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The effects of prophylactic intravenous injection of rhBNP on prognosis in patients with STEMI undergoing PPCI

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ABSTRACT

This experiment was carried out to observe the application value of recombinant human brain natriuretic peptide (rhBNP) in patients with ST-segment elevation myocardial infarction (STEMI) by primary percutaneous coronary intervention (PPCI), to provide reference for the future treatment of STEMI. In this study, we selected STEMI patients who underwent PPCI treatment in our hospital from October 2019 to December 2021 were selected as the study subjects, of which 46 received intravenous injections of rhBNP (research group), and 36 STEMI patients underwent PPCI (control group). There was no difference in clinical efficacy between the two groups (P>0.05). After treatment, high-sensitivity cardiac troponin I (hs-cTnI), creatine kinase-MB (CK-MB) and plasma N-terminal pro-BNP (NT-proBNP) levels decreased in both groups, with the research group lower than the control group; cardiac output (CO), cardiac index (CI) and mean arterial pressure (MAP) of the research group were lower than the control group's (P<0.05). The left ventricular ejection fraction (LVEF) in the research group was higher than that in the control group at 1 week and 1 month after treatment, while left ventricular end-diastolic diameter (LVEDD) and left ventricular end-systolic diameter (LVESD) were lower than those in the control group (P<0.05). There was also no difference in the rate of prognostic risk events between the two groups at 6 months of follow-up (P>0.05). Combining the results of these experiments above, we believe that the intravenous injection of rhBNP in STEMI patients undergoing PPCI treatment can improve cardiac function and promote the recovery of hemodynamics.

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Introduction

Myocardial infarction (MI) remains one of the leading causes of death from cardiovascular diseases, including non-ST-segment elevation MI (NSTEMI) and ST-segment elevation MI (STEMI) (1). STEMI accounts for approximately 60-80% of all MIs, posing a greater threat (2). Statistics show that the incidence of STEMI is increasing annually; in 2018, the number of new STEMI cases in China alone exceeded 500,000 (3). Thrombolytic therapy and interventional therapy are the main strategies for the clinical treatment of STEMI, and it is advocated that patients undergo primary percutaneous coronary intervention (PPCI) within 12 hours of onset to effectively ensure their safety (4). However, some STEMI patients still experience adverse events such as heart failure or cardiogenic shock during PPCI treatment due to ineffective reperfusion of myocardial cells, resulting in poor prognosis (5).

Recombinant human brain natriuretic peptide (rhBNP) is a derivative of brain natriuretic peptide (BNP) that effectively improves myocardial ischemia, has diuretic and sodium excretion-promoting effects, and can significantly alleviate symptoms such as dyspnea in patients (6). It has been proven to be effective in the treatment of patients with acute heart failure in clinical practice (7, 8). In patients with STEMI, MI is usually a high-risk complication that is difficult to avoid, and previous studies have repeatedly demonstrated that myocardial ischemic necrosis and activation of the renin-angiotensin-aldosterone system (RAAS system) occur after STEMI, only to varying degrees in different patients (Wang et al., 2022). We hypothesize that its prophylactic use in STEMI patients undergoing PPCI may reduce the occurrence of adverse events or complications such as heart failure and improve the prognosis of STEMI patients after PPCI treatment. However, no studies have confirmed our conjecture yet.

Therefore, this study aims to observe and analyze the impact of prophylactic intravenous injection of rhBNP on the short-term prognosis of STEMI patients undergoing PPCI, providing more research support for future clinical treatment.

Materials and Methods

Data collection

With the approval of our hospital's ethics committee, 82 STEMI patients who underwent PPCI treatment in our hospital from October 2019 to December 2021 were selected as the subjects of this study. Among them, 46 STEMI patients received intravenous injections of rhBNP before PPCI treatment (research group), and the other 36 STEMI patients underwent PPCI treatment (control group). All study subjects were informed about the study and signed informed consent forms.

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Inclusion and exclusion criteria

Inclusion criteria: Patients met the diagnostic criteria for STEMI (9), were experiencing their first episode, had an onset time of <12 hours, underwent PPCI treatment at our hospital's emergency department within 12 hours of symptom onset, had complete medical records, and demonstrated high compliance. Both groups of patients were informed and participated in this study. Exclusion criteria: Patients who had recently undergone major surgery or had significant diseases, patients with severe liver or kidney abnormalities, patients with thrombocytopenia or those intolerant to antiplatelet drug therapy, patients with atrial fibrillation, patients with recurrent infarction at the original site, patients undergoing thrombolytic therapy, patients with chronic heart failure before STEMI onset, and patients without normal communication abilities or those who were transferred to another hospital during treatment.

