ORIGINAL RESEARCH

The Efficacy and Mechanism of Xinhuosun + Shakubatra valsartan in the Treatment of CHF Patients with Atrial Fibrillation

Jiao Wang, MM; Qingqing Zhang, MM; Bo Miao, BM; Jiangman Cui, MM; Xuehong Du, BM; Xin Li, BM

ABSTRACT

Objective • Exploring the clinical efficacy of neomycin and sakubactria valsartan in the treatment of patients with chronic heart failure (CHF) and atrial fibrillation. This study investigates the potential benefits of combining neomycin with sakubactria valsartan, a medication with a background of demonstrated efficacy in cardiovascular conditions, to address the complex challenges presented by chronic heart failure and atrial fibrillation.

Methods • Using a single-center clinical randomized trial, 111 patients with CHF complicated with atrial fibrillation who were treated in the cardiovascular department of Xingtai Third Hospital from June 2019 to March 2021 were randomly divided into two groups. In the control group, 56 patients received treatment with Western Medicine Foundation + Shakubatra valsartan. In the experimental group, consisting of 55 patients, the treatment was identical to the control group, with the additional administration of neomycin.. After 12 weeks of continuous treatment, the echocardiograms, electrocardiogram parameters, and Differences in changes in serum soluble growth stimulating gene 2 protein (sST2) and galactose agglutinin 3 (Gal-3), clinical efficacy, and incidence of adverse reactions.

Results • Before treatment, no significant differences existed in LVEF, LVEDV, FS, and SV between the experimental and control groups ($P > .05$). Post-treatment, both groups exhibited significant improvements in these parameters, with the experimental group showing statistically higher values ($P < .05$).Similarly, pre-treatment comparisons of Pd, sST2, Gal-3, and NT-proBNP revealed no significant differences between the groups ($P > .05$). After treatment, both groups showed significant reductions, with the experimental group demonstrating lower values ($P < .05$).

Clinical efficacy assessment post-treatment showed significant differences. The experimental group had a basic cure rate of 45.45%, a significant effective rate of 43.64%, and an effective rate of 10.91%, while the control group had rates of 28.57%, 48.21%, and 23.21%, respectively ($P < .05$).Adverse reactions occurred in 9 and 4 patients in the experimental and control groups, respectively. The severity was not significant, and treatment was uninterrupted ($P > 0.05$).The treatment improved heart function and reduced atrial fibrillation occurrences, holding clinical significance by potentially enhancing patients' quality of life and decreasing cardiovascular events. These results highlight the clinical significance of this treatment, which may help improve patients' quality of life and reduce the occurrence of cardiovascular events.

Conclusion • The treatment of patients with CHF combined with atrial fibrillation using neomycin and sakubactria valsartan can more effectively improve their cardiac function and alleviate the condition of atrial fibrillation, which is worthy of clinical promotion and application. In actual clinical practice, physicians and healthcare providers may consider incorporating this treatment into their treatment regimens, especially for patients who need to improve heart function and reduce the risk of atrial fibrillation. Additionally, further research and clinical trials can further validate these findings to ensure their effectiveness and safety. These insights will help the medical community better understand how to apply this treatment to real patients and maximize its clinical effectiveness. (*Altern Ther Health Med.* [E-pub ahead of print.])

Jiao Wang, MM, Attending doctor**; Qingqing Zhang, MM,** Attending doctor**; Bo Miao, BM,** Attending doctor**; Xin Li, BM,** Associate chief physician**;** Department of Cardiology CCU, Xingtai Third Hospital, Xingtai, China; **Jiangman Cui, MM,** Attending doctor**; Xuehong Du, BM,** Nurse in Charge; Department of Cardiology, Xingtai Third Hospital, Xingtai, China.

