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Choice of RAAS blocker in the treatment of heart failure in acute myocarditis

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The aim – to evaluate the effectiveness of sacubitril/valsartan and enalapril in heart failure treatment in patients with acute severe myocarditis with reduced left ventricular ejection fraction based on dynamic analysis of the heart structural and functional changes.

Materials and methods. The study is based on the results of examinations of 90 patients with a severe course of acute myocarditis (AM) with reduced ejection fraction (EF) of the left ventricle (LV) – ≤40 %. The patients were divided into two groups: the 1st group included 48 patients who were treated with an angiotensin-converting enzyme (ACE) inhibitor – enalapril as part of heart failure (HF) therapy; the 2nd group included 42 patients with AM who received the sacubitril/valsartan combination instead of enalapril in the complex therapy of HF. All patients underwent a 6-minute walk test, echocardiography (EchoCG) with the speckle-tracking method, and cardiac magnetic resonance imaging (CMR). Examinations were carried out three times: in the 1st month from the onset of AM symptoms before the appointment of drug therapy, after 6 and 12 months of observation. Part of the patients from the 1st group, namely 25 patients (52.1 %) in whom the use of ACE inhibitors proved to be ineffective after six months, was transferred to the combination of sacubitril/valsartan (group 1A).

Results and discussion. After six months of treatment, compared to the 1st group, the patients of the 2nd group were distinguished by better indicators of the structural and functional state of the heart, which characterise the contractility and volume of the LV – the values of LV EF and LV longitudinal global systolic strain (LGSS) were higher by 13,7 and 26.2 % respectively, LV end-diastolic volume index (EDVi) was 13.2% lower, as well as a 21.7 % lower number of LV segments in which delayed contrast was detected on cardiac MRI. After six months of taking the sacubitril/valsartan combination in 1A group patients, an improvement in the structural and functional state of the heart was also achieved: the values of LVEF and LGSS increased by 19.2 % and 27.9 %, respectively, and LV EDVi decreased by 19.0 %; the number of LV segments in which delayed enhancement was determined on cardiac MRI decreased by 30.7 %. With the help of regression analysis, it was established the presence of a set of factors that determine the priority of prescribing the sacubitril/valsartan combination as initial therapy in patients with severe myocarditis: presence of reduced LVEF – ≤40 %; pronounced decrease in longitudinal and circular global LV strain – ≤8.5 and ≤9.0 %, respectively; pronounced dilatation of the LV – EDVi ≥102 ml/m^2; presence of III or higher HF functional class; presence of delayed enhancement in ≥ 5,0 LV segments according to cardiac MRI data.

Conclusions. In patients with a severe course of myocarditis, the sacubitril/valsartan combination prescribed as initial therapy showed higher effectiveness compared to ACE inhibitors in terms of improving contractility and reducing LV dilatation, as well as improving the functional class of heart failure. A complex of factors has been established that prove the expediency of prescribing the sacubitril/valsartan combination as initial therapy for heart failure in patients with acute myocarditis.

Key words: acute myocarditis, heart failure, optimal medical therapy, sacubitril/valsartan combination, angiotensin-converting enzyme inhibitors.

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Myocarditis is an inflammatory disease of the myocardium, the manifestations of which range from subclinical disease to cardiogenic shock, arrhythmias, and sudden death [6]. The dominant clinical manifestation of severe acute myocarditis (AM) is progressive heart failure (HF), which is associated with the heart muscle inflammatory lesion and, as a result, with the heart contractile function deterioration, left ventricle (LV) dilation, life-threatening arrhythmias and persistent hemodynamic disorders [3, 5, 9, 19]. In recent years, more and more publications have appeared testifying to the high effectiveness of the angiotensin-receptor neprilysin inhibitor sacubitril/valsartan (S/V) in the complex of optimal HF drug therapy [7, 11]. Among RAAS blockers, the potential advantages of S/V versus angiotensin-converting enzyme inhibitors (iACE) include the impact on the pathogenetic mechanisms of HF formation, in particular the recently established anti-inflammatory and antifibrotic effects, which are of significant relevance in the treatment of AM [13, 18, 20, 21]. Therefore, timely optimisation of therapy to prevent HF progression in patients with AM is one of the primary tasks in clinical practice and has prognostic significance.

