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Original Article

Effect of recombinant human brain natriuretic peptide on efficacy, hemodynamics and NT-proBNP in elderly patients with heart failure

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Abstract: Aim: To investigate the effects of recombinant human brain natriuretic peptide (rhBNP) on efficacy, hemodynamics, and N-terminal pro-brain natriuretic peptide (NT-proBNP) in elderly patients with heart failure (HF). Methods: In this retrospective analysis, the clinical data of 112 HF patients who visited the First Affiliated Hospital of Anhui University of Chinese Medicine between March 2019 and October 2022 were analyzed. On the basis of standard HF treatment, 52 patients additionally treated with milrinone intravenous were set as the control group (Con) and 60 patients with rhBNP were set as the observation group (Obs). The therapeutic efficacy and pre- and post-treatment echocardiographic indexes, NT-proBNP and hemodynamics were recorded and compared, and the adverse drug reactions and quality of life scores after treatment were counted. Results: The Obs group showed a markedly higher post-treatment overall response rate than the Con (*P=0.002*). Besides, more obvious improvement of NT-proBNP and hemodynamic indexes were determined in the Obs group compared to the Con (*P*=0.000). Evidently ameliorated left ventricular ejection fraction (LVEF), left ventricular end-diastolic dimension (LVEDD) and left ventricular end-systolic diameter (LVESD) were observed in both groups after treatment, with more pronounced improvement in the Obs group (all *P*=0.000). The Obs group also exhibited an evidently lower incidence of adverse reactions and a better quality of life than the Con after treatment (*P*=0.000). Conclusions: rhBNP can effectively improve the cardiac function and hemodynamics in elderly HF patients, with high safety and few adverse reactions.

Keywords: Recombinant human brain natriuretic peptide, heart failure in the elderly, hemodynamics, NT-proBNP

Introduction

Heart failure (HF) in the elderly, a widespread clinical condition of older adults, was shown by the World Health Organization statistics to account for about 2 to 3 percent of the global elderly population and more than 10% among the population aged over 65 [1, 2]. In addition to its serious impact on patients' quality of life (QoL) and prognosis, HF in old age also imposes a significant burden on the healthcare system and socioeconomics [3]. At present, the treatment of HF in the elderly mainly relies on drug treatment. But due to the complex and diverse causes of the disease, as well as the obvious differences in physiological characteristics and drug metabolic mechanism between the elderly and the young, the treatment of the disease has become complicated and difficult, and traditional treatment methods often fail to achieve ideal curative effect [4]. Therefore, the search for more safe and effective treatment has become a hotspot in the research of HF among senile patients.

NT-proBNP, also known as N-terminal pro-brain natriuretic peptide, is released by myocardial cells as a response to stimuli such as myocardial stretching and increased volume load. It is initially released as pro-brain natriuretic peptide (proBNP), which is then gradually degraded by enzymes into BNP and NT-proBNP. In clinical practice, BNP is widely used to detect and assess the severity of heart failure in patients. Furthermore, studies have confirmed a positive correlation between serum BNP levels and the

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severity of heart failure in patients. Therefore, NT-proBNP can reflect the severity of heart failure and serve as a reliable indicator for monitoring the condition of the disease. In recent years, more and more studies have focused on new drug treatment strategies, among which recombinant human brain natriuretic peptide (rhBNP) has attracted much attention. rhBNP is an endogenous hormone and one of the commonly used anti-HF drugs in recent years, which can significantly increase glomerular filtration rate, eliminate water and sodium retention in the body, modulate myocardial circulation, and alleviate cardiac burden [5, 6]. In addition, rhBNP is shown to inhibit the renin-angiotensin-aldosterone system (RAAS), reduce nervous system activity, effectively suppress posterior pituitary and brainstem sympathetic nerves, ameliorate hypothalamic vascular pressure and regulate peripheral circulation [7]. Clinical research shows that the drug is effective in treating HF and can effectively enhance cardiac function. Although the current clinical role of rhBNP in the treatment of HF has been unanimously recognized, with its efficacy and safety explored accordingly, there are relatively few comprehensive studies on its role in elderly HF patients [8].