Corresponding author: Xin Li, BM
E-mail: xingtailixin@sina.com

INTRODUCTION

Chronic heart failure (CHF) and atrial fibrillation (hereinafter referred to as AF) are both cardiovascular diseases with high clinical morbidity, and they have similar pathogenesis and often act as risk factors for each other.[1,2] When CHF is combined with AF, it will cause ventricular hypoplasia due to ventricular systolic arrhythmia and left atrial systolic function abnormality, activate the renin-angiotensin-aldosterone system and the vegetative nervous system, and aggravate cardiac function abnormality.[3] For this group of patients, both atrial fibrillation-related treatments such as heart rate control, thrombosis prevention, and rhythm restoration, as well as

Table 1. Comparison of the basic information of the two groups of patients

Group	n	Age (years)	BMI (kg/m²)	Gender (%)		Duration of heart failure (years)	Duration of atrial fibrillation (months)	NYHA classification (%)		
				Male	Female			Grade II	Grade III	GradeIV
Experimental group	55	54.1±7.2	23.44±1.94	32(58.18)	23(41.82)	7.6±2.4	17.4±4.0	8(14.55)	32(58.18)	15(27.27)
Control group	56	52.5±8.0	23.20±2.30	26(46.43)	30(53.57)	8.1±2.5	16.6±4.8	15(26.79)	27(48.21)	14(25.00)
t/χ^2		1.107	0.594	1.536		-1.075	0.953	2.580		
P value		.271	.554	.215		.285	.343	.275		

cardiotonic, diuretic, neuroendocrine inhibition, and improvement of ventricular remodeling treatments are needed to improve heart failure symptoms.[4,5]Supplementation of exogenous brain natriuretic peptide (BNP) is deemed crucial for cardiovascular management, acting as a potent vasodilator to reduce blood pressure and improve cardiac function. With diuretic effects, it aids in fluid balance, contributing to the alleviation of heart failure symptoms. The evidence supporting its positive impact on hemodynamics emphasizes its key role in cardiovascular care. Sacubitril valsartan is an effective antagonist of heart failure, which improves myocardial remodeling by inhibiting the renin-angiotensin system and modulating BNP and can effectively improve cardiac function in patients with CHF.[7] Some studies have used it in CHF patients with decreased ejection fraction and found that it can reduce the risk of heart failure and death.[8] However, sacubitril valsartan is an oral formulation and has a relatively slow onset of action. Recombinant human brain natriuretic peptide (trade name: Neovusin), which has a similar biological activity to human endogenous BNP, can be effective in treating heart failure, has a shorter half-life, requires intravenous administration, and has a faster onset of action.[9] Fewer studies have been reported about the efficacy of neuvosin and sacubitril valsartan in the treatment of CHF combined with atrial fibrillation, and the present study attempts to investigate the advantages of combination therapy to provide a basis for clinical treatment. The study aims to explore the advantages of combining neuvosin and sacubitril valsartan in treating CHF with atrial fibrillation, addressing a gap in existing research and providing insights for clinical treatment. Therefore, the primary goal of this study was to evaluate the effects of combination therapy on specific health markers, including heart function and atrial fibrillation. We hypothesize that this combination therapy will significantly improve patients' heart function and reduce atrial fibrillation, thereby improving patients' quality of life and reducing hospitalizations.

PATIENTS AND METHODS

Basic information about the research subjects

Using a single-center clinical randomized trial, 111 patients with CHF combined with atrial fibrillation who were treated in the cardiovascular internal medicine department of Xingtai Third Hospital from June 2019 to March 2021 were randomly grouped, of which 56 patients in the control group were treated with the western medicine base + sakubutraviral valsartan, and 55 patients in the experimental group were treated with neoactivin in addition to the control group medication. It's important to clarify that 'neoactivin' is the intended term, as its abstract mention as 'neuvosin' might cause confusion. Additionally, confirm whether this medication was administered independently of the 'control group medication. and the comparison of all the basic condition data of the patients of the experimental group and the control group, there is no significant difference between the two groups of patients ($P > .05$).This study used computer-generated randomization to assign patients to treatment groups. During the randomization process, we use specially designed random number generation software to ensure randomness and fairness. This process was performed by independent researchers who were not involved in subsequent data collection and analysis to reduce potential bias. Through this approach, we were able to ensure that the allocation of patients to different treatment groups was completely randomized, helping to reduce selection bias and increase the internal validity of the study. See Table 1.

