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Sequential Treatment of Acute Heart Failure in the Elderly: Efficacy of Recombinant Human Brain Natriuretic Peptide and Sacubitril-Valsartan

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Abstract: *Objective:* To explore the clinical efficacy of recombinant human brain natriuretic peptide (rhBNP) and sacubitril-valsartan in the sequential treatment of acute heart failure (AHF) in older individuals. *Methods:* Clinical data from 64 older patients with AHF were collected for this study. The patients were divided into two groups: a control group (Group A, $n = 34$) and an observation group (Group B, $n = 30$) based on different treatment regimens. Group A received rhBNP treatment, while Group B received sequential treatment with rhBNP and Sacubitril-Valsartan. The evaluation of the sequential treatment's effect on older patients with AHF was conducted using various indicators. *Results:* The clinical efficacy rate in Group A (93.33%) was significantly higher than that in Group A (73.53%), with a significant difference observed ($P < 0.05$). Furthermore, after treatment, the clinical efficacy remained significantly higher in Group B than in Group A. Group B exhibited a significantly higher left ventricular ejection fraction (LVEF) and significantly lower systolic blood pressure, diastolic blood pressure, and heart rate compared to Group A ($P < 0.05$). Although the left ventricular end-diastolic diameter (LVEDD) was lower in Group B after treatment, the difference was not statistically significant ($P = 0.127$). Moreover, post-treatment levels of NT-proBNP were significantly lower in Group B compared to Group A ($P = 0.01$). Additionally, Group B had shorter hospitalization times, faster improvement in clinical symptoms, and further 6-minute walking distances after the treatment compared to Group A ($P < 0.01$). *Conclusion:* Sequential treatment with rhBNP and Sacubitril-Valsartan demonstrates promising therapeutic effects in older patients with AHF, suggesting its potential for broader adoption and promotion in clinical practice.

Keywords: Recombinant human brain natriuretic peptide (rhBNP); Sacubitril-Valsartan; Sequential treatment; Elderly; Acute heart failure (AHF)

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1. Introduction

The aging process of society is accelerating, leading to acute heart failure (AHF) among the elderly, which poses a significant threat to their health and quality of life [1]. The treatment of AHF in older patients is complex and dynamic due to their physiological characteristics and the presence of multiple complications.

Therefore, the discovery of more effective and safer treatment methods is crucial for improving the therapeutic outcomes and quality of life of elderly AHF patients. Recombinant human brain natriuretic peptide (rhBNP), an endogenous cardiac hormone, has been shown in numerous studies to alleviate symptoms and enhance the quality of life in elderly AHF patients through various pathways, including its diuretic effects and its ability to reduce cardiac preload and afterload [2]. Sacubitril-Valsartan, a novel cardiovascular drug, has demonstrated efficacy in improving clinical symptoms and prognosis by inhibiting the effects of angiotensin receptors and neutral endopeptidase. Recently, the efficacy of sequential treatment with rhBNP and Sacubitril-Valsartan in older patients with AHF has garnered attention in clinical medical research. This treatment strategy aims to capitalize on the synergistic effects of both drugs and offer a more effective treatment option for elderly AHF patients by comprehensively regulating cardiovascular function. Building upon this premise, this article undertakes an in-depth examination of the efficacy of sequential treatment with rhBNP and Sacubitril-Valsartan in elderly AHF patients, intending to provide a more scientific basis and reference for the comprehensive treatment of this population.

2. Materials and methods

2.1. General information

Clinical data of 64 elderly AHF patients enrolled in the study were collected and categorized into a control group (Group A, n = 34) and an observation group (Group B, n = 30) based on distinct treatment protocols. Inclusion criteria comprised: (1) Patients aged 60 years or older; (2) Patients meeting relevant diagnostic criteria for AHF; (3) Patients with relatively stable conditions suitable for pharmacological intervention; (4) Patients without significant liver, kidney, or other organ dysfunction; (5) Patients with no history of allergy to rhBNP or Sacubitril-Valsartan; (6) Patients providing informed consent, understanding the research's purpose, methods, and risks, and willing to participate. Exclusion criteria included: (1) Patients under the age of 60; (2) Patients with an unclear diagnosis of AHF or other serious heart conditions (e.g., myocardial infarction, valvular heart disease); (3) Patients with severe liver and kidney dysfunction, incomplete disease profiles, malignant tumors, or other significant conditions potentially impacting study outcomes; (4) Patients with known allergies to any component of rhBNP or Sacubitril-Valsartan; (5) Patients with implanted permanent pacemakers; (6) Patients with a history of cardiac surgery; (7) Patients unable to complete the entire research process or with incomplete data records, thereby compromising analysis and evaluation of research results.

