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Original Article

Effects of Tirofiban combined with Betaloc on serum P-selectin, BNP levels, and cardiac function in patients with acute myocardial infarction after PCI

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Abstract: Objective: To investigate the effects of tirofiban combined with betaloc on serum P-selectin, brain natriuretic peptide (BNP) levels, and cardiac function in patients with acute myocardial infarction (AMI) after percutaneous coronary intervention (PCI). Methods: Ninety-five patients were randomly divided into the observation group and the control group. The control group was treated with betaloc alone, while the observation group was treated with tirofiban and betaloc. Patient serum P-selectin and BNP levels, hemodynamic parameters, cardiac function indexes, troponin T (TNT), and C-reactive protein levels were observed and compared. Results: The total effective rate of the observation group was significantly higher than that of the control group (P=0.015). Parameters were significantly lower in both groups after treatment, and there was significant difference between the two groups (both P=0.000). P-selectin and BNP levels in both groups significantly decreased after treatment, and there was significant difference between the two groups (both P=0.000). LVEF was significantly increased in both groups, with significant difference between the two groups (P=0.000). The LVEDD and LVESD of the observation group were significantly lower than those of the control group after treatment (both P=0.000). Both TNT and hs-CRP were significantly reduced and with significant differences between the two groups (all P=0.000). Conclusion: Treatment with tirofiban combined with betaloc after PCI in patients with AMI can improve clinical outcomes and has a high clinical value owing to its ability to reduce P-selectin and BNP levels and to improve cardiac function and hemodynamic status.

Keywords: Tirofiban, betaloc, acute myocardial infarction, cardiac function

Introduction

Acute or persistent ischemia and hypoxia of the coronary arteries may lead to myocardial necrosis and then acute myocardial infarction (AMI), potentially leading to severe sternal pain, arrhythmia, and heart failure [1-3]. Clinically, AMIs are mainly treated via percutaneous coronary intervention (PCI). During such surgical interventions, the coronary artery is dredged; hemodynamic functions are improved. This PCI approach has become the standard form of treatment for AMI [4-6].

Although PCI has been widely adapted therapeutically, clinical findings have shown that myocardial infarction (MI) patients are prone to a series of adverse reactions after PCI, including poor blood flow and myocardial reperfusion disorder [7]. In order to reduce the occurrence of those symptoms, platelet glycoprotein receptor antagonist is often administered following PCI. Betaloc is commonly administered for the treatment of MI and angina pectoris; it offers good therapeutic efficacy for heart failure; however, its long-term use can produce adverse effects such as nausea, vomiting and arrhythmia. Tirofiban is a common platelet glycoprotein receptor antagonist, and the combination of tirofiban and betaloc has been shown to yield a strong synergistic effect in certain contexts. There are, however, relatively few studies on the combination of these two drugs in patients who have undergone a PCI procedure.

In this study, betaloc was administered with or without Tirofiban in patients who had undergone PCI after AMI to investigate the clinical efficacy of this regimen.

Table 1. Comparison of the total effective rate (n, %)

Group	Case	Markedly effective	Effective	Ineffective	Total effective rate
Observation group	50	32	14	4	46 (92.00)
Control group	45	20	13	12	33 (73.33)
X^2					5.892
P					0.015

Materials and methods

General data

A total of 95 patients with AMI undergoing PCI in Dezhou People's Hospital from February 2017 to February 2018 were selected and divided into either the control group (n=45) or the observation group (n=50) according to the random number table. All patients were informed of the clinical plan before the trial and signed informed consent form. The trial protocol was approved by the Ethics Committee of Dezhou People's Hospital. In the control group, there were 28 males and 17 females with an average age of 53.43±6.09 years old. Infarction types in the control group were: 23 cases of inferior wall infarction, 19 cases of anterior wall infarction, and 3 cases of other infarctions. In the observation group, there were 33 males and 17 females with an average age of 55.43±6.17 years old. Infarction types in the observation group were: 20 cases of inferior wall infarction, 21 cases of anterior wall infarction, and 9 cases of other infarctions. There were no significant differences in age, gender, or type of infarctions between the two groups.

Inclusion criteria: all patients met the diagnostic criteria for AMI according to the European Society of Cardiology (2003) [8]; patients met the *standards for coronary revascularization*, indicating they were suitable for PCI; patients did not have other cardiovascular and cerebrovascular diseases; patients were diagnosed within 24 hours of onset; patients had no psychiatric diseases, had good compliance, and could actively cooperate with the medical staff.