The control group was the baseline level, with a total of 56 patients, with an average age of 52.5±8.0 years, and an average BMI of 23.20±2.30, of which 46.43% were male and 53.57% were female. The average duration of heart failure was 8.1±2.5 years and the average duration of atrial fibrillation. It is 16.6±4.8 months. According to the NYHA classification, 26.79% are Grade II, 48.21% are Grade III, and 25.00% are Grade IV.

Inclusion criteria: (1) The clinical diagnostic criteria of CHF patients were based on the criteria in the Chinese Guidelines for the Diagnosis and Treatment of Heart Failure 2018 Edition, and the diagnostic criteria for AF were those in the Guidelines for Primary Diagnosis and Treatment of Atrial Fibrillation (2019); (2) Cardiac function evaluation (NYHA classification ≥ class II) was performed on patients before treatment, and the duration of atrial fibrillation was more than 3 months, and the duration of continuous episodes was more than 3 days (the frequency of episodes was >3 times/week); (3) Patients age range 19-75 years; (4) Patients and their families were willing to accept the therapeutic measures associated with this study; (5) This study was approved by the Ethics Committee of Xingtai Third Hospital. Exclusion criteria: (1) Patients with cancer diseases; (2) Cerebral hemorrhage, ruptured cerebral aneurysm, cerebral infarction, etc.; (3) HIV-infected patients; (4) Acute myocardial infarction; (5) Patients with concomitant immune system disorders; (6) Haematological disorders; (7) History of drug abuse, psychiatric illnesses, and Alzheimer's disease. There is usually a clear rationale behind exclusion criteria, which helps ensure the internal and external validity of the study.

Treatment method

After admission, the two groups of patients were given routine treatment such as oxygen, cardiac monitoring, etc., and digoxin, nitrates, angiotensin-converting enzyme

inhibitors, angiotensin II receptor antagonists, and other medications were given appropriately according to the patient's conditions. Based on the above, the control group was given 25 mg sacubitril valsartan (Beijing Novartis Pharmaceuticals Co., Ltd., Beijing, China) 2 times/day, after which the dose was increased by 25 mg per week, with the maximum dose did not exceed 100 mg/dose. In the experimental group, participants were administered 0.0075 μg·kg-1·min-1 recombinant human brain natriuretic peptide (Neoactivin, Chengdu Nordicam Bio-Pharmaceutical Co., Ltd., Chengdu, China) at a loading dose of 1.5 μg/kg, in addition to the medication received by the control group, for 3 to 5 days. This clarification ensures that participants in the experimental group received both the control group medication and Neoactivin concurrently.

Observation indexes and examination methods

Observe the echocardiograms (left ventricular ejection fraction (LVEF), left ventricular diastolic volume (LVEDV), left ventricular short-axis rate (FS), and pacemaker volume (SV)), electrocardiographic parameters (P-wave dispersion (Pd)), serum soluble growth-stimulating expressed gene 2 protein (sST2), galactose agglutinin-3 (Gal-3), nitrogen-terminal brain natriuretic peptide precursor (NT- proBNP) change differences, clinical efficacy differences, and the occurrence of adverse reactions.

Clinical efficacy: basic cure: the clinical signs and symptoms that existed before treatment disappeared completely after treatment, and the results of cardiac function and electrocardiogram were back to normal; obvious effect: the clinical symptoms and signs of patients improved significantly compared with those before treatment, and the cardiac function of the patients improved by ≥2 grades compared with those before treatment, and the frequency of atrial fibrillation was significantly reduced by more than 50%; effective: patients' clinical symptoms and signs were relieved to a certain extent compared with those before treatment but still existed, cardiac function improved by ≥1 grade, and the frequency of atrial fibrillation was reduced by less than 50%; Ineffective: there was no significant change in patient's clinical symptoms and signs, cardiac function improved by <1 grade and biochemical indexes did not improve. This clarification ensures that participants in the experimental group received both the control group medication and Neoactivin concurrently, and this combined treatment approach serves as the standard for assessing clinical efficacy.

