Research Article

Interventional Cardiology

Impact of Sacubitril/Valsartan on Patient Outcomes in Chronic Heart Failure

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Abstract:

Background: Chronic Heart Failure (CHF) remains one of the most important problems in cardiology, despite the availability of various modern diagnostic methods and a number of advances in treatment. This is due to its widespread use, lowering the quality of life of patients, as well as high rates of recurrent decompensation and death. Despite the optimal use of modern treatments based on proven medical principles, the disease still has a high morbidity and mortality rate.

Aim: The aim of our study was to evaluate the conservative treatment which pathogenetic complementarity with the inclusion of a combination of sacubitril/valsartan in the treatment of patients with chronic heart failure with a comparison with device therapy of chronic heart failure.

Materials and Methods: The study included 64 patients over the age of 38 suffering from Chronic Heart Failure (CHF) (45 men, 19 women, 59.5 ± 0.9 years of age). Patients were divided into basic and control groups. 33 patients were included in the main group. In the main group, patients received sacubitril/valsartan twice daily in addition to the classic conservative treatment of CHF. The control group included 31 patients who underwent CRT surgery and classic conservative treatment without of sacubitril/valsartan. During the study, the clinical performance of patients before and after 6 months of treatment, the results of BNP tests, the results of a 6-minute walking test were compared.

Conclusion: Evaluation of the results of examinations of patients after 6 months revealed more positive changes in the indicators of the majority of patients in the main group (especially on functional class) than in 6 months ago.

Keywords: Chronic heart failure . Sacubitril /Valsartan combination . CRT

Background

In the treatment of patients with CHF, our main goal is to improve the clinical condition of patients, increase their functional capacity and quality of life, prevent re-hospitalization and, most importantly, reduce the number of deaths [1-3].

Chronic Heart Failure (CHF) remains one of the most important problems in cardiology, this is due to its widespread use, lowering the quality of life of patients, as well as high rates of recurrent decompensation and death. Despite the optimal use of modern treatments based on proven medical principles, the disease still has a high morbidity and mortality rate [4-9]. Many new drugs and devices are currently being used to treat patients with chronic heart failure [2].

Modern principles of existing pharmacological treatments are based on the pathogenetic concept of CHF, which develops as a result of long-term activation of the neurohumoral system. These include, first of all, renin-angiotensin-aldosterenone and sympathetic-adrenal systems, which are considered pathognomonic in patients with chronic heart failure with poor prognosis. Theoretically, the combined

use of different groups of neurohumoral modulators may provide additional benefits in the treatment of patients with chronic heart failure as a result of a more complete blockade of neurohormones. The essence of such a concept is very simple, so the higher the level of different levels of neurohumoral regulation, the better the result [2]. In recent years, a new pharmacological drug has been used in the conservative treatment of patients with chronic heart failure with a reduced emission fraction. This pharmacological drug is a pharmacological agent that can provide simultaneous blockade of both the angiotensin system and neprilisyn. Recently, a number of studies have been conducted on this drug, and a series of studies are ongoing.

In addition to drug treatment, the device is widely used in modern therapies. Of these, resynchron heart therapy is the most widely used treatment in recent years in all countries of the world. In patients with moderate to severe heart failure, CRT treatment may improve quality of life in two-thirds of patients and prolong life in one-third [10]. However, not all patients receiving this treatment respond positively to the CRT method. A number of features can affect the course of the disease after this treatment and the mortality rate. For example, in patients with ischemic etiology, left ventricular function develops less positively after this treatment due to scar tissue of the myocardium. This reduces the likelihood of favorable remodeling during the use of CRT in such patients [3].

Materials and Methods

The study included 64 patients over the age of 38 who were treated at the Eurasia Hospital with a diagnosis of CHF. The diagnosis of CHF was confirmed on the basis of anamnesis, objective and instrumental examination methods.

Eligibility criteria

History of chronic heart failure; circulatory failure (functional class II-IV, NHYA); left ventricular ejection fraction <40%.