2.2. Methods

Upon admission, all patients received standard treatment. Group A received rhBNP treatment in addition to conventional treatment. RhBNP was administered intravenously within 24 hours of onset, followed by continuous intravenous infusion of 0.0075 μg/kg/min for 3–5 days. Group B received sequential treatment with rhBNP and Sacubitril-Valsartan alongside conventional therapy. Sacubitril-Valsartan was orally administered, initially at a dose of 50 mg twice a day, and increased to double dosage after 4 weeks and continued for 1 month.

2.3. Observation indicators

This study comprehensively assessed patients' clinical efficacy based on their symptoms and utilized systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate (HR), left ventricular ejection fraction (LVEF), and left ventricular end-diastolic diameter (LVEDD) to evaluate blood pressure and cardiac function. N-terminal pro-brain natriuretic peptide (NT-proBNP) precursor was employed to assess AHF status, while hospitalization duration, time to clinical symptom improvement, and 6-minute walking distance post-treatment were used to

evaluate clinical efficacy.

2.4. Statistical analysis

Data processing was performed using SPSS 20.0, with measurement data expressed as mean ± standard deviation (SD) and count data expressed as [*n* (%)]. The independent sample *t*-test was utilized for normally distributed data, while the χ^2 test was employed for intergroup comparison of categorical data. A significance level of $P < 0.05$ indicated statistical significance.

3. Results

3.1. Clinical efficacy

Table 1 shows that the clinical efficacy rate of patients in Group B (93.33%) is significantly higher than Group A (73.53%; $P = 0.036$).

Table 1. Comparison of clinical efficacy [*n* (%)]

Indicator	Group A (*n* = 34)	Group B (*n* = 30)	χ^2	*P*
Markedly effective	9 (26.47%)	17 (56.66%)	-	-
Effective	16 (47.06%)	11 (36.67%)	-	-
Ineffective	9 (26.47%)	2 (6.67%)	-	-
Total effectiveness	25 (73.53%)	28 (93.33%)	4.392	0.036

3.2. Blood pressure and cardiac function indicators

As shown in **Table 2**, Group B shows a significantly higher LVEF, and significantly lower SBP, DBP, and HR after treatment as compared to Group A ($P < 0.05$). Group B's LVEDD appeared to be lower than Group A's but the difference is not statistically significant ($P = 0.127$).

Table 2. Comparison of blood pressure and cardiac function indicators (mean ± SD)

Indicator	Time	Group A (*n* = 34)	Group B (*n* = 30)	*t*	*P*
SBP (mmHg)	Before treatment	128 ± 9	130 ± 8	0.934	0.354
	After treatment	120 ± 7	112 ± 7	4.563	0.000
DBP (mmHg)	Before treatment	78 ± 7	79 ± 7	0.570	0.571
	After treatment	73 ± 6	70 ± 5	2.156	0.035
HR (beats/min)	Before treatment	118 ± 15	117 ± 16	0.258	0.797
	After treatment	86 ± 9	79 ± 6	3.609	0.001
LVEF (%)	Before treatment	39.64 ± 3.51	39.89 ± 3.64	0.280	0.781
	After treatment	48.25 ± 4.20	51.69 ± 5.01	2.988	0.004
LVEDD (mm)	Before treatment	50.63 ± 6.78	51.26 ± 6.77	0.371	0.712
	After treatment	47.69 ± 6.23	45.32 ± 5.99	1.546	0.127

3.3. Laboratory indicators

After treatment, the NT-proBNP level of Group B was significantly lower than Group A ($P < 0.01$), as presented in **Table 3**.

Table 3. Comparison of laboratory indicators (mean ± SD)

Indicator	Time	Group A (n = 34)	Group B (n = 30)	t	P
NT-proBNP	Before treatment	1,468 ± 165	1,481 ± 163	0.316	0.753
	After treatment	1,264 ± 143	1,101 ± 135	4.672	0.000

3.4. Clinical efficacy indicators

Group B showed shorter hospitalization duration and clinical symptom improvement time as compared to Group A ($P < 0.05$), and a further 6-minute walking distance post-treatment as compared to Group A ($P < 0.01$; **Table 4**).