Before and after treatment, LVEF, LVEDd, FS, and SV were detected by SSC-400 Doppler ultrasound diagnostic instrument (Shanghai Aloka Medical Instrument Co., Ltd., Shanghai, China). Pd was recorded using an applied 12-lead ECG.

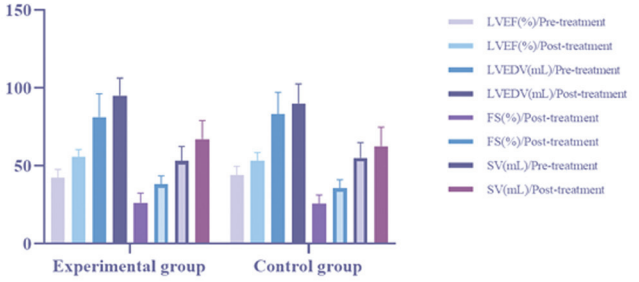
Serum factor level detection: 2 ml of patients' venous blood was drawn before and after treatment, and the serum was collected after centrifugation (15 min, 3500 rpm) to be measured, and sST2 and Gal-3 levels were detected by ELISA.

Table 2. Comparison of changes in cardiac function before and after treatment in the two groups of patients (±s)

Group	n	LVEF(%)		t	P value	LVEDV(mL)		t	P value
		Pre-treatment	Post-treatment			Pre-treatment	Post-treatment		
Experimental group	55	42.6±5.1	55.6±4.8	-13.832	.000	81.3±15.0	95.0±11.3	-5.441	.000
Control group	56	44.0±5.7	53.2±5.3	-8.808	.000	83.0±14.2	90.3±12.6	-2.866	.005
t		-1.363	2.499			-0.613	2.068		
P value		0.176	0.014			0.541	0.041		

Group	n	FS(%)		t	P value	SV(mL)		t	P value
		Pre-treatment	Post-treatment			Pre-treatment	Post-treatment		
Experimental group	55	26.3±6.2	38.0±5.6	9.688	.000	53.0±9.4	67.2±11.8	-7.005	.000
Control group	56	25.5±5.8	35.7±5.3	6.931	.000	55.1±9.8	62.5±12.3	-3.502	.001
t		0.702	-2.222			-1.152	2.054		
P value		.484	.028			.252	.042		

Figure 1. Comparison of changes in cardiac function before and after treatment in the two groups of patients



NT-proBNP level was detected by electrochemiluminescence immunoassay, and the kit was purchased from Shanghai Jianglai Biotechnology Company (Shanghai, China).

Postoperative follow-up was carried out for the two groups of patients, and the occurrence of adverse reactions such as angioedema, hypotension, hyperkalemia, headache, and nausea was observed and recorded in the two groups.

Statistical analysis

In this study, we analyzed the collected data using Statistic Package for Social Science (SPSS) 21.0 (IBM, Armonk, NY, USA). The measurements of QRS wave duration, sST2, Gal-3, and NT-proBNP in the study are presented as mean ± standard deviation. For the two groups of data, we used independent samples *t* test for statistical analysis. As for the occurrence of clinical efficacy and adverse reactions, we described them as percentages and compared them by the χ^2 test or Mann-Whitney U test. When the $P < .05$, we considered the statistical result to be significantly different.