Treatment methods

In the research group, rhBNP (Chengdu NuoDikang Biopharmaceutical Co., Ltd.) was administered 5 minutes before PPCI, with an initial bolus dose of 1.5 μg/kg intravenously, followed by a maintenance intravenous infusion of 0.0075-0.03 μg/kg/min until 5 days after PPCI. In the control group, nitroglycerin (Guangzhou Baiyunshan-Mingxing Pharmaceutical Co., Ltd.) was administered at 10-100 μg/min intravenously 5 minutes before PPCI until 5 days after PPCI. After surgery, both groups adhered to regular antiplatelet aggregation, anti-inflammatory lipid regulation, and angiotensin-converting enzyme inhibitor, β-blocker, and other conventional drug treatments.

Clinical efficacy evaluation

Referring to the MI treatment guidelines (10), the clinical efficacy was categorized as follows: Significant effect: After treatment, the patient's heart rate is normal, physical activity is not limited, mild pulmonary rales and dyspnea symptoms are present, and heart function improves by more than 2 levels. Effective: After treatment, the patient has no significant discomfort at rest, physical activity is limited to some extent, mild pulmonary rales and dyspnea symptoms are present, and heart function improves by 1 level. Ineffective: After treatment, the patient's indicators do not meet the above criteria or worsen. The total efficacy rate (significant effect + effective)/total number of patients × 100%.

Observation indicators

Venous blood samples were collected from patients immediately before treatment (upon admission) and after treatment (1 week after treatment). Plasma and serum were separated by centrifugation, and serum high-sensitivity cardiac troponin I (hs-cTnI), creatine kinase-myocardial band (CK-MB), and plasma N-terminal pro-BNP (NT-proBNP) levels were measured. Hemodynamic monitoring was used to observe cardiac output (CO), cardiac index (CI), and mean arterial pressure (MAP) after treatment. Echocardiography was performed 1 week and 1 month after PPCI to measure left ventricular ejection fraction (LVEF), left ventricular end-diastolic diameter (LVEDD), and left ventricular end-systolic diameter (LVESD). Prognosis was followed up for 6 months through regular checkups, and the incidence of risk events, such as recurrent heart failure, cardiac death, and other adverse reactions, was recorded for both groups.

Statistical methods

SPSS 25.0 software was used for statistical analysis. Count data were expressed as (%), and the chi-square test was used for intergroup comparisons; measurement data were expressed as ($\bar{\chi}$±s), and the independent samples t-test was used for intergroup comparisons, while the paired t-test was used for comparisons before and after treatment. A difference was considered statistically significant when $P<0.05$.

Results

Clinical data comparison

The basic clinical data of the two groups, including age, door-to-wire (D2W), BMI, medical history (diabetes mellitus, hypertension, etc.), and heart rate, were collected and statistically analyzed. The results showed that there were no statistically significant differences between the two groups in any of the data ($P>0.05$), confirming that the two groups were comparable. Table 1.

Clinical efficacy comparison

Statistically, the total efficacy rate of the research group was 86.96%, while that of the control group was 80.56%. The difference in the total efficacy rate between the two groups was not statistically significant ($P>0.05$).Table 2.

Table 1. Clinical data comparison.

	Research group (n=46)	Control group (n=36)	χ^2 or t	P
Age	60.7±7.6	59.4±6.8	0.805	0.423
BMI(kg/m^2)	28.2±2.8	27.4±2.5	1.345	0.182
D2W(min)	83.5±12.1	82.2±16.1	0.405	0.687
Gender			0.078	0.780
Male	28(60.87%)	23(63.89%)		
Female	18(39.13%)	13(36.11%)		
Diabetes mellitus			0.368	0.544
Yes	17(36.96%)	11(30.55%)		
No	29(63.04%)	25(69.44%)		
Heart rate (times/min)	82.9±4.4	84.4±3.7	1.641	0.105
Ethnicity			0.148	0.701
Chinese	41(89.13%)	33(91.67%)		
Minority	5(10.87%)	3(8.33%)		
Hypertension			0.293	0.589
Yes	28(60.87%)	24(66.67%)		
No	18(39.13%)	12(33.33%)		
Cerebrovascular disease			0.007	0.931
Yes	8(17.39%)	6(16.67%)		
No	38(82.61%)	30(83.33%)		
History of Smoking			0.200	0.655
Have	12(73.91%)	25(69.44%)		
none	12(26.09%)	11(30.56%)		

Table 2. Clinical efficacy comparison.

