Tropical Journal of Pharmaceutical Research December 2023; 22 (12): 2553-2559
ISSN: 1596-5996 (print); 1596-9827 (electronic)

Available online at http://www.tjpr.org
http://dx.doi.org/10.4314/tjpr.v22i12.19

Original Research Article

Efficacy of recombinant human brain natriuretic peptide as an adjuvant therapy for severe heart failure, and its impact on oxidative stress and quality of life in patients

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Sent for review: 23 June 2023 *Revised accepted: 26 November 2023*

Abstract

Purpose: *To evaluate the efficacy of recombinant human brain natriuretic peptide as an adjuvant therapy for severe heart failure, and its effect on oxidative stress and quality of life in patients.*
Methods: *The study was conducted on 100 patients with severe heart failure who met the screening criteria for this study. They were evenly but randomly divided into two groups. Patients in the control group were given routine treatment (diuretics and cardiac stimulants) for severe heart failure, while the study group received recombinant human brain natriuretic peptide adjuvant therapy in addition to the treatment administered to the control group. Cardiac function, heart rate, oxidative stress indicators, quality of life levels, and adverse drug reactions during treatment were compared before and after treatment.*
Results: *After the intervention, the NT-proBNP level in the study group was significantly lower than in the control group while LVEF level was significantly higher than in the control group ($p < 0.05$). Compared with the control group, the study group showed a significant decrease in heart rate ($p < 0.05$). The MDA level of the study group was significantly lower than that of the control group while the SOD and GSH-PX levels were significantly higher than those of the control group ($p < 0.05$). In addition, the GQOLI-74 score of the study group was significantly higher than that of the control group ($p < 0.05$). Furthermore, there was no statistically significant difference in incidence of adverse reaction between control and study groups (14.0 and 16.0 %, respectively, $p < 0.05$).*
Conclusion: *Recombinant human brain natriuretic peptide has a significant therapeutic effect on severe heart failure, thus improving patients' cardiac function, alleviating their oxidative stress state and enhancing their quality of life, and is also safe.*

Keywords: *Severe heart failure, Cardiac function, Recombinant human brain natriuretic peptide, Oxidative stress, Quality of life*

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INTRODUCTION

Heart failure refers to the syndrome of cardiac circulatory disorder resulting from the diastolic dysfunction of the heart. Based on the latest research numbers, there are about 22 million patients suffering from heart failure in the world, including 13 million in China, among which over

700,000 patients are severe cases [1-3]. The primary manifestations of severe heart failure are breathing difficulties and obvious edema of lower extremities, probably accompanied by changes in hemodynamics such as lower blood pressure, faster heart rhythm and arrhythmia. Severe heart failure poses a serious threat to patients' health and quality of life [4]. The best treatment for severe heart failure are heart transplant and an artificial heart. However, because of the limitations of the matching relationship between a donor and a receptor, every year, there are only about 600 cases of heart transplant in China. Most patients lose their survival opportunity when waiting for the donor [5]. The pathogenic mechanism of severe heart failure is complex. The contraction of peripheral blood vessels caused by decreased cardiac output, as well as the reduction of blocked blood flow in the kidneys and heart, are related to the occurrence of diseases. The key to its treatment is to open the infarct related arteries as soon as possible. Thus, theoretically, the application of positive inotropic drugs may alleviate its clinical symptoms [6]. Recombinant human brain natriuretic peptide is a kind of endogenous peptide, and also a kind of polypeptide cardiac neurohormone. It can dilate blood vessels and inhibit the sympathetic nervous system. Previous research have shown that it is effective in the clinical treatment of patients with acute myocardial infarction and heart failure by recovering the patient's heart functions and reducing vascular endothelial injury [7-9]. However, there are few reports about its effect on patients' blood pressure, quality of life and oxidative stress. Therefore, this study treated patients with severe heart failure with recombinant human brain natriuretic peptide on the basis of the conventional treatment, so as to explore its influence on patients' quality of life. The oxidative stress levels, and its effect on dilating vessels, as well as the inhibition of the sympathetic nervous system were evaluated to ascertain its safety.

METHODS

Patients

A total of 100 patients with severe heart failure who were admitted in Shaoxing Central Hospital Medical Alliance General Hospital from February 2022 to December 2022 were selected in this study.

Inclusion criteria

(1) Patients who were diagnosed with severe heart failure according to Practice of Cardiology [10]; (2) Patients whose cardiac functions were classified into Class 2 and Class 3 according to the New York Heart Association (NYHA) [11]; (3) Patients who were tolerant to the drugs in this study; (4) Patients who had complete clinical information and were totally informed of this study and had signed the informed consent form.