RESULTS

Comparative analysis of echocardiographic parameters of patients in the test group and control group

Before treatment, there was no significant difference in the comparison of the baseline measurement levels of LVEF, LVEDV, FS, and SV between the patients in the test group and the control group ($t = 0.702, -1.152$, $Ps > .05$). The results showed that there were no significant differences between the experimental and control groups on these measurement items. This suggests that the cardiovascular status of the two groups of patients was similar before treatment, making it easier to compare post-treatment effects. These data serve as baseline data for the study and help determine whether treatment has a significant impact on these

Table 3. Comparison of Pd, sST2, Gal-3, and NT-proBNP measurements before and after treatment between the two groups of patients (±s)

Group	n	Pd(ms)		*t*	*P* value	sST2(ng/L)		*t*	*P* value
		Pre-treatment	Post-treatment			Pre-treatment	Post-treatment		
Experimental group	55	44.72±6.91	32.19±5.10	14.840	.000	73.1±9.5	44.2±7.0	18.269	.000
Control group	56	42.08±7.12	33.87±5.51	14.006	.000	70.6±10.3	48.6±8.5	12.283	.000
t		1.982	-1.666			1.329	-2.974		
P value		0.050	0.099			0.187	0.004		
Group	n	Gal-3(μg/L)		*t*	*P* value	NT-proBNP(ng/L)		*t*	*P* value
		Pre-treatment	Post-treatment			Pre-treatment	Post-treatment		
Experimental group	55	8.96±2.00	4.51±1.43	13.503	.000	2568.3±344.0	1350.7±266.1	20.880	.000
Control group	56	9.43±2.26	5.13±1.50	11.831	.000	2620.5±395.1	1466.3±295.5	17.450	.000
t		-1.160	-2.228			-0.742	-2.165		
P value		.249	.028			.460	.033		

Table 4. Comparison of treatment effects between the two groups of patients [n (%)]

Group	n	Cured	Marked effect	Effective	Ineffective
Experimental group	55	25(45.45)	24(43.64)	6(10.91)	0(0.00)
Control group	56	16(28.57)	27(48.21)	13(23.21)	0(0.00)
Z		-2.146			
P value		.042			

Table 5. Comparison of adverse reactions between the two groups of patients

Group	n	Angioedema	Hypotension	Hyperkalaemia	Headache	Nausea	Adverse reactions
Experimental group	55	2	1	1	3	2	9(16.36)
Control group	56	1	2	0	1	0	4(7.14)
χ^2							2.282
P value							0.131

Figure 2. Comparison of Pd, sST2, Gal-3, and NT-proBNP measurements before and after treatment between the two groups of patients

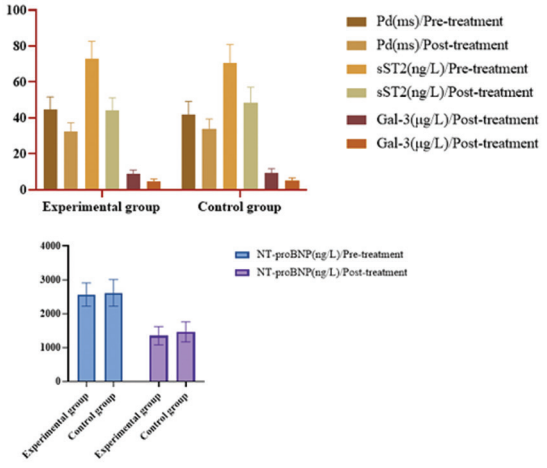
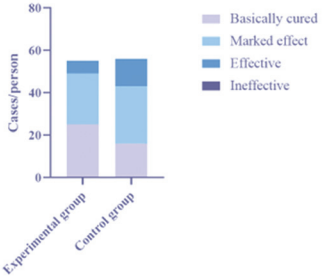


Figure 3. Comparison of treatment effects between the two groups of patients



cardiovascular parameters. After treatment, the measured values of LVEF, LVEDV, FS, and SV of patients in both groups were significantly higher than those before treatment in this group, and the differences in the above indicators were statistically significant (t = -2.222, P < .05); the measured values of LVEF, LVEDV, FS, and SV of patients in the experimental group were higher than those of the control group after treatment, and the differences between the data groups were significant (t = 2.045, P < .05); Table 2, Figure 1.

