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Effect of Sacubitril-valsartan Combined with Metoprolol in the Treatment of Refractory Heart Failure in the Elderly

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Abstract: *Objective:* To explore the effect of sacubitril-valsartan combined with metoprolol in the treatment of refractory heart failure in the elderly. *Methods:* 72 elderly patients with refractory heart failure were selected for data analysis in the outpatient clinic of our hospital from January 2024 to October 2025. They were divided into groups using the random number table method, with 36 patients in each group. The research group was treated with sacubitril-valsartan combined with metoprolol, and the control group was treated with metoprolol. The data between the groups were compared. *Results:* Compared with the control group, the total effective rate of the study group was significantly higher, the NT-proBNP index was significantly lower after treatment, and the inflammatory factors were significantly lower after treatment, $p < 0.05$; the NT-proBNP index and inflammatory factors before treatment were compared between the two groups, and the incidence of adverse reactions between the two groups was compared, $p > 0.05$. *Conclusion:* The effect of sacubitril-valsartan combined with metoprolol in the treatment of refractory heart failure in the elderly is ideal.

Keywords: Sacubitril-valsartan; Metoprolol; Elderly; Refractory heart failure; Effect

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1. Introduction

The most severe end-stage manifestation of various cardiovascular diseases is heart failure. The core pathological characteristics are ventricular remodeling and progressive decline in cardiac function. For elderly patients, the difficulty of treatment is significantly increased due to the decline of body function, multiple organ comorbidities, and poor drug tolerance. Therefore, clinical management of refractory heart failure is focused on the cardiovascular field. At present, our country is in the process of increasing population aging, so the number of elderly heart failure patients is increasing year by year. Among them, the special type is refractory heart failure, and the treatment dilemma is particularly prominent. Relevant data suggest that among the elderly, the prevalence of heart failure over the age of 80 is more than 10%, refractory heart failure accounts for more than 20%, and the 5-year survival rate is very low [1]. Metoprolol is currently used clinically in the treatment of elderly patients with refractory heart failure to improve hemodynamics and inhibit

neuroendocrine activation [2]. The patients slow down their heart rate, reduce myocardial oxygen consumption, and improve their cardiac function. However, single use of the drug has poor effects and cannot effectively control the patient's ventricular remodeling process. In clinical research, sacubitril-valsartan is effective in lowering blood pressure and inhibiting myocardial fibrosis, and it can be used as a combination drug in this article [3]. This article selected 72 patients to explore the effect of sacubitril-valsartan combined with metoprolol in the treatment of elderly patients with refractory heart failure.

2. Materials and methods

2.1. Information

From January 2024 to October 2025, 72 elderly patients with refractory heart failure were selected for data analysis in the outpatient clinic of our hospital. They were divided into groups using the random number table method, with 36 patients in each group. The study group included 20/16 men and women, aged 60–80 (66.26 ± 1.25) years old, including 23 patients with hypertension, 17 patients with diabetes, and 19 patients with coronary heart disease. The control group included 21/15 men and women, aged 61–79 (66.22 ± 1.36) years old, including 22 patients with hypertension, 18 patients with diabetes, and 20 patients with coronary heart disease. Comparison of the two sets of data resulted in $p > 0.05$.

2.1.1. Inclusion criteria

Consistent with the disease diagnostic criteria; expected survival time of more than 0.5 years; NYHA cardiac function class III-IV; heart failure that is refractory to recovery.

2.1.2. Exclusion criteria

Severe liver and kidney dysfunction; severe infection or autoimmune system disease; malignant tumor; drug contraindications or allergies; severe cognitive dysfunction or other mental illness; low treatment compliance.

2.2. Method

The control group is treated with metoprolol. Metoprolol is a sustained-release tablet, usually 12.5 mg/time. If the patient's basal heart rate is low (< 60 beats/min) or blood pressure is unstable, it can be started from 6.25 mg/time, once a day. Then gradually increase the dose, and increase the dose every 2–4 weeks according to the patient's tolerance (no obvious bradycardia, hypotension, or worsening of heart failure). The commonly used dose ladder is 12.5 mg → 25 mg → 50 mg → 100 mg → 200 mg, once a day. Target dose: The heart rate is controlled at 55–60 beats/min (resting state). The maximum tolerated dose was usually 200 mg/day (or adjusted according to body weight, such as 1 mg/kg/day). It is necessary to avoid heart rate < 50 beats/min.