The aim – to evaluate the effectiveness of sacubitril/valsartan and enalapril in patients with acute myocarditis heart failure and reduced left ventricular ejection fraction based on dynamic analysis of heart structural and functional changes.

MATERIALS AND METHODS

A total of 90 consecutive patients with AM and HF with reduced (≤40 %) ejection fraction (EF), NYHA II–IV functional class were enrolled in the study. Their age was 37.2±2.7 years, 57 of whom (63 %) were men. Diagnosis of myocarditis was based on the Ukrainian Association of Cardiology guidelines for the diagnosis and treatment of myocarditis [1, 2].

All patients provided written informed consent before being included in the study according to the Order of the Ministry of Health of Ukraine No. 110 from 14.02.2012. The study was conducted in accordance with the rules of the Declaration of Helsinki, «Ethical Principles of Medical Research Involving Humans», and the «General Declaration on Bioethics and Human Rights (UNESCO)», on the basis of the department of noncoronary heart diseases, rheumatology and therapy of the M.D. Strazhesko National Scientific Center of Cardiology, Clinical and Regenerative Medicine NAMS of Ukraine from January 2022 to November 2023.

All patients' medical history and clinical status were initially examined, and biochemical and functional studies were performed. The NYHA functional class evaluation is based on a 6-minute walking test (6MWT) [17].

Transthoracic echocardiography was performed using an Aplio Artida SSH-880CV ultrasound system (Toshiba Medical System Corporation, Japan). LV end-diastolic volume (EDV) and LV end-systolic volume (ESV) were measured, LVEF for study inclusion was calculated using the Simpson's biplane method. The LV end-diastolic volume (EDV) was adjusted for body surface area to obtain an EDV index (EDVi). Longitudinal global systolic strain (LGSS) was evaluated using 2D speckle tracking technique in the apical four-chamber, two-chamber, and three-chamber views. Segmentation of LV was based on the R. Lang's sixteen-segment model [14].

Circumferential global systolic strain (CGSS) and radial global systolic strain (RGSS) were assessed, video loops were recorded along the short axis of the LV at the level of the papillary muscles. The average deformation indicators of six segments were calculated, with one segment representing each LV wall in the middle section [14]. Values of strain and strain rate indicators were analysed using the Wall Motion Tracking software package. All strain indicators were presented in absolute values.

Cardiac magnetic resonance (CMR) imaging with Gadovist® contrast was performed on a Vantage Titan HSR 1.5 Tesla scanner (Toshiba, Japan). Images of the heart were evaluated along the short and long axes in three modes: T1 – (to detect hyperemia in the area of the inflammatory lesion), T2 – (to detect areas of edema) and late gadolinium enhancement (LGE) mode (10–15 minutes after contrast injection to detect necrotic or fibrotic changes) [8, 12, 13]. The severity of myocardial edema was evaluated, and a quantitative analysis of the areas of contrast accumulation in the early and delayed phases was performed according to the standardised imaging of the 17-segment structure of the LV myocardium with an assessment of the number of segments with inflammatory and fibrotic changes [8, 10].

Baseline HF treatment in all patients included beta-blockers, diuretics, mineralocorticoid receptor antagonists (MRA) according to current guidelines, and anticoagulants and antiarrhythmics if needed [17]. Depending on the RAAS blocker, 48 patients were started on ACEi enalapril in an initial dose of 5 mg bid (1st group), and 42 patients were started on S/V in the