Exclusion criteria: patients suffering from coagulopathy; allergic to the test drug; had acute infections or immune dysfunction.

Methods

Both groups of patients underwent routine PCI. Before surgery, patients received orally administered aspirin (Bayer Pharmaceuticals, Germany) 300 mg and clopidogrel (Sanofi (Hangzhou) Pharmaceutical Co., Ltd., China) 300 mg. After surgery, patients received orally administered aspirin 100 mg and clopidogrel 75 mg, and an injection of heparin calcium (Tianjin Biochemical Pharmaceutical Co., Ltd., China) for 7 days, once a day, 5,000 U/dose. Following surgery, the control group was treated with betaloc (AstraZeneca Pharmaceutical Co., Ltd., UK) once daily, with an initial dose of 12.25 mg. The observation group was treated with tirofiban (Iroko Cardio Australia Pty Ltd, Australia) at 10 μg/kg, along with the above Betaloc dose, and the injection was completed within 3 minutes. A micropump was used to pump tirofiban for approximately 36 h at an injection rate of 0.15 μg/kg•min^{-1}. The patient's hemodynamic parameters, P-selectin and cardiac function were recorded before treatment and 15 days after treatment. Serum natriuretic peptide (BNP) levels were recorded before treatment and 30 days after treatment.

Observation indicators and efficacy evaluation

Clinical efficacy criteria: If the patient's heart function reached grade I (NYHA classification) or cardiac function was improved by 2 grades, it was markedly effective; if the patient's cardiac function was improved by 1 grade, but did not reach level I, it was effective; if the patient's cardiac function grade did not change, it was ineffective. Total effective rate (%) = (markedly effective + effective)/total number of cases * 100% [9].

P-selectin levels: Fasting venous blood was collected before treatment and 15 days after treatment. Serum was collected following centrifugation. P-selectin concentration was determined by enzyme-linked immunosorbent assay (Thermo Fisher Scientific (China) Co., Ltd.). The procedure was carried out in strict accordance with the manufacturer's instructions [10].

BNP levels: Fasting venous blood was collected before treatment and 30 days after treatment. Serum was collected following centrifugation. BNP was determined by enzyme-linked immunosorbent assay (Thermo Fisher Scientific (China) Co., Ltd.). The procedure was car-

Table 2. Comparison of the mPAP (kPa, $\bar{x}$ ± sd)

Group	Before treatment	After treatment	Difference before and after treatment	t	P
Observation group	6.73±0.87	4.20±0.54	2.55±0.21	18.696	0.000
Control group	6.89±0.69	5.79±0.66	1.09±0.11	8.535	0.000
t	-0.986	-12.901	41.752		
P	0.327	0.000	0.000		

Note: mPAP, mean pulmonary arterial pressure.

Table 3. Comparison of the mMVP (kPa, $\bar{x}$ ± sd)

Group	Before treatment	After treatment	Difference before and after treatment	t	P
Observation group	2.48±0.21	0.93±0.10	1.55±0.11	52.175	0.000
Control group	2.45±0.26	1.69±0.11	0.70±0.09	14.941	0.000
t	0.621	-35.275	40.944		
P	0.536	0.000	0.000		

Note: mMVP, mean mitral valve pressure.

ried out in strict accordance with the manufacturer's instructions [11].

Hemodynamic indicators: The mean pulmonary arterial pressure (mPAP) and mean mitral valve pressure (mMVP) hemodynamic parameters from color doppler echocardiography were recorded.

Heart function indicators: The left ventricular ejection fraction (LVEF), left ventricular end-systolic diameter (LVESD) and left ventricular end-diastolic diameter (LVEDD) parameters from the cardiac color doppler ultrasonic apparatus were recorded.

Troponin T (TNT) and C-reactive protein (CRP) levels: Levels of both TNT and CRP were measured using enzyme-linked immunosorbent assays. The procedures were carried out in strict accordance with the kit manufacturer's instructions.

Statistical analysis

SPSS software, version 19.0, was used for all statistical analyses. Measurement data are expressed as mean ± standard deviation (mean ± SD). Measurements between two groups were compared using an independent sample t test, and intragroup comparisons were performed using a paired t test. Count data are expressed as percentage (rate), compared using χ^2 test. $P<0.05$ was considered to be significantly different.

Results

Comparison of clinical efficacy

The total effective rate in the observation group was 92.00%, while that in the control group was 73.33%. The total effective rate in the observation group was significantly higher than that in the control group (P=0.015; **Table 1**).