This study mainly discussed the efficacy of rhBNP treatment in elderly HF patients and its influence on hemodynamics and N-terminal pro-brain natriuretic peptide (NT-proBNP), in order to provide more reference for the selection of clinical treatment plans. The report is as follows.

Materials and methods

Patient Selection A retrospective analysis was conducted on heart failure patients who visited the First Affiliated Hospital of Anhui University of Chinese Medicine from March 2019 to October 2022. Both groups of patients received standard heart failure treatment, with the control group receiving additional milrinone and the observation group receiving rhBNP treatment.

Inclusion and exclusion criteria

Inclusion criteria: (1) Patients meeting the diagnostic criteria for heart failure; (2) Patients aged 70 years and above; (3) Patients with complete clinical data.

Exclusion criteria: (1) Patients with concomitant other heart diseases; (2) Patients with significant organ dysfunction such as liver or kidney impairment; (3) Patients with severe infectious diseases or immune disorders; (4) Patients with malignant tumors. This study has been approved by the hospital's ethics committee and complies with the Helsinki Declaration.

Data acquisition

Patient data was obtained by reviewing electronic medical records. Treatment methods included standard heart failure therapies according to current guidelines, such as angiotensin receptor blockers (ARBs) or angiotensin-converting enzyme inhibitors (ACEIs), beta-blockers, diuretics, and inotropic agents upon admission. The observation group received intravenous infusion of freeze-dried recombinant human brain natriuretic peptide (produced by Chengdu Nodican Biopharmaceutical Co., Ltd., with National Medical Products Administration approval number S20050033) on top of standard treatment. The initial dose was 1.5 μg/kg given as a bolus injection, followed by a continuous intravenous infusion at a rate of 0.0075-0.01 μg/kg per minute for 1 week. The control group received intravenous milrinone (from Shanghai Yuanye Biotechnology Co., Ltd., with code S31430) as an injection. The initial dose was 50 μg/kg, followed by an intravenous infusion at a rate of 0.5 μg/(kg·min) for 3-5 days after a 10-minute injection, once daily for 1 week.

Outcome measurement and data statistical analysis

During the study period, a total of 180 heart failure patients received treatment. After applying the exclusion criteria, 112 patients were finally included in the study, with 52 in the control group and 60 in the observation group (see **Figure 1** for details).

Main observational indicators: (1) In this study, the treatment effect of patients was evaluated according to the NYHA classification standard [9]. Restoring heart function to NYHA class I, or reducing NYHA class IV to class II, with significant relief or disappearance of clinical symptoms and signs, is considered as markedly effective. Improvement of patient symptoms and signs by one NYHA class is considered