Table 1
Baseline characteristics of patients

Indicators	The value of the indicator (M±m)		
	1st group (n=48)	2nd group (n=42)	p
Age, years	36.8 ± 2.4	37.6 ± 2.8	>0.05
Female, %	18 (37.5 %)	15 (35.7 %)	–
Mean systolic blood pressure	106.1 ± 5.9	103.6 ± 5.6	>0.05
Mean diastolic blood pressure	63.1 ± 3.8	62.2 ± 3.6	>0.05
Serum creatinine level, mmol/l	81.9 ± 7.6	78.7 ± 6.8	>0.05
Serum K^+ level, mmol/l	4.71 ± 0.22	4.66 ± 0.23	>0.05
NYHA functional class, %			
II	29.2	28.5	–
III	60.4	61.9	–
IV	10.4	9.5	–
6MWT, m	263.3 ± 21.2	271.0 ± 23.2	>0.05
LV EDVi, ml/m^2	106.4 ± 5.7	104.2 ± 8.2	>0.05
LV EF, %	36.2 ± 2.8	36.7 ± 2.5	>0.05
LGSS, %	8.64 ± 0.63	11.71 ± 0.81	>0.05
The total number of affected LV segments	6.98 ± 0.73	7.23 ± 0.69	>0.05

NYHA – New York Heart Association; 6MWT – 6 Minute Walk Test; LV – Left Ventricle; EDVi – End-Diastolic Volume Index; EF – Ejection Fraction; LGSS – Longitudinal Global Systolic Strain.

initial dose of 24/26 mg bid (2nd group). Enalapril and S/V doses were doubled every 2–4 weeks up to an optimal target of 20 mg bid and 97/103 mg bid, respectively. Beta-blocker (Carvedilol) was prescribed in an initial dose of 6,25 mg bid for all patients with further up-titration to a dose of 25 mg bid or maximal tolerated. Eplerenone and Torasemide were prescribed once a day in doses of 25 and 5 mg, respectively.

The statistical analysis was performed using SPSS Advanced Statistics 27.0 L-CZAA-BT2KCD version. The calculated quantitative indicators are presented as the mean value and standard deviation of the mean (M±m). By using the student's t-test, average indicators across all groups were compared. A critical level of statistical significance was set at $p<0.05$ for all types of analysis. Limit values of indicators that served as predictors of the presence of certain clinical characteristics were determined using the Student's criterion through multivariate regression analysis.

RESULTS

Basal clinical characteristics of the studied groups, as well as structural and functional echocardiographic parameters, were comparable, as shown in *Table 1*. Cardiac MRI data did not show any significant difference in the total number of LV segments affected by inflammatory changes or with the presence of delayed contrast. Groups were homogeneous in terms of optimal medical therapy.

After six months of treatment, patients in both groups were marked by achieved doses of Enalapril and S/V, Carvedilol, Eplerenone and Torasemide, as well as by the values of mean systolic and diastolic BP *(Table 2)*. However, most patients in the 2nd group (60.0 %) demonstrated a significant reduction of HF symptoms and had NYHA I functional class, while in the 1st group, only 21.9 % of patients improved to NYHA I functional class. In addition, among the patients from the 2nd group, only 11.9 % had NYHA III functional class, and none of the patients corresponded to NYHA IV functional class, while in the 1st group, more than half of patients corresponded to NYHA III (41.6 %) and IV (10.4 %) functional class.

The 2nd group of patients showed a significant improvement in EDVi (13.2 % lower), EF (13.7% higher), LGSS (26.2 % higher), 6MWT (18.8 % longer) compared to those in the 1st group *(table 2)*. A comparative analysis of cardiac MRI results showed that in the