Exclusion criteria

Acute myocardial infarction; hypertrophic cardiomyopathy; congenital heart defects; Patients under 25 years of age; heart failure in oncology patients. According to the admission criteria, a total of 64 patients were included in the study, 45 men (70.3% ± 5.7%) and 19 women (29.7% ± 5.7%). The mean age of the patients was 59.5 ± 0.9. During the study, each patient in the main group was given a combination of sacubitril / valsartan twice a day for 6 months in addition to the conservative treatment received for CHF. CRT surgery was performed on patients in the control group. Demographic and clinical characteristics of the patients included in the study are given in Table 1. Thus, no statistically significant differences were obtained during the analysis of the indicators between of patients divided into two groups P>0.05.

Table 1: Demographic and clinical characteristics of patients.

Characteristics	Groups	
	I group (n=33)	II group (n=31)
Age	59.6 ± 1.3	59.5 ± 1.4
	(38-70)	(39-73)
Male	25	20
	75.8% ± 7.5%	64.5% ± 8.6%
Female	8	11
	24.2% ± 7.5%	35.5% ± 8.6%
BMI	36.9 ± 0.5	35.9 ± 0.3
	(31.6-43.6)	(32.1-38.7)
Obesity		
I grade	8	6
	24.2% ± 7.5%	19.4% ± 7.1%
II grade	18	25
	54.5% ± 8.7%	80.6% ± 7.1%
III grade	7	0
	21.2% ±7.1%	0.00%
Action		
Activ	4	4
	12.1% ± 5.7%	12.9% ± 6.0%
Non-activ	29	27
	87.9% ± 5.7%	87.1% ± 6.0%
Smoking		
Does not smoke	8	11
	24.2% ± 7.5%	35.5% ± 8.6%
A few	8	4
	24.2% ± 7.5%	12.9% ± 6.0%
A lot	17	16
	51.5% ± 8.7%	51.6% ± 9.0%
Diabetus mellitus	27	26
	81.8% ± 6.7%	83.9% ± 6.6%
Arterial hypertension	21	20
	63.6% ± 8.4%	64.5% ± 8.6%
Family		
Mother	5	7
	15.2% ± 6.2%	22.6 ± 7.5%
Father	8	4
	24.2% ± 7.5%	12.9% ± 6.0%
Both	20	20
	60.6% ± 8.5%	64.5% ± 8.6%

Results

During the study, the clinical performance of patients before and 6 months after the start of treatment, the results of a 6-minute walking test were compared. Statistical analyzes included the Wilcoxon Signed Ranks Test (Tables 2 and 3) and the Mann-Whitney Test (Table 4), and the Pearson Chi-Square Tests (Table 5).

Table 2: Wilcoxon Signed ranks testi–Group 1.

Ranks		n	Mean rank	Sum of ranks	p
Shortness of breath a- Shortness of breath	Negative ranks	30	15,50	465,00	0
	Positive ranks	0	0,00	0,00	
	Ties	3			
	Total	33			
Heartbeat a – Heartbeat	Negative ranks	28	14,50	406,00	
	Positive ranks	0	0,00	0,00	
	Ties	5			
	Total	33			
Cough a–Cough	Negative ranks	15	8,00	120,00	0
	Positive ranks	0	0,00	0,00	
	Ties	18			
	Total	33			
Pulmonary auscultation a-pulmonary auscultation	Negative ranks	33	17,00	561,00	0
	Positive ranks	0	0,00	0,00	
	Ties	0			
	Total	33			
Edema in the legs a-edema in the legs	Negative ranks	33	17,00	561,00	0
	Positive ranks	0	0,00	0,00	
	Ties	0			
	Total	33			
Pulse fullness a - Pulse fullness	Negative ranks	1	1,00	1,00	0.317
	Positive ranks	0	0,00	0,00	
	Ties	32			
	Total	33			
Pulse rate a - Pulse rate	Negative ranks	32	16,50	528,00	0
	Positive ranks	0	0,00	0,00	
	Ties	1			
	Total	33			
SaO2 a–SaO2	Negative ranks	0	0,00	0,00	0
	Positive ranks	33	17,00	561,00	
	Ties	0			
	Total	33			
Decompentation a-Decompentation	Negative ranks	26	14,29	371,50	0
	Positive ranks		6,50	6,50	
	Ties	6			
	Total	33			
6 min. walk test a-6 min. walk test	Negative ranks	32	16,50	528,00	0
	Positive ranks	0	0,00	0,00	
	Ties	1			
	Total	33			
FC a–FC		Ties	0at		0
		Total	33		
	SPATs - SPAT	Negative Ranks	21au	11,00	
	Total	33			
SAH a–SAH	Negative Ranks	21	11,00	231,00	0
	Positive Ranks	0	0,00	0,00	
	Ties	12			
	Total	33			
DAH a–DAH	Negative Ranks	21	11,00	231,00	0
	Positive Ranks	0	0,00	0,00	
	Ties	12			
	Total	33			

