Effect of recombinant human brain natriuretic peptide on patients with non-ST segment elevation acute coronary syndrome

Wubin Wu
LiZhi Liu
Jiacai Chen

Wubin Wu Department of Cardiovascular, Fenghua People's Hospital of Ningbo City of Zhejiang Province, China, LiZhi Liu Department of Cardiovascular, Fenghua People's Hospital of Ningbo City of Zhejiang Province, China, Jiacai Chen Department of Cardiovascular, Fenghua People's Hospital of Ningbo City of Zhejiang Province, China, * Corresponding author:Wubin Wu, Email: 2889689365@qq.com*

Objective: To investigate the effect of recombinant human brain natriuretic peptide on patients with non-ST segment elevation acute coronary syndrome. Methods: 80 patients with non-ST segment elevation acute coronary syndrome diagnosed and treated in our hospital from January 2017 to December 2019 were randomly divided into study group (n = 41) and control group (n = 39). All patients were treated with basal therapy, the control group was treated with isosorbide dinitrate, and the study group was treated with recombinant human brain natriuretic peptide on the basis of the control group. The changes of cardiac function indexes, renal function indexes and hemodynamic parameters before and after treatment were observed and compared between the two groups. Results: The total effective rate of the study group was 87.80%, which was significantly higher than that of the control group (69.23%) (P<0.05). There was no significant difference in left ventricular end-diastolic dimension (LVEDD), left ventricular end-systolic dimension (LVESD) and left ventricular ejection fraction (LVEF), hemodynamic parameters' cardiac index (CI), central venous pressure (CVP), mean arterial pressure (MAP), systemic vascular resistance index (SVRI) and glomerular filtration rate (eGFR) between the two groups before treatment (P>0.05). After treatment, LVEDD, LVESD and SVRI were all decreased than that before treatment in the two groups, LVEF, CI, CVP, MAP and eGFR were higher than those before treatment (P<0.05), and LVEDD, LVESD and SVRI in the study group were lower than those in the control group, and LVEF, CI, CVP, MAP and eGFR were higher than those in the control group (P<0.05). Conclusion: Recombinant human brain natriuretic peptide is effective in the treatment of non-ST segment elevation acute coronary syndrome, which is beneficial not only for the recovery of cardiac function, but also for the improvement of hemodynamic status and renal function.

Key words: Recombinant human brain natriuretic peptide; Non-ST segment elevation acute coronary syndrome; Hemodynamics; Renal function
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Acute coronary syndrome (ACS) refers to a series of clinical syndromes caused by acute or subacute myocardial ischemia caused by unstable plaque rupture and thrombosis of coronary arteries, which are mainly divided into ST-segment elevation type and non-ST segment elevation type. Non-ST segment elevation acute coronary syndrome is more common in clinic, has the characteristics of high incidence, rapid disease progression and poor prognosis, and seriously endangers human health [1-3]. Therefore, early standardized and effective treatment of patients with non-ST segment elevation acute coronary syndrome is of paramount importance, which can effectively improve the prognosis of patients and reduce the occurrence of adverse cardiovascular events. At present, anti-myocardial ischemia drugs and β-receptor blockers are commonly used in clinical treatment of this disease to improve myocardial ischemia and relieve clinical symptoms of patients, but their efficacy is poor [4]. Recombinant human brain natriuretic peptide is a biological product synthesized by gene

recombination technology and has the same mechanism of action and biological activity as endogenous brain natriuretic peptide (produced by ventricular muscle) [5]. It has been found that [6, 7] recombinant human brain natriuretic peptide is effective in blocking ventricular remodeling and restoring cardiac function. However, the efficacy of this drug in combination with isosorbide dinitrate in the treatment of non-ST segment elevation acute coronary syndromes has not been reported. Based on this, this study focuses on the effects of recombinant human brain natriuretic peptide on hemodynamics and renal function in patients with non-ST segment elevation acute coronary syndromes and reports the following results:

ATA AND METHODS

Clinical data

From January 2017 to December 2019, 80 patients with non-ST segment elevation acute coronary syndrome were selected as study objects, and randomly divided into study group (n = 41) and control group (n = 39) by random number table method. There was no significant difference in gender, age, course of disease, body mass index, combined underlying disease and blood lipid index between the two groups (P>0.05), showing comparability.