Table 2
Characteristics of the studied groups after six months of treatment

Indicators	The value of the indicator (M±m)		
	1st group	2nd group	p
Mean achieved daily dose of Enalapril, mg	33.5 ± 2.6	–	–
Mean achieved daily dose of S/V, mg	–	320.5 ± 24.8	–
Mean achieved dose of Carvedilol, mg	39.5 ± 4.7	36.8 ± 4.5	>0.05
Mean dose of Eplerenone, mg	21.5 ± 2.1	22.5 ± 2.3	>0.05
Mean dose of Torasemide, mg	4.15 ± 0.35	4.24 ± 0.35	>0.05
Mean systolic blood pressure	115.3 ± 7.2	122.1 ± 7.2	>0.05
Mean diastolic blood pressure	68.5 ± 5.1	67.4 ± 5.7	>0.05
Serum creatinine level, mmol/l	69.5 ± 5.4	74.2 ± 5.6	>0.05
Serum K^+ level, mmol/l	4.75 ± 0.31	4.72 ± 0.27	>0.05
NYHA functional class, %			
I	21.9	60.0	–
II	27.1	30.1	–
III	41.6	11.9	–
IV	10,4	–	–
6MWT, m	298.2 ± 26.7	397.2 ± 29.4	<0.01
LV EDVi, ml/m^2	94.7 ± 5.4	82.2 ± 5.1	<0.05
LV EF, %	41.5 ± 2.4	48.1 ± 2.5	<0.05
LGSS, %	8.64 ± 0.63	11.71 ± 0.81	<0.01
CGSS, %	8.90 ± 0.82	10.54 ± 1.08	>0.05
RGSS, %	18.35 ± 2.64	21.2 ± 2.76	>0.05
Number of LV segments with inflammatory changes	3.14 ± 0.28	2.47 ± 0.27	<0.05
Number of LV segments with LGE	4.14 ± 0.38	3.24 ± 0.36	<0.05
The total number of affected LV segments	7.28 ± 0.53	5.71 ± 0.51	<0.01

NYHA – New York Heart Association; 6MWT – 6 Minute Walk Test; LV – Left Ventricle; EDVi – End-Diastolic Volume Index; EF – Ejection Fraction; LGSS – Longitudinal Global Systolic Strain; CGSS – Circumferential Global Systolic Strain; RGSS – Radial Global Systolic Strain; LGE – late Gadolinium Enhancement.

2nd group of patients, the number of LV segments with inflammatory lesions and the number of those in which DE was detected was 21.3 and 21.7 % less, respectively; also, the total number of affected LV segments was significantly less (21.4 %) compared to those in the 1st group.

Therefore, after six months of treatment, patients in the S/V group demonstrated significantly better results versus patients in the enalapril treatment group: reduced LV dilation, improved left ventricular contractility as indicated by LVEF and LGSS, and better exercise tolerance.

The analysis of results in the 1st group showed that after six months of enalapril treatment 25 patients (52.1 %) did not show significant differences between baseline and 6-month follow-up in echocardiographic parameters: they still had reduced LVEF (35.7±2.3 %) and LGSS (7.32±0.51 %); NYHA functional class ≥ III, significant LV dilatation (LV EDVi 107.8±6.9 ml/m²). The number of LV segments with LGE and the total number of affected LV segments was 6.31±0.54 and 8.49±0.62, respectively. These patients (group 1A) were switched to S/V after a minimum of 36 hours from ACEi withdrawal, initially prescribed at 48/52 mg dose bid and up-titrated to dose 97/103 mg bid. Patients who experienced improvement in structural and functional parameters continued treatment with enalapril 20 mg bid (1B group, n=23).

Table 3
Differences in echocardiographic and cardiac magnetic resonance imaging parameters after 12-month follow-up

Indicators	The value of the indicator (M±m)		
	1A group	1B group	2nd group
LV EDVi, ml/ml	87,3 ± 5,9	88,8 ± 5,7	76,4 ± 5,7 *
LVEF, %	44,2 ± 2,4	43,3 ± 2,6	50,6 ± 2,6 *°
LGSS, %	10,15 ± 0,79 *	8,19 ± 0,78	12,31 ± 0,84 **°
CGSS, %	9,06 ± 0,98	8,45 ± 0,83	10,06 ± 0,98
RGSS, %	17,23 ± 2,45	17,01 ± 2,51	21,23 ± 2,85
Number of LV segments with inflammatory changes	2,54 ± 0,27	2,65 ± 0,26	2,23 ± 0,24
Number of LV segments with LGE	4,37 ± 0,39 *	5,32 ± 0,41	2,84 ± 0,42 **°
The total number of affected LV segments	6,91 ± 0,51	7,97 ± 0,54	5,07 ± 0,46 **°