Group	n	Significant effect	Effective	Ineffective	Total efficacy rate
Research	46	17(36.96)	23(50.00)	6(13.04)	86.96%
Control	36	10(27.78)	19(52.78)	7(19.44)	80.56%
χ^2					0.620
P					0.431

Comparison of cardiac function biomarkers before and after treatment

Before treatment, there were no statistically significant differences in hs-cTnI, CK-MB, and NT-proBNP between the two groups (P>0.05). After treatment, the levels of these biomarkers in both groups were lower than before treatment (P<0.05). The post-treatment levels of hs-cTnI, CK-MB, and NT-proBNP in the research group were respectively (3.05±0.90) ng/L, (14.00±2.10) U/L, and (416.60±46.40) ng/L, which were lower than those in the control group (P<0.05). Figure 1

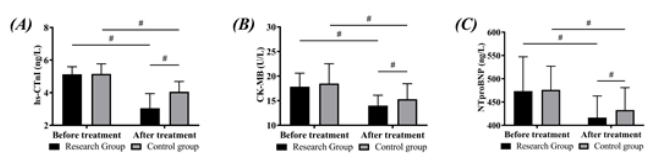

Figure 1. Comparison of cardiac function biomarkers. (A) hs-cTnI before and after treatment in both groups. (B) CK-MB before and after treatment in both groups. (C) NT-proBNP before and after treatment in both groups. Note: #P<0.05.

Comparison of hemodynamics

After treatment, the CO, CI, and MAP were lower in the research group than in the control group (P<0.05), indicating that the hemodynamics were more stable in the research group after treatment. Figure 2

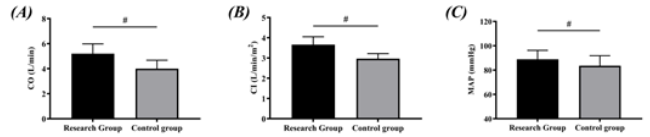

Figure 2. Comparison of hemodynamics. (A) CO for both groups. (B) CI for both groups. (C) MAP for both groups. Note: #P<0.05.

Comparison of echocardiography results after treatment

Echocardiography results showed that the LVEF in the research group was higher than that in the control group at both 1 week and 1 month after treatment, while LVEDD and LVESD were lower than those in the control group (P<0.05). In both groups, LVEF was higher in 1 month after treatment than in 1 week after treatment, while LVEDD and LVESD were lower (P<0.05). Figure 3

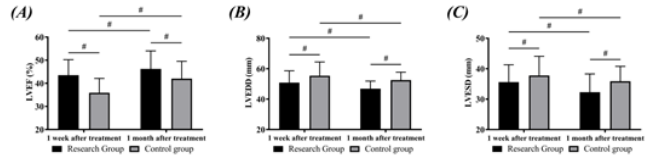

Figure 3. Comparison of echocardiography results. (A) LVEF at 1 week and 1 month after treatment in both groups. (B) LVEDD at 1 week and 1 month after treatment in both groups. (C) LVESD at 1 week and 1 month after treatment in both groups. Note: #P<0.05.

Comparison of prognostic risk events

During the 6-month follow-up period, both groups experienced adverse reactions such as nausea and vomiting, dizziness, and headache. In the control group, 2 patients experienced cardiac death, while no patients in the research group died. There was no statistically significant difference in the overall incidence of prognostic risk events between the two groups (P>0.05). Table 3

Discussion

PPCI is the most direct and effective means of restoring myocardial perfusion, and for STEMI patients, it can rapidly and sufficiently open the infarct-related artery, reduce the area of myocardial ischemia, and salvage the dying myocardium. This is of utmost importance in preventing and treating complications related to STEMI (11). However, during the process of PPCI and revascularization, platelet activation and sympathetic nerve stimulation may still occur, potentially leading to endothelial damage and increased blood osmotic pressure (12). This undoubtedly exacerbates the deterioration of cardiac function and increases the occurrence of no-reflow in the myocardium (13). Therefore, finding ways to further reduce the negative impact of myocardial ischemia and minimize the threat to patients' cardiac function is crucial for ensuring the safety of STEMI patients' prognosis.

BNP is an endogenous peptide mainly secreted by the atria and ventricles of the heart. Its secretion is minimal under physiological conditions, but it can be synthesized

Table 3. Prognostic risk events.