Comparison of Pd, sST2, Gal-3, and NT-proBNP measurements before and after treatment between the two groups of patients

Before treatment, the comparison of Pd, sST2, Gal-3, and NT-proBNP measurements between patients in the test group and the control group was not statistically significant (t = 1.160, -0.742, P > .05); after treatment, the measured values of Pd, sST2, Gal-3, and NT-proBNP of patients in both groups were significantly lower than those before treatment in this group, and the differences in the above indicators were statistically significant (t = -2.228, P < .05); the sST2, Gal-3, and NT-proBNP measurements of the patients in the test group were lower than those of the control group after treatment, and the differences were all statistically significant (t = -2.165, P < .05); Table 3, Figure 2.

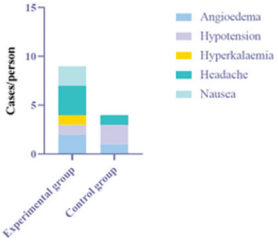
Comparison of treatment effects between the two groups

Clinical effect evaluation was carried out after treatment, the basic cure rate of the experimental group was 45.45%, the apparent efficiency was 43.64%, the effective rate was 10.91%, and the basic cure rate of the control group was 28.57%, the apparent efficiency was 48.21%, and the effective rate was 23.21%, and the difference was statistically significant (Z= -2.146, P < .05); Table 4, Figure 3.

Comparison of the occurrence of adverse reactions between the two groups

A total of 9 patients in the experimental group (2 cases of angioedema, 1 case of hypotension, 1 case of hyperkalaemia, 3 cases of headache, 2 cases of malignancy) experienced different types of adverse reactions, and 4 cases in the control group, the degree of adverse reactions were not serious, and the patients did not have any interruption of treatment due to adverse reactions, and the comparison of the occurrence of adverse reactions in patients of the two groups showed that the differences between the two groups were not significant (χ^2= 2.282, P > .05). Regarding adverse reactions, the results showed that there was no significant difference in the incidence of adverse events between the experimental group and the control group, which helps to evaluate the safety of the treatment. Although adverse effects occurred, they were generally manageable and did not lead to treatment discontinuation. This is critical in determining the practical feasibility of treatment and patient safety. Table 5, Figure 4.

Figure 4. Comparison of adverse reactions between the two groups of patients



DISCUSSION

Patients with CHF who develop atrial fibrillation will lose the function of the atrial auxiliary pump, which will cause serious harm to cardiac function, and also reduce cardiac output, inducing serious consequences such as palpitations, tachycardia, congestive heart failure, and the risk of patient's death is significantly increased. This study aimed to investigate the effect of treatment with neoactivin + sacubitril valsartan in patients with CHF combined with atrial fibrillation.

The results of this study showed that after treatment, the measured values of LVEF, LVEDV, FS, and SV of the two groups of patients were significantly higher than those before the treatment of this group, and the above indexes of the patients in the experimental group were significantly higher than those in the control group. It is suggested that the combined treatment program of neoactivin + sacubitril valsartan has a more significant effect on the improvement of patients' cardiac function. The reasons are analyzed as follows: sacubitril valsartan can inhibit both RAAS and natriuretic peptide system, which in turn can play a role in reversing ventricular remodeling and reducing ventricular flutter and ventricular fibrillation. The effects of this drug in reducing the number of recurrences of atrial fibrillation and improving cardiac function have been clinically proven.[10,11] The test group used neovasculin + sacubitril valsartan, which was found to be more effective in improving cardiac function than the control group regimen in this study. Neovusin has the same structure and biological activity as endogenous brain natriuretic peptide and has become a first-line drug for the treatment of heart failure secondary to acute myocardial infarction.[12,13] Combined with the analysis of the results of this study, neovasculin can effectively antagonize the activity of RAAS, the sympathetic nervous system, and the endothelin system, and superimposed on the effect of blocking ventricular remodeling in combination with sacubitril valdecoxib, it can more effectively reduce the cardiac load, improve the cardiac function, and promote symptomatic relief.