Table 1.
Comparison of general data between the two groups ($\bar{x} \pm s$)

Group	Number of cases	Gender (M / F)	Age (years old)	Duration of disease (d)	Body mass index (kg/m^2)	Hypertension (case)	Diabetes (case)	Total cholesterol (mmol/L)	Triacylglycerol (mmol/L)	Low density lipoprotein cholesterol (mmol/L)	High density lipoprotein cholesterol (mmol/L)
Control group	39	21/18	64.21±6.87	2.57±0.79	22.85±2.51	21	15	4.79±0.75	2.11±0.38	3.27±0.71	1.22±0.37
Study group	41	23/18	63.47±7.01	2.64±0.82	22.67±2.63	24	16	4.86±0.81	2.16±0.33	3.36±0.65	1.17±0.34
χ^2		0.041	0.477	0.389	0.313	0.179	0.003	0.401	0.629	0.592	0.630
P		0.840	0.635	0.699	0.755	0.673	0.959	0.690	0.531	0.556	0.531

Inclusion criteria and exclusion criteria

Inclusion criteria: ① Patients met relevant diagnostic points in the "Guidelines for the Diagnosis and Treatment of Non-ST-Segment Elevation Acute Coronary Syndrome"[8] and were diagnosed; ② None of the patients received coronary intervention; ③ Patients were able to tolerate the drugs used in this study; ④ Patients with good compliance and complete cooperation in treatment; ⑤ Patients with complete clinical data. This study complies with the principles of informed consent, voluntary participation, and has been approved and supported by the hospital ethics committee.

Exclusion criteria: ① Cardiogenic shock; ② Patients with malignant tumor, severe infectious disease or immune system disease; ③ Patients with severe hepatic and renal insufficiency or patients requiring mechanical ventilation; ④ Patients with surgical operation or trauma history in the past month; ⑤ Patients with severe / acute cerebrovascular disease or severe hypotension; ⑥ Patients with mental disease; ⑦ Patients with contraindications to the use of this study drug.

Treatment methods

After admission, patients in both groups received lipid regulation, conventional anticoagulation, anti-platelet aggregation, anti-arrhythmia, diuresis and other basic treatments including β-receptor blocker and angiotensin receptor inhibitor. Patient with hypertension and diabetes were also given symptomatic treatment.

Patients in the control group were treated with isosorbide dinitrate (specification: 5mg/5mL, approval No.: GYZZ H10960036, manufacturer: Qilu Pharmaceutical Co., Ltd.) on the basis of basic treatment. Isosorbide dinitrate was intravenously infused at a rate of 10 μg/min, then the infusion rate was adjusted to be within 10 ~ 100 μg/min, and the intravenous infusion was maintained for 72h.

The study group was treated with recombinant human brain natriuretic peptide (specification: 0.5 mg, approval document No.: GYZZ: S20050033,

manufacturer: Chengdu Nuodikang Biopharmaceutical Co., Ltd.) on the basis of the control group. First, the drug was injected intravenously at a loading dose of 1.5 μg/kg, and the drug was administered within 1-2 min, followed by intravenous drip at a rate of 0.0075 g/(kg · min) for 72h.

Observational indexes

① Efficacy [9]: According to the specific situation of the patient after treatment, the clinical symptoms and physical signs of the patient disappeared completely, or the frequency and duration of angina pectoris episodes were reduced by more than 75%, and the ischemic changes (ST segment depression) in ECG were alleviated. Effective: The patient's clinical symptoms and signs were relieved, the times and duration of angina attack were less than 75% or more than 50%, and ECG showed no change. Ineffective: The patient's clinical symptoms and signs were not relieved or even aggravated, or the number and duration of angina attack was less than 50% or increased by less than 50%, and the ST segment of ECG showed no change. Ineffective: The patient's clinical symptoms and signs were not relieved or even aggravated, or the times and duration of attack were more than 50%, and the ischemic changes in ECG were aggravated. Total effective rate = (number of effective cases + number of effective cases) / total number of cases × 100%.

② Cardiac function indexes: Cardiac function in 2 groups before and after treatment was measured and evaluated by ECG and Doppler ultrasound, including left ventricular end-diastolic dimension (LVEDD), left ventricular end-systolic dimension (LVESD) and left ventricular ejection fraction (LVEF).

③ Hemodynamics: Right internal jugular vein puncture was performed in the two groups before and after treatment. The changes of hemodynamic parameters including cardiac index (CI), central venous pressure (CVP), mean arterial pressure (MAP) and systemic vascular resistance index (SVRI) before and after treatment were monitored.