The difference in indicators is statistically significant compared to those in the 1B group: * – p<0.05; ** – p<0.01. The difference in indicators is statistically significant compared to those in the 1A group: ° – p<0.05. LV – Left Ventricle; EDVi – End-Diastolic Volume Index; EF – Ejection Fraction; LGSS – Longitudinal Global Systolic Strain; CGSS – Circumferential Global Systolic Strain; RGSS – Radial Global Systolic Strain; LGE – Late Gadolinium Enhancement.

After 12 months of treatment with S/V, 1A group patients showed significant positive dynamics of indicators of the structural and functional state of the heart: the value of LVEF and LGSS increased by 19.2 % and 27.9 %, respectively, LV EDVi decreased by 19.0 %. The number of LV segments in which LGE was detected decreased by 30.7 %, and the total number of affected LV segments also decreased from (8.49±0.62) to (6.91±0.51) segments (p<0.05). In addition, the replacement of ACE inhibitors with the S/V after six months of treatment made it possible to improve the result of the 6MWT: the walking distance increased from 257.8±22.9 m to 325.1±24.8 m (p<0.01).

After 12 months of follow-up, the results of treatment in all studied groups were analysed, and it was found that the best response to RAAS blockers was achieved in the 2nd group of patients who were prescribed the S/V from the baseline *(Table 3)*. These patients, after 12 months of treatment, were characterised by better LV contractility compared to the patients of the 1A and 1B groups, which was evidenced by the practically normal average value of LVEF and a significantly higher value of LGSS. The differences were observed against the background of a smaller number of both segments with the presence of LGE and a smaller total number of affected LV segments in the 2nd group. No significant differences in LGSS and RGSS values were seen between the groups after 12 months of follow-up.

The comparative analysis of indicators of the structural and functional state of the heart in the 1A group showed that after switching from enalapril to S/V after 12 months of observation, the values of EF and EDVi of LV corresponded to the average level of those in 1B group *(Table 3)*. Furthermore, in 1A group patients after six months of S/V, the value of LGSS was significantly higher, and the number of LV segments with LGE was significantly less compared to 1B group.

In order to establish independent prognostic factors that are predictors of effectiveness and may serve as indications for priority prescription of S/V, multivariate regression analysis was performed in group 1A and a multivariate model was created. The regression model looked as follows:

$$y=a_0+a_1x_1+a_2x_2+\ldots+a_nx_n,$$

where y – represents the initial function of the model (expediency of prescribing the S/V instead of ACE inhibitors as a component of HF therapy as a priority RAAS blocker in patients with severe AM), x_1, …, x_n – represent independent variables (limit values of the factors determined during the initial study), a_0, …, a_n – are the model coefficients.

According to the values of the β coefficients, the greatest contribution to the future effectiveness of prescribing the S/V instead of ACE inhibitors according to the results of the 6-month treatment course had the following indicators determined during the 1st month from the onset of the disease before prescribing of the treatment: reduced LVEF ≤40 % (β=0.601; p=0.016); significant reduction of LV LGSS and CGSS – ≤8.5 (β=0.687; p=0.012) and ≤9.0 % (β=0.611; p=0.024), respectively; significant LV dilatation – LV EDVi ≥102 ml/m² (β=0.712; p=0.006); NYHA functional class ≥ III according to the results of the 6MWT (β=0.425; p=0.047); delayed contrast in ≥5.0

LV segments according to cardiac MRI (β=0.548; p=0.031).

DISCUSSION

To the best of our knowledge, this is the first study suggesting significant advantages of S/V over enalapril in patients with AM and HF with severe left ventricular dysfunction during 12-month follow-up.