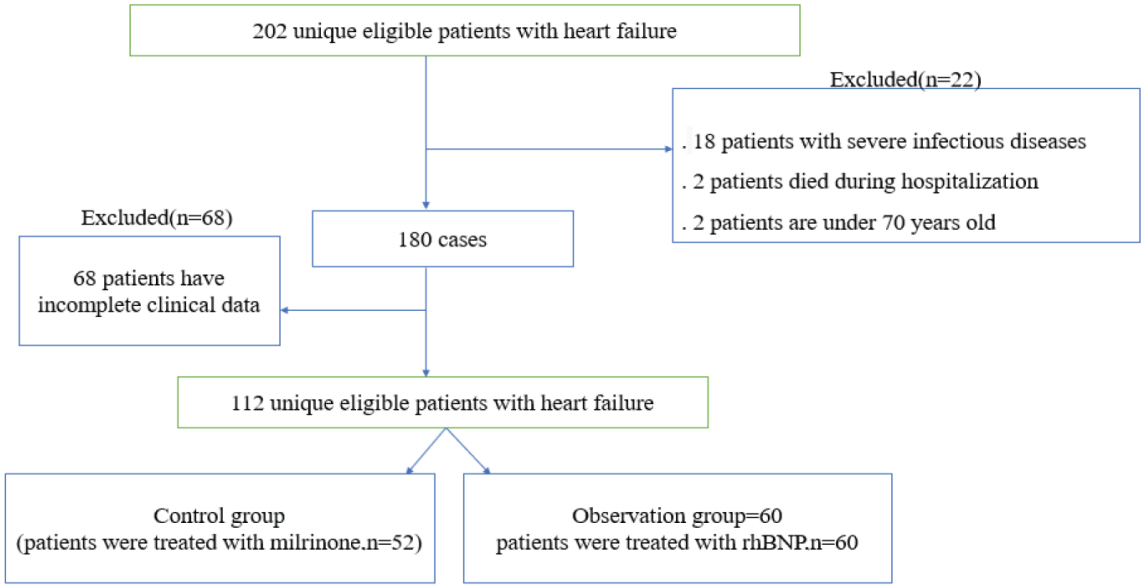

Figure 1. Flow diagram detailing the selection of patients included in the retrospective analysis.

effective. Treatment is considered ineffective if patient symptoms and signs worsen, and NYHA classification remains unchanged or deteriorates. The effectiveness rate is calculated as (markedly effective + effective)/total number × 100%. (2) Records and comparisons of heart function indicators before and after treatment for both groups of patients were conducted, including left ventricular ejection fraction (LVEF), left ventricular end-diastolic diameter (LVEDD), and left ventricular end-systolic diameter (LVESD). (3) Comparison of N-terminal pro-brain natriuretic peptide (NT-proBNP) levels before and after treatment for both groups of patients.

Secondary observational indicators: (4) Records and comparisons of the incidence of adverse reactions during treatment for both groups of patients, including hypotension, worsening renal function, hyperkalemia, and exacerbation of heart failure leading to rehospitalization. (5) Assessment of post-treatment quality of life for both groups of patients using the Minnesota Living with Heart Failure Questionnaire (MLHFQ) [10], which includes three domains: physical, emotional, and other. A higher score indicates a poorer quality of life.

Statistical methods

In this study, SPSS20.0 software and GraphPad Prism 8 software were used to process, analyze and visualize the collected data. Between-group and intra-group comparisons of quantitative data were made by the independent sample t test and the paired t test (represented by t), respectively; a chi-square test was used for the analysis of counting data. The significance level has been defined as $P<0.05$.

Results

General information

As can be seen in **Table 1**, the Con and the Obs were not statistically different in gender, age, BMI, and other general data ($P>0.05$), with comparability.

Comparison of therapeutic effects

The number of marked response, response and non-response patients in the Obs was 34, 24, and 2, respectively, compared with 21, 19, and 12 in the Con. The overall response rate in the Obs was 96.67%, which was significantly higher than 76.92% in the Con. See **Table 2** for details.

Comparison of pre- and post-treatment cardiac function indexes

The cardiac function indexes LVEDD, LVESD and LVEF did not differ significantly between the Con and the Obs prior to treatment ($P>0.05$). A reduction in LVEDD and LVE-

Table 1. Comparison of general data

Factors	Observation group (n=60)	Control group (n=52)	t/χ^2	P
Sex			0.082	0.775
Male	33 (55.00)	30 (57.69)		
Female	27 (45.00)	22 (42.31)		
Age (years)	72.8±5.4	72.1±5.2	0.016	0.654
BMI (kg/m^2)			0.001	0.978
≥23	31 (51.67)	27 (51.92)		
<23	29 (48.33)	25 (48.08)		
Smoking history			0.019	0.891
Yes	35 (58.33)	31 (59.62)		
No	25 (41.67)	21 (40.38)		
Drinking history			0.010	0.919
Yes	41 (68.33)	36 (69.23)		
No	19 (31.67)	16 (30.77)		
Educational level			0.084	0.772
Primary school and below	40 (66.67)	36 (69.23)		
Above primary school	20 (33.33)	16 (30.77)		
Diabetes			0.001	0.978
Yes	29 (48.33)	27 (51.92)		
No	31 (51.67)	25 (48.08)		

Table 2. Comparison of curative effects [n (%)]

Group	Marked response	Response	Non-response	Overall response rate
Observation group	34 (56.67)	24 (40.00)	2 (3.33)	58 (96.67)
Control group	21 (40.38)	19 (36.54)	12 (23.08)	40 (76.92)
X^2	0.556		9.928	
P value	0.542		0.002	

SD and an elevation in LVEF were determined in both groups after treatment (P<0.05), with better cardiac function in the Obs than in the Con (P<0.05) (**Figure 2**).