Inflammatory factors will participate in the body's inflammatory and immune responses, causing damage to cardiomyocytes and inducing heart failure, and their levels can reflect the degree of heart failure as well as prognostic assessment.[14,15] sST2, Gal-3, and NT-proBNP can be used as the target of the treatment and prognostic assessment indexes for the treatment of CHF combined with heart failure. The results of this study showed that after treatment, the measured values of Pd, sST2, Gal-3, and NT-proBNP in both groups were significantly lower than those before treatment in this group; the levels of the above indicators in the patients of the test group were significantly lower than those in the control group after treatment. It is suggested that the test group program reduces cardiotoxicity significantly and can effectively improve cardiac function. Sacubitril valsartan sodium tablets combine two main drug components, valsartan and sacubitril. Together, these components act on angiotensin II receptors and enkephalinase, thereby contributing to vasodilatation, as well as enhancing urinary sodium excretion and reversing structural changes in the ventricles. However, their ability to modulate inflammation-related factors is relatively weak.[16] In contrast, neopterin can counteract the renin-angiotensin-aldosterone system and neutralize the activity of this system, thus helping to mitigate the structural changes in the ventricles. "Neopterin" is a biomarker commonly used as an indicator of the activity of the body's immune system. It is often associated with inflammation and immune responses. In medical research, measuring neopterin levels in the blood can provide information about the body's immune activity and disease conditions. This effect further helps to mitigate the adverse effects on the heart by increasing Pd values and alleviating myocardial damage, while significantly reducing the serum levels of sST2, Gal-3, and NT-proBNP in patients. Combined with the significant modulation of NT-proBNP levels with sacubitril valsartan and neoactivin, this study further validates the association of improved cardiac function with enkephalin inhibitors.

This study evaluated the clinical outcome after treatment and found a significant difference in the cure rate between the test and control groups. The difference in the incidence of adverse reactions between the two groups was not statistically significant. It suggests that neovasculin + sacubitril valsartan has a better effect in the treatment of patients with CHF combined with atrial fibrillation, and has a certain degree of safety, without increasing the incidence of adverse reactions. Neoctreotide is a biological preparation based on genetic recombination technology, which has the effect of antagonizing sympathetic nerves, inhibiting aldosterone, and endothelin secretion, and can effectively dilate blood vessels. The drug can dilate volume vessels, reduce peripheral vascular resistance, effectively correct hemodynamics, reduce patients' heart rate and blood pressure, and improve the symptoms of heart failure.[17] it can combine with the specific receptors on the surface of the cardiac muscle cell membrane, causing an increase in intracellular cyclic guanosine monophosphate (cGMP) concentration, causing arterial and venous vascular smooth muscle diastole, reducing the cardiac load, and improving the cure rate.[18] In the experimental group of neuvosin +s acubitril valsartan regimen, the lower dose of neuvosin used in this study was able to achieve a better therapeutic effect with less drug accumulation effect and a better safety profile.

Due to the small sample size included in this study, the short follow-up time, and the long-term efficacy of all patients were not counted, so the conclusion still needs to be confirmed by a large-sample, high-quality randomized study.

In conclusion, the treatment of CHF combined with atrial fibrillation with neuvosin + sacubitril valsartan can more effectively improve cardiac function and reduce the condition of atrial fibrillation, which is worthy of clinical promotion and application.

ETHICAL COMPLIANCE

This study was approved by the ethics committee of Xingtai Third Hospital. Signed written informed consent was obtained from the patients and/or guardians.

CONFLICT OF INTEREST

The authors have no potential conflicts of interest to report relevant to this article.

AUTHOR CONTRIBUTIONS

JW and XL designed the study and performed the experiments, QZ and BM collected the data, JC and XD analyzed the data, and JW and XL prepared the manuscript. All authors read and approved the final manuscript.

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