Specifically, the positive impact of the S/V on improving the structural and functional state of the heart, such as a notable increase in LVEF and LGSS, along with a reduction in LV EDVi, was particularly evident in the 1A group of patients with insufficient response to enalapril treatment. These findings align with numerous prospective studies that have highlighted the benefits of this combination in the comprehensive management of HF [11, 18, 22, 23]. As a result, S/V has been incorporated into contemporary guidelines for treating chronic HF [17].

Nevertheless, studies devoted to the effectiveness of the S/V in patients with AM, accompanied by significant dilatation and impairment of LV systolic function and the development of HF with reduced EF, have not been conducted to date. Our study contributes to understanding the superior effectiveness of S/V compared to enalapril, primarily attributed to a reduction in the number of LV segments showing delayed contrast, indicative of fibrotic/necrotic changes in the myocardium. These changes often contribute to persistent LV contractility impairment and hinder its reverse remodeling despite optimal drug therapy for HF. Additionally, international studies have also highlighted the antifibrotic and anti-inflammatory effects of the S/V, particularly relevant in the context of AM [4, 15, 23].

The early indicators of higher efficiency of the S/V versus enalapril identified in our study using multivariate regression analysis will make it possible to make a timely correction of HF drug therapy in patients with AM and in numerous clinical situations to make a decision to prescribe the S/V combination as starting therapy. Prospects for further studies of the S/V in patients with AM should include conducting multicenter randomised clinical trials with analysis of its efficacy and safety and impact on classic endpoints, such as the frequency of hospitalisations and death.

CLINICAL CASE

We present a clinical case that demonstrates the importance of timely prescription of HF treatment to patients with AM. Patient L., 38 years old, combatant was hospitalised in July 2023 at M.D. Strazhesko National Scientific Center of Cardiology, Clinical and Regenerative Medicine NAMS Ukraine with complaints of shortness of breath during moderate physical exertion, palpitations, fatigue, reduced tolerance to physical exertion, bilateral edema of the feet and shins. From the anamnesis, it is known that she got sick 3–4 weeks after acute viral infection and hypothermia.

The 6MWT showed 258 m, corresponding to NYHA III functional class. Echocardiography revealed dilatation and diffuse hypokinesis, resulting in

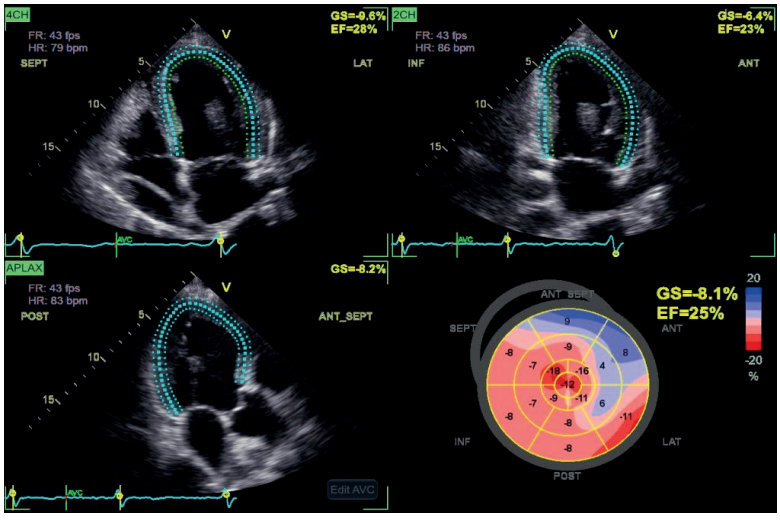

Fig. 1. **Baseline echocardiography in patient L. STEchocardiography showed significant impairment of LGSS and LVEF.**