Comparison of pre- and post-treatment NT-proBNP levels

No significant inter-group difference was identified in the pre-treatment NT-proBNP level (P>0.05); but the NT-proBNP level decreased after treatment (P<0.05), with an even lower level in the Obs (P<0.05) (**Figure 3**).

Comparison of the incidence of adverse reactions during treatment

Comparing the adverse reactions between the two groups, it was found that the incidence of adverse reactions was significantly lower in the Obs versus the Con, with statistical significance (P<0.05) (**Table 3**).

Comparison of post-treatment MLHFQ scores

Markedly lower post-treatment QoL scores were determined in the Obs compared with the Con (P<0.05), indicating better QoL in patients treated by rhBNP versus those treated by milrinone (**Table 4**).

Discussion

Heart failure is a common cardiovascular disease in clinical practice, prone to recurrent episodes and associated with a high mortality rate. Clinical investigations have shown that the hospitalization rate for heart failure in cardiovascular diseases is as high as 21%, with an approximate mortality rate of 40%, especially prevalent in the elderly population [11]. Research indicates a significant correlation between the pathogenesis of heart failure and the Renin-Angiotensin-Aldosterone System (RAAS). Current clinical interventions typically

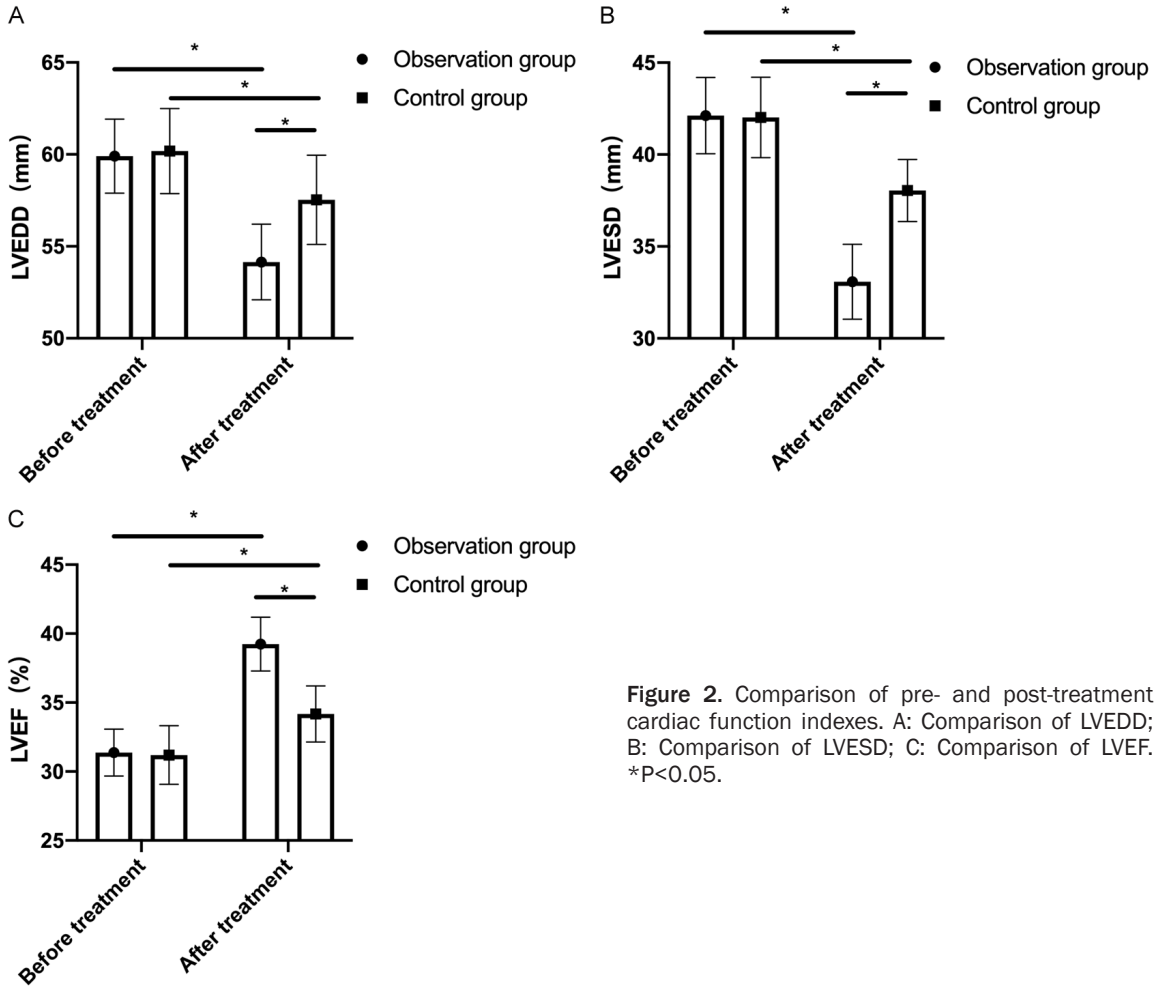

Figure 2. Comparison of pre- and post-treatment cardiac function indexes. A: Comparison of LVEDD; B: Comparison of LVESD; C: Comparison of LVEF. *P<0.05.

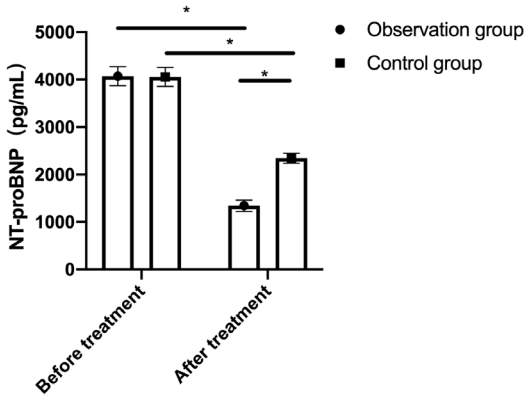

Figure 3. Comparison of pre- and post-treatment NT-proBNP levels. *P<0.05.

involve vasodilators, diuretics, and other medications to alleviate symptoms in patients, but the outcomes are often suboptimal, leading to frequent relapses. Moreover, these treatment methods may exert excessive influence on the sympathetic nervous system, increasing the risk of recurrence [12]. Therefore, the development of novel anti-heart failure drugs is crucial for enhancing efficacy and safety in clinical practice.