The research group was treated with sacubitril-valsartan combined with metoprolol, and based on the intervention in the control group, the following was increased: starting dose: those who have not used angiotensin-converting enzyme inhibitors (ACEI)/angiotensin II receptor blockers (ARB): 50 mg/time, 2 times a day times; those who switch from ACEI/ARB: they need to stop taking ACEI for at least 36 hours before starting again, with a starting dose of 50 mg/time, twice a day (if the patient has previously tolerated the regular dose of ACEI/ARB, they can directly start 100 mg/time, twice a day). Adjust according to blood pressure, renal function (to avoid significant elevation of serum creatinine, serum potassium > 5.5 mmol/L) and heart failure symptoms every 2–4 weeks, the dose ladder is 50 mg → 100 mg → 200 mg, twice a day. Target dose: usually 200 mg/time, 2 times a day (or adjusted according to body weight, such as those weighing < 40 kg, start with 25 mg/time, 2 times a day).

During the treatment of the patient, an outpatient review was conducted every four weeks to monitor the patient's heart rate, blood pressure, liver and kidney function, electrolytes, NT-proBNP, hs-CRP and other indicators, and adjust the patient's medication dosage in a timely manner to avoid adverse reactions in the patient.

Treatment for 1 year.

2.3. Observation indicators

(1) Compare the total effectiveness of the two groups. After treatment, if the symptoms are significantly improved and the NYHA cardiac function classification is raised to level 2 or above, it is judged to be effective; if the symptoms are improved and the NYHA cardiac function classification is raised to 1 level, it is judged to be effective; in other cases, it is judged to be ineffective. Total efficiency = 100% – inefficiency.
(2) Compare the NT-proBNP indicators of the two groups.
(3) Compare the inflammatory factors between the two groups.
(4) Compare the occurrence of adverse reactions between the two groups.

2.4. Statistics

Use SPSS 28.0 software, use mean ± standard deviation ($\bar{x} \pm s$) to describe measurement data, *t* test; use rate (%) to describe count data, χ^2 test, $p < 0.05$, statistically significant.

3. Results

Compared with the control group, the total effective rate of the study group was significantly higher, the NT-proBNP index was significantly lower after treatment, and the inflammatory factors were significantly lower after treatment, $p < 0.05$; the NT-proBNP index and inflammatory factors before treatment were compared between the two groups, and the incidence of adverse reactions between the two groups was compared, $p > 0.05$. See **Table 1, 2, 3** and **4**.

Table 1. Comparison of the total effective rate (%) between the two groups

Group	Effective	Valid	Invalid	Always efficient
Research group (n = 36)	13 (36.11)	21 (58.33)	2 (5.56)	94.44
Control group (n = 36)	8 (22.22)	19 (52.78)	9 (25.00)	75.00
χ^2	-	-	-	5.2578
p	-	-	-	< 0.05

Table 2. Comparison of NT-proBNP indicators between the two groups

Group	NT-proBNP (ng/L)	
	Before treatment	After treatment
Research group (n = 36)	3352.37 ± 650.45	1504.35 ± 280.71
Control group (n = 36)	3365.28 ± 653.07	1943.89 ± 368.78
t	0.0840	5.6903
p	> 0.05	< 0.05

Table 3. Comparison of inflammatory factors between the two groups

Group	hs-CRP (ng/mL)	
	Before treatment	After treatment
Research group (n = 36)	14.15 ± 2.44	6.27 ± 1.88
Control group (n = 36)	14.13 ± 2.32	11.05 ± 2.16
t	0.0356	10.0155
p	> 0.05	< 0.05

Table 4. Comparison of the incidence of adverse reactions between the two groups (%)

Group	Dizziness	Weakness	Hypotension	Bradycardia	Elevated blood potassium	Total
Research group (n = 36)	1 (2.78)	1 (2.78)	1 (2.78)	0	1 (2.78)	4 (11.11)
Control group (n = 36)	2 (5.56)	1 (2.78)	0	1 (2.78)	0	4 (11.11)
χ^2	-	-	-	-	-	0.0000
p	-	-	-	-	-	> 0.05

4. Discussion

The core contradiction in elderly patients with refractory heart failure is progressive ventricular remodeling and cardiac function decline induced by neuroendocrine overactivation, which requires combined medication. This article studied the therapeutic value of sacubitril-valsartan combined with metoprolol and obtained the following results.

The improvement in treatment efficiency is due to the advantages of combined medication. The research data in this article show that the total effectiveness of the study group is 94.44%, which is significantly higher than that of the control group. The reason is the mechanism synergy. Metoprolol can block β1 receptors for patients, slow down the patient's heart rate, reduce myocardial oxygen consumption and improve myocardial energy metabolism [4]. However, it cannot effectively antagonize vasoconstriction, water and sodium retention, and myocardial fibrosis caused by RAAS activation. For patients, Sacubitril-valsartan uses the inhibitory effect of neprilysin to enhance patients' sodium and water excretion, help patients relax blood vessels, block angiotensin II type 1 receptors, and inhibit RAAS-mediated myocardial damage. This "inhibition of sympathetic nerves + dual regulation of the RAAS/natriuretic peptide system" can intervene in the pathological links of heart failure with multiple targets [5]. In line with the complex pathophysiological characteristics of elderly patients, the research group significantly improved symptoms and improved cardiac function classification. For elderly patients, due to decreased blood vessel elasticity and weakened myocardial contractility, the use of a single drug during treatment cannot cover multiple pathological mechanisms. Therefore, it is clinically recommended for patients to use combined drugs to use complementary mechanisms to comprehensively intervene in the pathological process of heart failure. Therefore, the treatment effect of the research group studied in this article is better.