④ The indexes of renal function: 3 mL of fasting peripheral venous blood was collected before and after treatment in the two groups, the upper serum was retained after centrifugation, and the serum creatinine content of the patients was determined. The modified simplified MDRD equation [10] was used to estimate the glomerular filtration rate (eGFR) before and after treatment.

Statistical processing

SPSS 25.0 was used to analyze and process the study data. The measurement data were expressed in the form of ($\bar{x} \pm s$), and t-test was performed. The enumeration data were expressed in percentage (%), and chi-square test was performed. $P<0.05$ was used to indicate that the difference had statistical significance.

RESULTS

Comparison of efficacy between the two groups

The total effective rate of the study group was 87.80%, which was significantly higher than that of the control group (69.23%). The difference between the two groups had statistical significance ($P<0.05$). See Table 1 for details.

Table 1.
Efficacy comparison between the two groups [n (%)]

Group	Number of cases	Produce effect	Effective	Ineffective	Total effective rate
Control group	39	14（35.90）	13（33.33）	12（30.77）	27（69.23）
Study group	41	20（48.78）	16（39.02）	2（12.20）	36（87.80）
χ^2		-	-	-	4.121
P		-	-	-	0.042

Comparison of cardiac function indexes before and after treatment in the two groups

Before treatment, there was no significant difference in LVEDD, LVESD and LVEF between the two groups ($P>0.05$). After treatment, LVEDD and LVESD in the two groups were lower than those before treatment, LVEF was higher than that before treatment ($P<0.05$). After treatment, LVEDD and LVESD in the study group were much lower than those in the control group, LVEF was much higher than that in the control group ($P<0.05$). See Table 2.

Comparison of changes of hemodynamic parameters before and after treatment in the two groups

Before treatment, there was no significant difference in CI, CVP, MAP and SVRI between the two groups (P>0.05). Compared with those before treatment, CI, CVP and MAP were significantly increased and SVRI significantly decreased in both groups (P<0.05). After treatment, CI, CVP and MAP in the study group were significantly higher and SVRI significantly lower than that in the control group (P<0.05). See Table 3.

Table 2.
Comparison of cardiac function indicators before and after treatment in the two groups ($\bar{x}\pm s$)

Group	Number of cases	LVEDD (mm)		LVESD (mm)		LVEF (%)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control group	39	58.12±5.46	50.78±5.23$^{\#}$	46.74±4.77	40.02±4.35$^{\#}$	42.78±5.13	48.24±6.10$^{\#}$
Study group	41	58.33±5.62	45.65±4.96$^{*\#}$	46.67±4.85	34.26±4.11$^{*\#}$	43.26±5.24	54.13±6.23$^{*\#}$

Note: Compared with control group, *P<0.05; compared with the same group before treatment, $^{\#}$P<0.05.

Table 3.
Comparison of changes of hemodynamic parameters before and after treatment in the two groups ($\bar{x}\pm s$)

Group	Number of cases	CI (L·min^{-1}·m^{-2})		CVP (mmHg)		MAP (mmHg)		SVRI (dyn·s·m^{2}·cm^{-5})	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control group	39	2.56±0.51	3.13±0.62$^{\#}$	5.04±1.24	6.26±1.17$^{\#}$	65.14±5.48	76.34±6.35$^{\#}$	3322.24±138.65	2267.64±124.25$^{\#}$
Study group	41	2.60±0.55	3.78±0.74$^{*\#}$	5.10±1.33	7.38±1.41$^{*\#}$	65.23±5.32	83.15±7.01$^{*\#}$	3306.15±142.03	1512.20±119.87$^{*\#}$

Note: Compared with control group, *P<0.05; compared with the same group before treatment, $^{\#}$P<0.05.

Comparison of renal function indexes between the two groups before and after treatment

Before treatment, there was no significant difference in eGFR between the two groups (P>0.05); compared with that before treatment, eGFR increased in both groups after treatment (P<0.05); and eGFR in the study group after treatment was significantly higher than that in the control group (P<0.05). See Table 4.