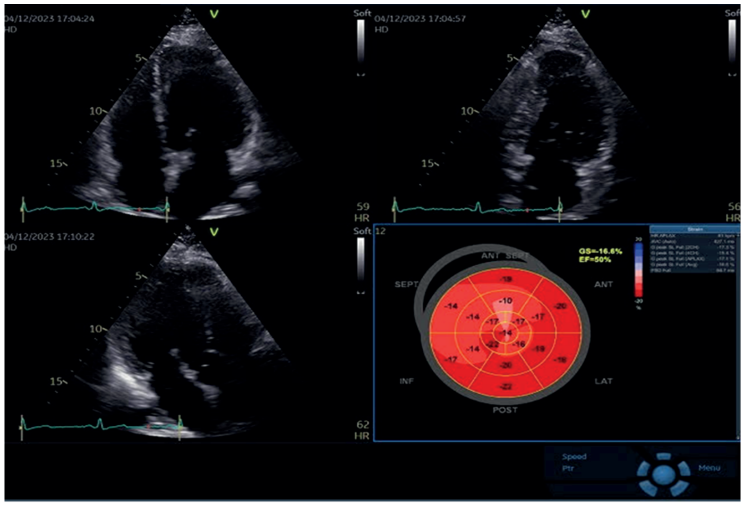

Fig. 2. **Echocardiography in patient L. after six months of S/V treatment.**

decreased LVEF to 25.0 %, LGSS and GCSS to 8.1 % and 8.8 %, respectively, and LV EDVi was 106.2 ml/m² *(Fig. 1)*. Cardiac MRI indicated signs of diffuse myocarditis with damage of at least eight segments of the LV, along with the simultaneous presence of all 3 Lake Louise criteria *(Fig. 1)*. These findings collectively met all the criteria established in our study, supporting the priority prescription of the S/V as RAAS blocker in HF treatment. The dose of S/V 50 mg twice a day was prescribed and up-titrated to the target of 200 mg twice a day. Also, Carvedilol was prescribed in the dose 6.25 mg twice a day with further up-titration to target 25 mg twice a day; Eplerenone and Torasemide were administered once a day in doses 25 and 5 mg, respectively. Target doses of S/V and Carvedilol were achieved in 60 days.

Significant positive changes were noted after six months: LVEF increased to 50 %, and LV LGSS improved to 16.6 % *(Fig. 2)*. Cardiac MRI showed no signs of the inflammatory process, with delayed contrast noted only in 2 segments of the LV intramurally, indicating residual fibrotic changes. The patient's clinical condition improved significantly, with reduced complaints of shortness of breath and palpitations, disappearance of leg swelling, and a 6MWT distance of 490 m, corresponding to NYHA I functional class.

The presented clinical case demonstrates the effectiveness of the timely prescription of S/V which resulted in reverse heart structural and functional remodeling in a patient with severe AM.

CONCLUSIONS

1. In patients with a severe course of myocarditis, the initial S/V prescription for heart failure with reduced ejection fraction treatment showed higher effectiveness compared to ACE inhibitors in terms of improving contractility and reducing LV dilatation, as well as improving the NYHA functional class.

2. In lack of ACE inhibitors effectiveness, sacubitril/valsartan is advisable for intake for faster restoration of LV contractile function, reduction of LV dilatation and improvement of heart failure functional class by reducing the number of LV segments affected by inflammatory and fibrotic lesions

3. The basis of the higher efficiency of treatment with the sacubitril/valsartan versus ACE inhibitors was its antifibrotic and anti-inflammatory effects, which caused a reduction in the volume of LV lesions according to cardiac MRI and, as a result, a faster recovery of LV contractility.

4. Based on regression analysis, a set of factors was established that prove the expediency of prescribing the sacubitril/valsartan as initial therapy for heart failure in patients with severe acute myocarditis: reduced LV ejection fraction – ≤40 %; reduction of longitudinal and circular global LV systolic deformation – ≤8.5 and ≤9.0 %, respectively; pronounced LV dilatation – end-diastolic volume index ≥102 ml/m²; III or higher functional class of heart failure; the presence of delayed enhancement in ≥5.0 segments of the LV according to cardiac MRI data.

There is no conflict of interest.

Author contribution: conception and design – E.N., V.K.; collection of material – Ie.T., I.H., R.K., O.D.; database creation – A.S., Ie.T., I.H.; statistical analysis of results – S.Ch., A.S., R.K.; article writing – E.N., S.Ch., A.S.; editing of the article – V.K., E.N., S.Ch.