Exclusion criteria

(1) Patients who had other severe organ dysfunctions; (2) Patients who couldn't communicate with researchers; (3) Patients with other factors that influenced the results; (4) Patients who had cardiogenic shock; Patients whose heart rate was less than 60 beats/min and systolic blood pressure was less than 90 mmHg; Patients who had heart block of Class II or above; (5) Patients who had heart valve hypertrophy, stenosis or restrictive cardiomyopathy; (6) Patients with abnormal coagulation function, immune system diseases and malignant tumors; (7) Patients who were allergic to all drugs or one of the ingredients used in the study; (8) Patients who had no complete clinical information and were unwilling to sign the informed consent form and refused to participate in the study.

Patient profile and ethical approval

The patients were randomly distributed into two groups - control group and study group. The average age of patients in the control group was (60.45 ± 6.17) years old, with a gender ratio of 27/23. The causes were coronary heart disease in 18 cases, hypertensive heart disease in 7 cases, rheumatic heart disease in 8 cases, and dilated cardiomyopathy in 17 cases. The average age of patients in the study group is (58.20 ± 10.17) years old, with a gender ratio of 29/21. The causes include 16 cases of coronary heart disease, 10 cases of hypertensive heart disease, 6 cases of rheumatic heart disease, and 18 cases of dilated cardiomyopathy. Differences in the basic information of all the patients were not significant and comparable. All procedures performed in this study which involved human participants were approved by the Ethics Committee of Shaoxing Central Hospital Medical Alliance General Hospital (approval no. 2023-020), and complied with the guidelines of 1964 Helsinki Declaration and its later amendments for Ethical Research involving human subjects [12].

Treatments

The control group patients were given routine treatment such as diuretics and cardiac enhancers. After the treatment phase was completed, cardiac function indicators and

inflammatory factor indicators were recorded, and a one-year follow-up was conducted.

First, isosorbide mononitrate (Zhuhai UCB Co. Ltd, specification: 10 ml: 10 mg) was injected intravenously, and the infusion speed was adjusted according to the patient's blood pressure. The duration of treatment was 1 month. Digoxin tablets (Shanghai Sphsine Pharmaceutical Co. Ltd, specification: 0.25 mg) were used as cardiac stimulant and given orally (0.125 mg) once a day for one month if the patients had no side effects. Furosemide injection (Shanghai Harvest Pharmaceutical Co. Ltd, specification: 20 mg) was used as diuretic and injected intravenously, 10 mg/h every day. Water and electrolyte balance was maintained after treatment. If the mean urine volume in 24 h was greater than 2500 ml, the dose of furosemide was reduced or stopped and if the urine volume was still small on the second day, patients receive the original dose. The duration of treatment was 1 month.

For patients in the study group, recombinant human brain natriuretic peptide (Chengdu Rhodiola Pharmaceutical Co. Ltd, specification: 0.5 mg) was given. The first dose was 1.5 ug /kg intravenously. The flow rate was maintained at 0.0075 - 0.0200 ug /kg /min, and the dose was adjusted based on the hemodynamics of the patients. The course of treatment was continued for 1 month if patients had no obvious toxic and side effects.

Evaluation of parameters/indices

Cardiac function

Cardiac function indices before and after treatment including amino terminal brain natriuretic peptide precursor (NT-proBNP) and left ventricular ejection fraction (LVEF) were assessed. Blood pressure was determined while the heart rhythm of the patients during treatment was measured by a heart rate meter. Extract the patient's serum to detect NT proBNP using a dual antibody sandwich ABC-ELISA method. The assay kit is provided by Shanghai Xitang Biotechnology Co. Ltd. LVEF is measured using echocardiography.

Oxidative stress indices

Oxidative stress indices were evaluated and venous blood was collected from each patient in fasting state before and after treatment respectively, and the serum preserved in a refrigerator at -20 ℃. Malondialdehyde (MDA), glutathione peroxidase (GSH-PX), and superoxide dismutase (SOD) levels in the serum were assayed. Both MDA and GSH-PX were determined using colorimetric methods, using an assay kit (Shanghai Yaji Biotechnology Co. Ltd), while SOD evaluated spectrophotometrically with the aid of an assay kit provided by Shanghai Enzymes Biotechnology Co. Ltd.

Prognostic quality of life

A survey questionnaire was used to evaluate the quality of life of patients. The questionnaire is the General Quality of Life Inventory-74 (GQOLI-74), which includes four dimensions: physical function, psychological function, social function, and material life status. The first three dimensions each have 5 factors, the material life dimension has 4 factors, and there is also an overall quality of life factor, totaling 20 factors, The higher the total score, the higher the quality of life.