Changes in core indicators of cardiac function further confirmed the effectiveness of the combined medication. Clinical studies have shown that NT-proBNP levels are positively related to the severity of heart failure. After treatment, the NT-proBNP levels of the study group (1504.35 ± 280.71 ng/L) were significantly lower than those of the control group. From the perspective of pharmacological mechanism, using metoprolol for patients can restore myocardial sensitivity to catecholamines by upregulating β-receptor density [6]. Sacubitril-valsartan can promote arterial dilation and venous dilation in patients, help patients reduce cardiac pre- and post-load, and reduce myocardial compensatory hypertrophy. This drug can provide favorable conditions for the recovery of myocardial contractile function. In synergy with the two, patients

can significantly improve myocardial blood pumping efficiency, reduce ventricular end-diastolic volume, and reduce the synthesis and release of NT-proBNP, forming a virtuous cycle [7]. In addition, the significant reduction of NT-proBNP also fully reflects the effect of combined medication on inhibiting ventricular remodeling. The progression of heart failure in patients is delayed, and the long-term prognosis of patients is significantly improved.

Patients reduce the levels of inflammatory factors because the combination of drugs has an anti-inflammatory mechanism [8]. In the occurrence and development of heart failure, chronic inflammatory response plays an important role. Inflammatory factors such as hs-CRP can aggravate cardiac function damage by damaging myocardial cells and promoting collagen deposition. This study shows that the levels of the above-mentioned inflammatory factors in the research group after treatment were significantly lower than those in the control group. From a mechanism analysis, when metoprolol was used for patients, sympathetic nerve activation was inhibited and the release of inflammatory factors was reduced. Using sacubitril-valsartan for patients has a strong anti-inflammatory effect, blocking the activation of RAAS and reducing the activation of inflammatory pathways such as nuclear factor-κB, and the anti-inflammatory activity of natriuretic peptides is significantly enhanced. The two drugs can inhibit the inflammatory response in patients and reduce acute myocardial damage. When used in combination, the drugs can also inhibit chronic inflammation-mediated ventricular remodeling, significantly improving the patient's therapeutic effect. This result suggests that the use of combined drugs for patients can significantly improve the patient's clinical symptoms and cardiac function, intervene in the patient's disease progression from the inflammatory mechanism level, and effectively treat the condition of elderly patients with refractory heart failure.

In terms of safety, the incidence of adverse reactions in the two groups was consistent at 11.11%. The patients' adverse reaction symptoms were relatively mild. After symptomatic treatment for the patients, all patients were relieved and no serious adverse reactions occurred in the patients. It can be fully confirmed that sacubitril-valsartan combined with metoprolol can effectively and safely treat elderly patients with refractory heart failure. It adapts to the poor drug tolerance of elderly patients and can be used in the long-term clinical treatment of elderly patients with refractory heart failure. What needs attention is that the heart rate, blood pressure, and liver and kidney functions need to be closely monitored during the patient's medication to avoid adverse reactions such as bradycardia, hypotension, and elevated blood potassium, and to ensure the safety of patient drug treatment.

Analyzing the limitations of this article, the first is that the sample size is small and it is a single-center outpatient study, so there is selection bias. The second is that there are few observation indicators in this study, and only NT-proBNP and hs-CRP are included. Due to hospital conditions, no objective indicators related to the patient's cardiac function are monitored, and the patient's treatment effect cannot be fully evaluated. In addition, the follow-up time is 1 year, and the patient's long-term prognosis and drug safety are not observed. Based on this, in subsequent studies, the sample size can be expanded, multi-center studies can be carried out, the follow-up period can be extended, observation indicator monitoring can be increased, and the conclusions can be improved.

In summary, the treatment effect of sacubitril-valsartan combined with metoprolol in the treatment of elderly patients with refractory heart failure is ideal. The NT-proBNP index of patients after treatment is significantly lower, and the inflammatory factors are significantly lower after treatment. The drug is safe and worthy of clinical use and promotion.

About the author

Zhou Yuyan (1982.3—), female, Han, native of Wuxi, Jiangsu Province, with a bachelor's degree, works at the Community Health Service Center of Wangzhuang Street, Wuxi City, Jiangsu Province. Her research interests include general practice, chronic diseases of the elderly, and diagnosis and treatment of common diseases.

Disclosure statement

The author declares no conflict of interest.

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