The treatment strategies for heart failure are diverse, covering various aspects from medication and lifestyle adjustments to high-tech surgical interventions. In terms of medication, ACE inhibitors, beta-blockers, diuretics, and potassium-sparing agents have become the cornerstone of heart failure treatment. These drugs improve heart function, alleviate symptoms, and prolong survival through different mechanisms. However, even with such standard treatment, not all patients can fully adapt. The effectiveness of drug therapy is influenced by individual differences, comorbidities, and patient compliance, necessitating personalized adjustments and optimization of treatment plans. Therefore, novel drug treatment approaches

Table 3. Comparison of adverse reactions

Curative effect	Observation group (n=60)	Control group (n=52)	χ^2	P
Hypotension	3 (5.00)	2 (3.85)	0.556	0.663
Worsening renal function	1 (1.67)	1 (1.92)	0.443	0.552
Hyperkalemia	1 (1.67)	4 (76.92)	0.760	0.412
Readmission due to heart failure aggravation	2 (3.33)	8 (15.38)	0.654	0.669
Total incidence	7 (11.67)	15 (28.85)	5.209	0.023

Table 4. Comparison of MLHFQ scores after treatment

Classification	Observation group (n=60)	Control group (n=52)	t	P
Physical field	13.18±1.54	15.8±1.35	9.504	<0.001
Emotional field	8.14±0.39	9.9±0.35	24.97	<0.001
Other fields	16.15±0.4	17.92±0.41	23.09	<0.001

hold significant practical significance. Recombinant human brain natriuretic peptide (rBNP) is one of the commonly used anti-heart failure medications in recent years, demonstrating favorable clinical outcomes [13-15]. The results of this study indicate that the overall treatment effectiveness was higher in patients receiving additional rBNP compared to the control group. Additionally, the levels of N-BNP were lower in the observation group, suggesting that the degradation of natriuretic peptides by Neutral Endopeptidase (NEP) plays a role in the diagnosis and prognosis of heart failure. The study also found that NT-proBNP levels, which are not affected by NEP inhibition, can reflect changes in heart function and prognosis. Patients in the observation group showed a more significant improvement in NT-proBNP levels compared to the control group after treatment, consistent with previous research findings [16]. The mechanisms underlying these effects include the ability of rBNP to enhance glomerular filtration rate, regulate fluid balance, and improve cardiac function [17, 18]. Furthermore, rBNP can inhibit the RAAS system, reduce neural activity, and regulate vascular pressure, thereby enhancing peripheral circulation [19-21].

