III FC as reliably as in patients with CHF II FC. In the first group, before and after treatments, a highly reliable difference of 28.3±0.5% and 30±0.4% ($p<0.05$), and in the second group, 27.92±0.5% and 30±0.4% ($p<0.01$). Changes in pulmonary artery diameter were reliable in both groups before and after treatments (decrease between groups from 27±0.3 mm to 25.8±0.4 mm and from 26.8±0.3 mm to 26±0.2 mm, respectively, $p<0.01$).

In the first group of patients, the changes in the end systolic and diastolic volume of the left ventricle after treatments were positive, but the difference was not reliable ($P>0.05$). In the second group of patients, the final systolic volume before and after the treatment was 79.24±2.04 ml and 72±2.1 ml, respectively, and the diastolic volume was equal to 172.8±2.53ml and 164.2±2.45ml, respectively, and a reliable difference was noted in both indicators ($P< 0.05$). The final systolic size in the first group of patients was 43.4±1.45 mm and 40.1±1.54 mm before and after treatment, and no reliable difference was observed ($P>0.05$). In the second group, reliable changes were noted after treatments (45.54±1.45 mm and 40.3±1.4 mm, respectively, $P<0.05$). The end-diastolic size was 61.8±1.36 mm and 56.6±1.4 mm in the first group before and after the treatments, and 63.6±1.36 mm and 58.8±1.3 mm in the second group, and reliable differences were noted in both groups ($P<0.05$).

Pulmonary artery systolic pressure in the first group was 37.9±1.3 mmHg before treatments and 33.8±1.2 mmHg after treatment, reliable changes were found ($P<0.05$). In the second group, these indicators were 39.7±1.4 mm.sim.ust and 33.5±1.3 mm.sim.ust, respectively, before and after the treatments, and a highly reliable difference was noted ($P<0.01$). Left ventricular ejection fraction reliably increased from 38.5 ± 1.1% to 42.5 ± 1.2% after treatment in the first group ($P<0.05$). In the second group, this indicator was equal to 36.3±1.1% and 41±1.04%, respectively, and a reliable difference was found when comparing them ($P<0.01$). In the first group, the post-treatment changes in the systolic amplitude of the tricuspid valve neck (TVNSA) were not reliable. In the second group, a highly reliable difference of 15.8±0.18 mm and 16.5±0.21 mm was recorded before and after the treatment, respectively.

Conclusion

Therefore, the obtained results showed that the second group of patients compared to the first group of patients after the procedures were reliable in parameters such as right ventricular size, systolic area, fractional change of right ventricular area, pulmonary artery diameter and systolic pressure, systolic amplitude of tricuspid valve annulus (TVNSA). Such changes can be attributed to the effective reduction of the pressure in the pulmonary artery of sildenafil drug in patients with PH who underwent CHF II - III FC, as well as the standard treatment of CHF, enalapril, bisoprolol, eplerenone, empagliflozin (Diampa), not only on the activity of the left but also the right parts of the heart. Both FC show a high positive effect when empagliflozin and eplerenone are added to the complex treatment, GNK2 group drugs moderate pulmonary hypertension by reducing endothelial dysfunction.

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