a: after 6-month (after treatment)

Table 3: Wilcoxon Signed ranks testi–Group 2.

Ranksa		n	Mean Rank	Sum of Ranks	p
Shortness of breath a-Shortness of breath	Negative ranks	18	9,50	171,00	0
	Positive ranks	0	0,00	0,00	
	Ties	13			
	Total	31			
Heartbeat a–Heartbeat	Negative ranks	27	14,00	378,00	0
	Positive ranks	0	0,00	0,00	
	Ties	4			
	Total	31			
Cough a-Cough	Negative ranks	12	6,50	78,00	0.001
	Positive ranks	0	0,00	0,00	
	Ties	19			
	Total	31			
pulmonary auscultation a-pulmonary auscultation	Negative ranks	28	14,50	406,00	0
	Positive ranks	0	0,00	0,00	
	Ties	3			
	Total	31			
edema in the legs a-edema in the legs	Negative ranks	30	15,50	465,00	0
	Positive ranks	0	0,00	0,00	
	Ties	1			
	Total	31			
Pulse fullness a-Pulse fullness	Negative ranks	4	2,50	10,00	0.046
	Positive ranks	0	0,00	0,00	
	Ties	27			
	Total	31			
Pulse rate a-Pulse rate	Negative ranks	31	16,00	496,00	0
	Positive ranks	0	0,00	0,00	
	Ties	0			
	Total	31			
SaO2 a–SaO2	Negative ranks	0	0,00	0,00	0
	Positive ranks	31	16,00	496,00	
	Ties	0			
	Total	31			
Decompentation a-Decompentation	Negative ranks	24	14,25	342,00	0
	Positive ranks	2	4,50	9,00	
	Ties	5			
	Total	31			
6 min. walk test a-6 min. walk test	Negative ranks	31	16,00	496,00	0
	Positive ranks	0	0,00	0,00	
	Ties	0			
	Total	31			
Total	Negative ranks	18	9,50	171,00	0
	Positive ranks	0	0,00	0,00	
	Ties	13			
	Total	31			
SAH a–SAH	Negative ranks	24	12,50	300,00	0
	Positive ranks	0	0,00	0,00	
	Ties	7			
	Total	31			
DAH a–DAH	Negative ranks	22	11,50	253,00	0
	Positive ranks	0	0,00	0,00	
	Ties	9			
	Total	31			

a: after 6-month (after treatment)

Table 4: Mann-Whitney Test.