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Вибір блокатора ренін-ангіотензин-альдостеронової системи для лікування серцевої недостатності при гострому міокардиті

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Мета – оцінити ефективність сакубітрилу/валсартану та еналаприлу для лікування серцевої недостатності (СН) у хворих з тяжким перебігом міокардиту зі зниженою фракцією викиду (ФВ) лівого шлуночка (ЛШ) на основі динамічного аналізу структурно-функціонального стану серця.

Матеріали і методи. Дослідження ґрунтується на результатах обстежень 90 хворих із тяжким перебігом гострого міокардиту (ГМ) зі зниженою ФВ ЛШ ≤ 40 %. Хворі були розподілені на 2 групи: 1-ша група – 48 хворих із ГМ, які в комплексі терапії СН отримували інгібітор ангіотензинперетворювального ферменту (іАПФ) еналаприл; 2-га група – 42 хворих із ГМ, які в комплексі оптимальної медикаментозної терапії СН замість еналаприлу отримували комбінацію сакубітрил/валсартан. Усім хворим проводили тест із 6-хвилинною ходьбою, ехокардіографію (ЕхоКГ) зі спекл-трекінг методикою, магнітно-резонансну томографію (МРТ) серця. Обстеження проводили тричі: в 1-й місяць від початку симптомів ГМ до призначення медикаментозної терапії, через 6 та 12 місяців спостереження. Частина пацієнтів з 1-ї групи, а саме 25 (52,1 %) хворих, в яких застосування іАПФ виявилось неефективним, через 6 місяців була переведена на прийом комбінації сакубітрил/валсартан (1А група).

Результати та обговорення. Через 6 місяців лікування у хворих 2-ї групи порівняно з 1-ю були кращі показники структурно-функціонального стану серця, що характеризують скоротливу здатність та об'єм порожнини ЛШ, більші величини ФВ та поздовжньої глобальної деформації ЛШ відповідно на 13,7 та 26,2 %, менший на 13,2 % індекс кінцеводіастолічного об'єму (іКДО) ЛШ, а також менша на 21,7 % кількість сегментів ЛШ, в яких на МРТ серця виявляли відстрочене контрастування. Через 6 місяців прийому комбінації сакубітрил/валсартан у хворих 1А групи також було досягнуто покращення структурно-функціонального стану серця: величини ФВ та поздовжньої глобальної деформації ЛШ зросли на 19,2 % та 27,9 % відповідно, а іКДО ЛШ зменшився на 19,0 %; кількість сегментів ЛШ, у яких при проведенні МРТ серця визначалось відстрочене контрастування, зменшилась на 30,7 %. За допомогою регресійного аналізу було встановлено комплекс факторів, що визначають пріоритетність призначення комбінації сакубітрил/валсартан як стартової терапії у хворих із тяжким перебігом міокардиту: наявність зниженої ФВ ЛШ ≤ 40 %; виражене зниження поздовжньої та циркулярної глобальної деформації ЛШ ≤ 8,5 та ≤ 9,0 % відповідно; виражена дилатація ЛШ – іКДО ЛШ ≥ 102 мл/м^2; наявність III функціонального класу СН або вище; наявність відстроченого контрастування в ≥ 5,0 сегментах ЛШ за даними МРТ серця.

Висновки. У хворих з тяжким перебігом міокардиту комбінація сакубітрил/валсартан, призначена як стартова терапія, показала більшу ефективність порівняно з іАПФ щодо поліпшення скоротливої здатності і зменшення дилатації ЛШ, а також покращання функціонального класу СН. Визначено комплекс факторів, що засвідчують доцільність призначення комбінації сакубітрил/валсартан як стартової терапії СН у хворих із ГМ.

Ключові слова: гострий міокардит, серцева недостатність, оптимальна медикаментозна терапія, комбінація сакубітрил/валсартан, інгібітори ангіотензинперетворювального ферменту.