Table 4.
Comparison of renal function indicators before and after treatment in the two groups of patients ($\bar{x}\pm s$)

Group	Number of cases	eGFR		*t* value	*P* value
		Before treatment	After treatment		
Control group	39	68.24±8.67	77.41±11.02	4.084	0.000
Study group	41	68.53±9.10	86.79±12.34	7.626	0.000
t value		0.146	3.579	———	———
P value		0.884	0.001		

DISCUSSION

With the change of diet structure, life style and aging of population, the incidence rate of non-ST segment elevation acute coronary syndrome has been increasing year by year. It is also the main cause of heart failure and cardiogenic shock in clinical practice. Serious cases can induce death and greatly threaten the life safety of patients [11,12]. Clinical treatment of this disease is based on the principle of alleviating the symptoms of myocardial ischemia, stabilizing plaque and preventing thrombosis as soon as possible, aiming at reducing the occurrence of complications and mortality [11].

Clinically, vasodilators such as nitroglycerin and isosorbide dinitrate are commonly used to relax vascular smooth muscle, dilate arteriovenous and

reduce cardiac load, thus reducing myocardial oxygen consumption and relieving myocardial ischemia symptoms, but the therapeutic effect is poor [4]. In patients with non-ST segment elevation acute coronary syndromes, excessive activation of the renin-angiotensin-aldosterone system (RAAS system) and the sympathetic nervous system results in increased ventricular filling pressure and decreased cardiac function[4,13]. Brain natriuretic peptide is a compensatory cardioprotective factor produced by the human body, mainly distributed in the heart, with multiple functions such as diuresis, natriuresis, regulation of blood pressure and blood volume balance, vasodilation, and inhibition of RAAS system and sympathetic nervous system activity [14-16]. Clinical studies have shown that treatment with isosorbide dinitrate combined with recombinant human brain natriuretic peptide in patients with acute myocardial infarction complicated with heart failure can significantly improve clinical efficacy, improve cardiac function and reduce adverse reactions, with satisfactory results [17].

In this study, the total effective rate after treatment in the study group was significantly higher than that in the control group, suggesting that recombinant human brain natriuretic peptide can improve the therapeutic effect, relieve clinical symptoms and improve cardiac function in patients with non-ST segment elevation acute coronary syndrome on the basis of isosorbide dinitrate treatment. After treatment, the levels of LVEDD, LVESD and SVRI of the two groups were decreased, LVEF, CI, CVP and MAP were increased, and the levels of LVEDD, LVESD and SVRI in the study group were much lower than those in the control group. The levels of LVEF, CI, CVP and MAP in the study group were much higher than those in the control group. The results indicated that recombinant human brain natriuretic peptide therapy could effectively improve hemodynamics and restore cardiac function in patients as soon as possible. Because recombinant human brain natriuretic peptide is a synthetic exogenous brain natriuretic peptide, its amino acid sequence is the same as that of endogenous brain natriuretic peptide. Therefore, supplementation of exogenous brain natriuretic peptide can not only balance arterio-venous vasodilation, reduce vascular systemic resistance and improve hemodynamics, but also effectively inhibit activation of RAAS system and sympathetic nervous system and protect patients' cardiac function. Therefore, hemodynamic and cardiac function indicators can be restored to normal levels as soon as possible [18]. After treatment, eGFR in both groups was higher than that before treatment, and eGFR in the study group was significantly higher than that in the control group after treatment, indicating that treatment with recombinant human brain natriuretic peptide can enhance the glomerular filtration and protect the renal function of patients.

In conclusion, recombinant human brain natriuretic peptide has a good effect in the treatment of non-ST segment elevation acute coronary syndrome, can effectively improve the patient's hemodynamics and protect the patient's heart and kidney function, and has the value of being widely applied in clinical practice. However, due to the small number of study objects included in the study, there are some deficiencies in the results. More objective observation indicators and sample size should be included in the subsequent study for confirmation.