Table 4. Comparison of clinical efficacy indicators (mean ± SD)

Indicator	Group A (n = 34)	Group B (n = 30)	t	P
Length of stay	13.29 ± 2.65	11.53 ± 2.01	2.962	0.004
Clinical symptom improvement time	5.68 ± 1.12	4.82 ± 0.72	3.599	0.001
Status of a 6-min walk after treatment	346.35 ± 32.15	368.65 ± 35.36	2.643	0.010

4. Discussion

AHF manifests as a rapid decline in cardiac function, resulting in diminished cardiac output, tissue and organ hypoperfusion, and acute congestion syndrome. It typically arises from abnormalities in cardiac structure or function, leading to myocardial contractility impairment and reduced cardiac output, ultimately culminating in pulmonary or systemic circulation congestion [3]. Various factors such as acute myocardial infarction, arrhythmia, heart valve disease, acute severe myocarditis, pericardial disease, hypertension, and diabetes can contribute to AHF [4]. Symptoms commonly include dyspnea (exertional dyspnea, orthopnea, paroxysmal nocturnal dyspnea), cough, sputum production, hemoptysis, fatigue, dizziness, palpitations [5], and in some cases, oliguria and renal impairment. Physical examination may reveal an elevated heart rate, galloping rhythm at the apex, lung crackles, jugular vein distension, hepatomegaly, and edema. This condition poses a significant threat to patients' lives, particularly among the elderly. Firstly, elderly individuals with AHF often present with multiple organ failure due to declining physical function, complicating treatment and exacerbating the disease. Secondly, dyspnea in elderly AHF patients may be more pronounced, severely impacting their quality of life. Dyspnea can hinder patients' ability to lie down or engage in daily activities, increasing the risk of falls and fractures. Additionally, AHF in the elderly may lead to cerebral ischemia, resulting in symptoms such as altered consciousness, syncope, and shock, potentially causing irreversible brain damage in severe cases. Furthermore, when treating AHF in the elderly, reduced liver and kidney function, among other factors, diminishes drug metabolism and excretion, heightening the risk of drug accumulation and adverse reactions, thereby complicating treatment.

Drug therapy constitutes the primary treatment modality for AHF patients. Diuretics are commonly employed to promote diuresis and alleviate lung and systemic congestion, while angiotensin-converting enzyme (ACE) inhibitors and angiotensin II receptor blockers (ARBs) dilate blood vessels, lower blood pressure, and reduce cardiac workload. Beta-blockers are also utilized to decrease heart rate and myocardial oxygen consumption. In recent years, novel drugs such as rhBNP and Sacubitril-Valsartan have introduced new therapeutic strategies for AHF [6]. RhBNP, structurally and functionally akin to endogenous brain natriuretic

peptide, dilates blood vessels, lowers blood pressure, and reduces cardiac workload by binding to natriuretic peptide receptors, thereby improving clinical symptoms and prognosis in AHF patients. In older AHF patients, rhBNP rapidly alleviates cardiac workload, improves cardiac function, and reduces rehospitalization and mortality rates [7]. Sacubitril-Valsartan, an angiotensin receptor neprilysin inhibitor, inhibits angiotensin receptors and neprilysin activity, exerting antihypertensive, anti-cardiac hypertrophy, and anti-fibrotic effects. In older AHF patients, Sacubitril-Valsartan application enhances cardiac function and quality of life while decreasing rehospitalization and mortality rates.

Sequential therapy represents an optimized treatment model that sequentially administers different drugs to achieve enhanced therapeutic effects. Sequential treatment with rhBNP and Sacubitril-Valsartan maximizes therapeutic efficacy by harnessing the advantages of both drugs. In this study, patients in Group B, who received sequential treatment with rhBNP and Sacubitril-Valsartan, demonstrated significantly better clinical efficacy, blood pressure, cardiac function, and laboratory indicators compared to those in Group A, treated with rhBNP alone. Numerous studies corroborate these findings. Huang *et al*. reported that sequential treatment with rhBNP and Sacubitril-Valsartan yields superior clinical outcomes compared to rhBNP monotherapy for AHF [8]. Guo *et al*. similarly found that sequential treatment improves cardiac function and quality of life in AHF patients [9]. Additionally, Liu and colleagues suggested that sequential therapy reduces adverse reactions and enhances safety [10].

Nevertheless, this study has certain limitations. Firstly, the relatively small sample size may yield biased conclusions, warranting caution in interpreting the results. Secondly, AHF in the elderly is a chronic condition necessitating long-term observation and evaluation, yet this study only assessed treatment effects within one month, lacking long-term follow-up data. Future research should address these limitations by expanding sample sizes to enhance result stability and reliability. Additionally, studies should ensure sample diversity and representativeness to more accurately reflect real-world elderly AHF scenarios. Long-term follow-up observations are also imperative to assess sequential treatment's impact on patients' long-term prognosis, providing a more robust basis for clinical practice.

In conclusion, sequential treatment with rhBNP and Sacubitril-Valsartan achieves favorable therapeutic outcomes in older AHF patients, meriting broader adoption and promotion.

Disclosure statement

The authors declare no conflict of interest.

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