Group	n	Nausea and vomiting	Dizziness, and headache	Cardiac death	Heart palpitations	Insomnia	Overall incidence
Research	46	3(6.52)	2(4.35)	-	3(6.52)	2(4.35)	21.74%
Control	36	4(11.11)	1(2.78)	2(5.56)	2(5.56)	3(8.33)	33.33%
χ^2							1.383
P							0.240

and released in large amounts when the ventricular wall pressure increases or the ventricular muscle is subjected to stretching forces. This is actually a compensatory cardiac protective effect, but its elevated concentration is not sufficient to antagonize the activated renin-angiotensin-aldosterone system (RAAS) (14). rhBNP is a synthetically produced peptide with the same amino acid sequence, spatial structure, and biological activity as endogenous BNP. It can bind to specific BNP receptors, increase cyclic guanosine monophosphate (cGMP) levels in cells, relax smooth muscle cells, and have vasodilatory effects on both arteries and veins. Therefore, it can reduce systemic vascular resistance, pulmonary artery wedge pressure, and cardiac preload and afterload, effectively alleviating symptoms of heart failure. Previous studies have shown that intravenous administration of rhBNP has excellent effects on patients with NYHA class II heart function impairment (15). In this paper, we applied rhBNP in all STEMI patients, which is clearly over-indicated. However, the pre-use regimen, has a higher clinical significance for better prevention and control of MI in STEMI patients in the future. In this study, although there was no significant difference in the overall clinical efficacy between the two groups, we found that after the application of rhBNP, the levels of hs-cTnI, CK-MB, and NT-proBNP in the research group were further reduced compared to the control group, and echocardiographic examination results also showed more significant improvement in cardiac function in the research group patients. This indicates that rhBNP can effectively assist PPCI treatment and more effectively improve patients' cardiac function. This is consistent with the research results of Zhu P et al. (16), which can corroborate the accuracy of this study.

At the same time, rhBNP can antagonize RAAS and catecholamines, reduce the impulse threshold of the vagus nerve, inhibit the excitability of the sympathetic nerves, and suppress the synthesis and release of substances such as adrenocortical hormones, reducing the pressure in the blood vessels of the thalamus, effectively balancing water and sodium metabolism and blood pressure (17). In this study, we also found that the hemodynamics of the research group patients were better than those of the control group after treatment, further indicating the excellent therapeutic effect of rhBNP on patients with STEMI. We believe that this may be due to rhBNP's ability to relieve peripheral circulation and cardiac load, increase coronary artery blood supply, promote the recovery of myocardial cell function, further increase myocardial contractility, and dilate blood vessels while treating, thereby improving the patient's overall condition. In addition, studies have shown that rhBNP can maintain vascular and renal hemodynamic balance by reducing the secretion of renin and aldosterone, an antagonizing antidiuretic hormone from the posterior pituitary gland, and preserving sodium in the sympathetic nerves (18), which is more conducive to the recovery of patients' hemodynamics.

Finally, in the comparison of the prognosis safety between the two groups of patients, we observed that although both groups experienced symptoms such as nausea, vomiting, and dizziness, no cases of cardiogenic death were observed in the research group, while two patients in the control group experienced cardiogenic death. Pharmacological studies of rhBNP have found that it does not undergo hepatic or renal metabolism and has fewer toxic side effects on the human body (19). In previous studies, we also found that Liang L et al. reported that the use of rhBNP can improve the treatment safety of coronary heart disease patients (20). Therefore, although there was no difference in the total incidence of risk events between the two groups of patients in this study, based on the above experimental results and previous studies, we believe that the use of rhBNP may be beneficial in improving the safety of PPCI, reducing the risk of adverse events in patients' prognosis. The lack of statistically significant differences between the two groups in this study may be due to the small number of cases and the resulting randomness.

In summary, this study suggests that the use of rhBNP in conjunction with PPCI may effectively improve cardiac function and hemodynamics in patients with STEMI, potentially enhancing safety and reducing the risk of adverse events in patients' prognosis. However, further research with larger sample sizes and more rigorous study designs is needed to confirm these findings and explore the optimal dosing and treatment strategies for rhBNP in the context of PPCI for STEMI patients.

However, although rhBNP has demonstrated excellent effects in various cardiovascular diseases, its specific mechanisms and pathways of action remain unclear, which is a focus for further in-depth research in the future. At the same time, it is necessary to increase the number of cases and extend the follow-up period to verify the accuracy of this study. Moreover, this study focuses on the effects of rhBNP in the context of PPCI treatment; future research could also explore the effects of rhBNP combined with other treatment methods for STEMI patients, providing more comprehensive reference opinions for clinical practice.

Prophylactic intravenous injection of rhBNP in conjunction with PPCI treatment for STEMI patients can effectively improve treatment outcomes, enhance cardiac function, and promote the recovery of hemodynamics. In addition, the use of rhBNP may also increase the safety of PPCI, providing more reliable safety guarantees for patients' prognosis, and having a high clinical application value.

Consent for publications

The author read and proved the final manuscript for publication.

Ethics approval and consent to participate

The study protocol was approved by the Ethics Committee of (No.2022-09-035-H00)

Interest conflict

The authors report no conflict of interest.

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Availability of data and material

All data generated during this study are included in this published article.

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