Statistical analysis

The data obtained were kept in a database. SPSS24.0 was used to analyze the data. Count data are presented as % and tested by χ^2 test while measurement data are presented as mean ± standard deviation (SD) and tested by *t* test. $P < 0.05$ was considered statistically significant.

RESULTS

Cardiac function

The NT-proBNP and LVEF levels are shown in Table 1. Prior to intervention, the cardiac function indices were similar in the two groups were similar and the difference was not statistically significant (t = 0.651, 1.167; p = 0.516, 0.246). The NT-proBNP levels in both groups after intervention were lower than those before intervention, but the level in the study group was significantly lower than in the control group. LVEF levels after intervention were higher than those before intervention, with the values for the study group significantly higher than those of the control group ($p < 0.05$).

Clinical indices

The blood pressure and heart rhythm data of the patients in the two groups are shown in Table 2. Before intervention, the systolic blood pressure, diastolic blood pressure and heart rhythm of the two groups were similar and the difference was not statistically significant (t = 0.106, 1.685, 0.179; p = 0.916, 0.095, 0.858).

Table 1: Comparison of cardiac function indices between two groups of patients (mean ± SD, N = 50)

Group	Time	NT-proBNP (pg/ml)	LVEF (%)
Control	Before intervention	2485.61±388.28	41.15±3.26
	After intervention	1244.40±174.26	52.23±6.88
Study	Before intervention	2534.70±365.02	40.35±3.56
	After intervention	956.43±121.06	59.28±4.28
t-value		9.597	6.156
P-value		0.000	0.000

Table 2: Comparison of clinical indices (mean ± SD, N = 50)

Group	Time of intervention	Systolic blood pressure (mmHg)	Diastolic blood pressure (mmHg)	Heart rhythm (beats/min)
Control	Before	139.04±12.87	94.87±7.17	92.71±2.99
	After	130.16±9.72	85.53±8.66	80.59±1.45
Study	Before	139.35±16.46	92.50±6.90	92.60±2.96
	After	126.23±11.88	82.54±7.18	71.30±1.78
t-value		1.814	1.875	28.634
P-value		0.073	0.064	0.000

Table 3: Comparison of oxidative stress indices (mean ± SD, N = 50)

Group	Time of intervention	MDA	SOD	GSH-PX
Control	Before	7.14±0.95	83.52±6.47	99.50±12.90
	After	6.31±0.73	92.74±7.16	108.35±16.06
Study	Before	7.33±0.91	84.60±6.63	100.89±12.13
	After	4.63±0.82	116.28±8.96	139.84±19.72
t-value		10.856	14.523	9.252
P-value		0.000	0.000	0.000

The 3 indices of the patients after intervention were lower than those before intervention. Systolic blood pressure and diastolic blood pressure of the study group were lower than those of the control group but the differences were not significant ($p < 0.05$). However, heart rhythm was significantly lower ($p < 0.05$).

Oxidative stress indices

Oxidative stress indices are shown in Table 3. The differences between MDA, SOD and GSH-PX levels in the two groups before intervention were not significant (t =1.050, 0.827, 0.558, p = 0.296, 0.410, 0.578). However, the MDA level of the two groups after intervention were lower than before intervention, while the SOD and GSH-PX levels were higher. The MDA level of the study group was significantly lower than that of the control group, while SOD and GSH-PX levels were significantly higher.

Quality of life

The differences between the scores of GQOLI-74 that patients in two groups got before intervention were not statistically significant (t=0.735, p=0.464). However, the of GQOLI-74 scores in both groups were significantly higher ($p < 0.05$) after intervention than those before intervention.

Table 4: Comparison of quality of life among the groups (mean ± SD, N = 50)

Group	Time of intervention	GQOLI-74 (point)
Control	Before	41.49±5.95
	After	62.88±6.32
Study	Before	40.67±5.22
	After	71.98±4.88
t-value		8.050
P-value		0.000

Adverse reactions

Among the 50 patients in the control group, 7 patients (14.0 %) had adverse reactions while 8 patients (16%) in the study group experienced adverse reactions. However, the difference was not statistically significant ($p > 0.05$).

Table 5: Comparison of adverse reactions among the two groups {N (%)}

Group	Cardiac death	Ventricular tachycardia	Severe arrhythmia	Second heart failure	Total adverse reaction (%)
Control	1 (2.00)	2 (4.00)	1 (2.00)	3 (6.00)	14.0
Study	2 (4.00)	3 (6.00)	1 (2.00)	2 (4.00)	16.0
χ^2 value					0.078
P-value					0.779

DISCUSSION

Severe heart failure is the end state of many cardiovascular diseases such as cardiomyopathy and coronary heart disease [13]. Clinical studies have found that with the increase in the aging population, people are facing a higher risk of heart failure and a more challengeable treatment method [14]. Besides, in daily life, increasing work pressure, changes in living habits and diet are risk factors of heart failure [15].