Ranks				
Gr1		**n**	**Mean rank**	**Sum of ranks**
	Group 1	33		
	Group 2	31		
	Total	64		
Test Statisticsa				
	Mann-Whitney U	Wilcoxon W	Z	Asymp. Sig. (2-tailed)
Shortness of breath	5,03,000	10,64,000	-0,139	0,890
Shortness of breath a	3,80,000	9,41,000	-2,517	0,012
Heartbeat	4,49,500	9,45,500	-0,985	0,325
Heartbeat a	4,48,000	9,44,000	-1,042	0,298
Cough	4,87,000	10,48,000	-0,368	0,713
Cough a	3,91,500	9,52,500	-2,309	0,021
Pulmonary auscultation	4,07,000	9,03,000	-1,913	0,056
Pulmonary auscultation a	4,92,500	9,88,500	-0,376	0,707
Edema in the legs	4,75,500	10,36,500	-0,844	0,399
Edema in the legs a	2,74,000	8,35,000	-3,521	0,000
Pulse fullness	5,02,500	10,63,500	-0,155	0,877
Pulse fullness a	4,70,000	9,66,000	-0,800	0,424
Pulse rate	4,97,000	9,93,000	-0,195	0,845
Pulse rate a	4,90,000	9,86,000	-0,290	0,772
SaO2	4,08,000	9,69,000	-1,485	0,138
SaO2 a	4,55,500	9,51,500	-0,775	0,439
QRS	4,82,000	9,78,000	-0,447	0,655
Decompentation	4,46,500	10,07,500	-0,892	0,373
Decompentation a	4,99,500	10,60,500	-0,178	0,859
6 min. walk test	4,66,000	10,27,000	-1,315	0,189
6 min. walk test a	3,41,500	9,02,500	-3,105	0,002
FC	5,10,500	10,71,500	-0,021	0,983
FC a	3,49,500	9,10,500	-2,390	0,017
Initial compensation period	3,73,000	9,34,000	-1,958	0,050
SAH	4,75,500	10,36,500	-0,496	0,620
SAH a	5,06,000	10,67,000	-0,079	0,937
DAH	4,86,500	10,47,500	-0,360	0,718
DAH a	4,71,500	10,32,500	-0,564	0,573
a: after 6-month (after treatment)				

Table 5: Pearson chi-square tests.		
Ranks	**Significance**	
Shortness of breath	Chi-square	0,020
	Df	2
	Sig.	0,990
Shortness of breath a	Chi-square	8,165
	Df	3
	Sig.	0,043
Heartbeat	Chi-square	4,478
	Df	2
	Sig.	0,107
Heartbeat a	Chi-square	5,142
	Df	2
	Sig.	0,076
Cough	Chi-square	5,379
	Df	2
	Sig.	0,068
Cough a	Chi-square	5,531
	Df	2
	Sig.	0,063
Pulmonary auscultation	Chi-square	3,718
	df	1
	Sig.	0,054
Pulmonary auscultation a	Chi-square	3,541
	df	2
	Sig.	0,170
edema in the legs	Chi-square	0,724
	df	1
	Sig.	0,395
Edema in the legs a	Chi-square	16,263
	df	3
	Sig.	0,001
Pulse fullness	Chi-square	0,024
	df	1
	Sig.	0,876
Pulse fullness a	Chi-square	0,650
	df	1
	Sig.	0,420
6 min. walk test	Chi-square	1,756
	df	1
	Sig.	0,185
6 min. walk test a	Chi-square	13,706
	df	2
	Sig.	0,001
FC	Chi-square	0,414
	df	2
	Sig.	0,813
FCa	Chi-square	6,687
	df	3
	Sig.	0,083
Initial compensation period	Chi-square	7,212
	df	3
		0,065

Discussion

As can be seen from the tables above, during the study, the pulse and blood pressure readings, anamnesis, physical examination results of all patients, as well as the results of the 6-minute walking test were examined in detail by statistical analysis. Both qualitative and quantitative tests were used in statistical analysis. During the Wilxson test, statistical accuracy was obtained in the results of other indicators 6 months later, except for pulse fulness in group 1. $p<0.05$ Calculation of pulse fullness results 6 months before and after did not give statistically accurate results ($p= 0.317$). There are also positive changes in the comparison of pre- and post-treatment outcomes of patients in group 2. Thus, statistically accurate results were obtained. That is, positive results were obtained from the treatments carried out separately in both groups. An intergroup analysis of patients' results was performed with the Mann-Whitney Test. Although statistical accuracy was not obtained in all indicators during this analysis, statistical accuracy was obtained in some indicators (history of shortness of breath, cough complaints, 6-minute walking test) as shown in Table 3. The most important of these is the acivite of patients and functional class indicator. The intergroup 6 minutes' walk test index gave a statistically accurate result ($p=0.000$). The intergroup functional class index gave a statistically accurate result ($p=0.017$). In the Pearson Chi-Square Test, a qualitative analysis, no statistical accuracy was obtained in most indicators, nor in the functional class ($p=0.083$).

Conclusion

OIn summary, a statistical analysis of the results of our study concluded that the addition of sacubitril/valsartan complex to the treatment of patients had a better effect on the reduction of complaints in the anamnesis of patients, activity of patients and functional class performance than other treatments.

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