REFERENCES

1. Sun Yazhao, Sun Dongxu, Huang Shutian. Application of platelet-lymphocyte ratio in the evaluation of acute coronary syndrome[J]. Chinese Journal of Prevention and Control of Chronic Diseases, 2019, 27 (3): 231-233.
2. Wong DTL. Plaque characterization by coronary computed tomography angiography and association with acute coronary syndrome[J]. J Am Coll Cardio, 2016, 67(4):458-459.
3. Liu Yong, Liu Yanli, Mo Songliu, et al. Comparison of Effects of Different Doses of Atorvastatin in the Treatment of Non-ST-Segment Elevation Acute Coronary Syndrome[J]. Chinese Journal of Clinical New Medicine, 2019, 12 (10): 1071-1074.
4. Zheng Zhigang, Duan Baomin, Chen Lantao. The effect of freeze-dried recombinant human brain natriuretic peptide on senile acute NSTEMI complicated with acute left heart failure and its hemodynamic parameters[J]. Practical Integrated Traditional and Western Medicine Clinics, 2018, 18 (1): 10-11.
5. Feng Junpeng, Liang Meifang, Wang Youheng, et al. Effect of Tanshinone IIA Sodium Sulfonate Combined with Recombinant Human Brain Natriuretic Peptide on Myocardial Infarction, Improvement of Cardiac Function and Prognosis[J]. Drug Evaluation Research, 2019, 42 (8): 1576-1579.
6. Wu Qiong, Chen Huanzhen, Gai Wanli. Effect of recombinant human brain natriuretic peptide in treatment of acute myocardial infarction complicated with heart failure[J]. Chinese Journal of Cardiovascular

Medicine, 2019, 24 (3): 250-253.
7. Li Ruina. Efficacy and prognosis of recombinant human brain natriuretic peptide in patients with acute myocardial infarction complicated with cardiogenic shock[J]. Anhui Medical Journal, 2019, 23 (4): 696-699.
8. Chinese Society of Cardiology, Editorial Committee of Chinese Journal of Cardiovascular Diseases. Guidelines for the Diagnosis and Treatment of Non-ST-Segment Elevation Acute Coronary Syndrome (2016) [J]. Chinese Journal of Cardiovascular Diseases, 2017, 45 (5): 359-376.
9. Du Yuming. Comparative Study of Nitroglycerin and Recombinant Human Brain Natriuretic Peptide in the Treatment of Acute Non-ST Segment Elevation Myocardial Infarction Complicated with Heart Failure[J]. Hebei Medical Journal, 2012, 18 (5): 579-579.
10. Ren Li, Zhang Congli, Pan Yan, et al. Correlation between estimated glomerular filtration rate and pathological damage of IgA nephropathy by modified simplified MDRD equation[J]. Journal of Bengbu Medical College, 2019, 44 (7): 908-910.
11. De Rosa R, Palmerini T, De Servi S, et al. High on-treatment platelet reactivity and outcome in elderly with non-ST-segment elevation acute coronary syndrome - Insight from the GEPRESS study[J]. Int J Cardiol, 2018, 259(1):20-25.
12. Rodriguez F, Mahaffey KW. Management of patients with NSTE-ACS: a comparison of the recent AHA/ACC and ESC guidelines[J]. J Am Coll Cardiol, 2016, 68(3): 313-321.
13. Zheng Fang, Wang Qin, Dong Shimin, et al. The effect of intravenous injection of recombinant human brain natriuretic peptide on ventricular remodeling in patients with acute coronary syndrome[J]. Hebei Medical Journal, 2010, 32 (23): 3272-3275.
14. Han Peng, Xu Jirui, Wang Jizheng. Effect of recombinant human brain natriuretic peptide on ventricular remodeling and cardiac function in patients with middle and high risk acute coronary syndrome[J]. Shandong Medical Journal, 2015, 55 (2): 56-58.
15. Liu Jichao, Liu He. Effect of isosorbide dinitrate combined with freeze-dried recombinant human brain natriuretic peptide on myocardial deformation and cardiac function after PCI in patients with acute anterior myocardial infarction[J]. Modern Journal of Integrated Traditional Chinese and Western Medicine, 2017, 26 (4): 409-411.
16. Zhao Shaohui, Niu Xiaolong, Xiao Hua. Application of freeze-dried recombinant human brain natriuretic peptide combined with tirofiban in patients with acute ST-segment elevation myocardial infarction after PCI[J]. Medical Theory and Practice, 2020, 33 (1): 39-40.
17. Chen Qi, Li Na, Liu Hengliang. Clinical study of recombinant human brain natriuretic peptide combined with isosorbide dinitrate in patients with acute myocardial infarction complicated with heart failure[J]. Internal Medicine, 2019, 14 (6): 699-701.
18. Du Yuming. Comparative Study of Nitroglycerin and Recombinant Human Brain Natriuretic Peptide in the Treatment of Acute Non-ST-Segment Elevation Myocardial Infarction Complicated with Heart Failure[J]. Hebei Medical Journal, 2012, 18 (5): 579-582.