Severe heart failure is harmful, complicated and difficult to treat. If patients are not given appropriate treatment in time, it will lead to the organ dysfunction. Exacerbated heart failure is often fatal, which is not conducive to its prognosis. Therefore, this study focused on finding effective treatment plans [16]. Drug therapy is a conventional treatment plan and though progress has been made in drug therapy in recent clinical practice, its curative effect is still not satisfactory. The key to its treatment is to reduce the mortality of the disease by opening the infarct artery as soon as possible, saving the dying myocardia, preventing remodeling of the left ventricular, and improving patients' cardiac function [17].

Previous studies have shown that the rising level of NT-proBNP of patients with severe heart failure indicates the lack of endogenous B-type natriuretic peptide. Thus, exogenous B-type natriuretic peptide should be given to these patients [18]. Recombinant human brain natriuretic peptide is a new biologic drug with the same therapeutic effect as B-type urinary natriuretic peptide. It mainly regulates hemodynamics by activating vascular endothelial protein kinase so as to promote vasodilation. Previous studies have proven that it is effective in treating myocardial infarction and other diseases [19,20].

By comparing conventional treatment and conventional treatment combined with recombinant human brain natriuretic peptide, this study found that NT-proBNP, LVEF, heart rate and other cardiac function indices of patients who had recombinant human brain natriuretic peptide were significantly improved compared to those of patients who only received conventional treatment. Their systolic and diastolic blood pressures improved as well, but the degree of improvement was not significantly different from that of the control group. Overall, the results indicate that recombinant human brain natriuretic peptide improves patients' cardiac functions and this result is in lines with previous studies[21]. The reason may be related to the fact that recombinant human brain natriuretic peptide selectively dilates pulmonary capillaries and pulmonary veins and reduces the resistance and pressure of pulmonary circulation [22,23].

Previous studies have found that oxygen free radicals are generated during myocardial ischemia re-perfusion, consuming large amounts of SOD and GSH-PX and increasing the MDA levels. Thus, the patient is obviously in a state of oxidative stress which greatly affects the incidence and development of the disease [24]. The present study indicate that both treatments alleviated the state of oxidative stress. However, patients who were treated with recombinant human brain natriuretic peptide showed better indices, indicating that recombinant human brain natriuretic peptide control the state of oxidative stress of patients with severe heart failure. It is related to the fact that this drug can reduce oxygen radicals and suppress the release of stress hormones, effectively protecting the cardiac muscles [25].

In order to determine the influence of the combination treatment on patients' quality of life, the GQOLI-74 scores of that patients in the two groups were compared. The results showed that the scores for the study group were significant higher, indicating that the drug may improve patients' quality of life and their prognosis.

Finally, by comparing the adverse reactions in the two groups, this study found that there was no significant difference in adverse reactions between patients who were treated with conventional treatment and recombinant human brain natriuretic peptide and patients who were only treated with conventional treatment. Thus, the combination treatment seems safe for patients.

CONCLUSION

Recombinant human brain natriuretic peptide improves the clinical ameliorates of patients with severe heart failure such as cardiac dysfunction and heart rhythm problem, improve patients' quality of life and prognosis, and is relatively safe. Its mechanism of action may be related to the fact that it control patients' state of oxidative stress, alleviates the damage from oxidative stress, and enhances patients' antioxidant capacity. However, this study was relatively limited by the small sample size and limited content. In the future, more patients should be enrolled into this study, the follow-up visits extended, and the research content expanded to further investigate the mechanism of action of recombinant human brain natriuretic peptide.

DECLARATIONS

Acknowledgements

None provided.

Funding/Sponsorship

This work was supported by Medical and Health Self financing Technology Plan Project in Keqiao District, Shaoxing City, Zhejiang Province. (Grant No. 2021KZ43).

Conflict of Interest

No conflict of interest associated with this work.

Contribution of Authors

We declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by the authors. Yanping Zeng designed the study and carried them out; Yanping Zeng, Weixing Ma, Hua Xue, Cheng Ma, Yan Wang, Xiaohui Ren, Zhenhua Jiang supervised the data collection, analyzed and interpreted the data; Yanping Zeng prepared the manuscript for publication and reviewed the draft of the manuscript. All authors read and approved the manuscript for publication.

Ethical Approval

This study was approved by the Ethics Committee of Shaoxing Central Hospital Medical Alliance General Hospital (approval no. 2023-020).

Availability of Data and Materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

*Use of Artificial Intelligence/*Large Language Models

None provided.

Use of Research Reporting Tools

None provided.

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