Stable hemodynamics are a crucial factor in triggering BNP secretion, highlighting the importance of monitoring hemodynamics in clinical practice [22]. The results of this study revealed that the improvement in cardiac function and hemodynamic parameters in the observation group was significantly superior to that in the control group, indicating that rBNP not only effectively improves heart failure but also enhances hemodynamic stability in patients. This improvement can be attributed to the activation of protein kinase in vascular endothelium by rBNP, leading to vasodilation without affecting electrolyte balance and improving myocardial ischemia [23]. Quality of life assessment in patients post-treatment is an essential indicator of treatment effectiveness. Both groups of patients in this study showed improved quality of life after treatment, with the observation group exhibiting greater improvement, likely due to significant enhancement in cardiac function post-treatment [24, 25]. Adverse drug reactions are reliable indicators of the safety of drug therapy. Milrinone, as a phosphodiesterase inhibitor, works by increasing the heart's contractility to improve cardiac output, and is widely used in treating cardiovascular diseases such as heart failure. While its therapeutic effects are significant, the associated side effects cannot be overlooked. These side effects mainly include but are not limited to headaches, tachycardia, and blood pressure fluctuations. Among these side effects, some may only be temporary discomfort, while others could have long-term impacts on the patient's health. Let's first delve into the side effect of headaches. Headaches are one of the most common side effects of milrinone, and their occurrence may be related to drug-induced vasodilation. The severity and duration of headaches vary from person to person; they could be mild discomfort or escalate to severe pain, significantly affecting the patient's daily life and work. Next, tachycardia is another side effect of milrinone that cannot be ignored. Tachycardia not only makes patients feel palpi-

tations and unease but can also increase the heart's workload. For patients already dealing with heart issues, this is undoubtedly an added burden. Furthermore, tachycardia could lead to other heart conditions like arrhythmias, and in extreme cases, even cardiac arrest. Milrinone can cause fluctuations in a patient's blood pressure, which may manifest as either an increase or decrease in blood pressure. For patients with originally unstable blood pressure, these fluctuations could pose serious risks such as stroke or heart attacks. Therefore, doctors must closely monitor changes in the patient's blood pressure and adjust the treatment plan promptly when using milrinone. In addition to the aforementioned side effects, milrinone may also trigger other adverse reactions such as nausea, vomiting, allergic reactions, etc. While these side effects are relatively mild, they should not be disregarded as they could impact the patient's adherence to medication and consequently affect the treatment outcomes. The study results did not show statistically significant differences in the occurrence of various complications between groups, possibly due to the relatively small sample size, which may impact the overall incidence rate [26].

Limitations of this study include the small sample size, short observation period, lack of inclusion of heart failure history duration, absence of clinical data on other drug dosages, and uncontrolled confounding factors, necessitating further extensive and long-term research. Additionally, a more comprehensive evaluation of cardiac function parameters would serve as a valuable supplement to the study conclusions. Long-term follow-up results are essential for consolidating the findings of this study. In conclusion, elderly heart failure patients treated with recombinant human brain natriuretic peptide demonstrated improved outcomes, effectively enhancing cardiac function and hemodynamic parameters with good safety profiles, ultimately enhancing patients' quality of life. These findings underscore the potential for clinical application and further research in this field.

In conclusion, elderly patients with heart failure have shown better outcomes after treatment with recombinant human brain natriuretic peptide. This treatment can effectively improve heart failure and hemodynamic parameters with good safety profile, enhancing patients' quality of life. Therefore, it is worth promoting in clinical practice.

Disclosure of conflict of interest

None.

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