Comparison of hemodynamics

There were no significant differences in mPAP or mMVP between the two groups before treatment (P=0.327, P=0.536). After treatment, mPAP and mMVP were both significantly decreased in both groups, and there was significant difference between the two groups (all P=0.000; **Tables 2** and **3**).

Comparison of P-selectin

There was no significant difference in P-selectin between the two groups before treatment. Both groups were lower after treatment and the P-selectin of the observation group was significantly lower than that of the control group (t=-14.161, P=0.000; **Table 4** and **Figure 1**).

Comparison of BNP levels before and after treatment

There were no differences in BNP levels before treatment between the two groups. After 30 days of treatment, BNP levels had decreased in

Table 4. Comparison of P-selectin before and after treatment (μg/L, $\bar{x} \pm sd$)

Group	Before treatment	After treatment	Difference before and after treatment	t	P
Observation group	12.78±0.82	8.70±0.88	4.08±0.76	26.361	0.000
Control group	12.91±1.16	10.85±0.54	2.06±0.29	13.192	0.000
t	-0.636	-14.161	16.758		
P	0.527	0.000	0.000		

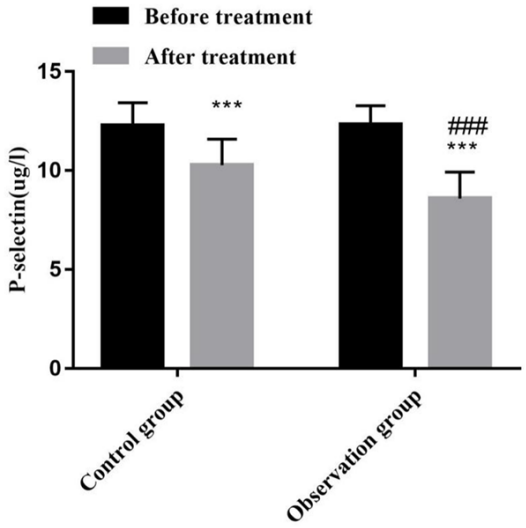

Figure 1. Comparison of P-selectin before and after treatment between the two groups. ***, relative to before treatment, the observation group: t=26.361, P=0.000; the control group: t=13.192, P=0.000. ###, differences before and after treatment in the observation group relative to the control group: t=16.758, P=0.000.

both groups, and there was a significant difference between the two groups (t=5.512, P=0.000; **Table 5** and **Figure 2**).

Comparison of cardiac function before and after treatment

There were no significant differences in LVEF, LVEDD, or LVESD between the two groups at baseline (P=0.506; P=0.465; P=0.728). After treatment, LVEF was significantly increased in both groups, and there was a significant difference between the two groups (all P=0.000). The LVEDD and LVESD of the observation group were significantly lower than those of the control group after treatment (both P=0.000; **Tables 6**-**8**).

Comparison of hs-CRP and TNT

There were no differences in hs-CRP or TNT between the two groups before treatment (both P>0.05). After treatment, the hs-CRP and TNT levels in patients in the observation group were significantly lower than those in the control group, and the difference in the observation group before and after treatment was significantly larger than that in the control group (all P=0.000; **Tables 9** and **10**).

Discussion

AMI is due to acute myocardial ischemic necrosis caused by decreased coronary blood flow. The onset of this disease is both sudden and severe [12]. Clinically, there are a series of reactions including severe chest pain, cardiac dysfunction, and myocardial ischemia that seriously endanger the safety of AMI patients [13]. Clinical treatment of AMI primarily relies upon intravenous thrombolysis and cardiac intervention [14]. The former approach refers to the dissolution of newly formed thrombi; however, this approach is less widely employed because it does not improve atherosclerotic plaques. The latter approach dredges up the stenosis and blocks blood vessels, improves hemodynamics, and is therefore widely used. Among cardiac interventions, PCI is the most widely used form of interventional therapy. The procedure consists of the insertion of a catheter with a balloon dilator into the coronary artery, allowing for arterial expansion and dredging. This approach causes minimal damage, and is highly efficacious. However, clinical studies have found that during PCI procedures, thrombi shedding may be caused by the squeezing of atherosclerotic plaques by the inserted balloon, and the balloon's stimulation on the coronary artery wall may lead to slow coronary flow, thereby ultimately causing cardiac dysfunction and affecting myocardial perfusion [15]. In order to reduce the impact of PCI on the body, thrombolytic and anticoagulant drugs are often used following surgery. The latest drug, betaloc, is a cardiac selective beta-blocker that lowers blood pressure. Long-term use reduces the incidence of MI. Post-MI use results in

Table 5. Comparison of BNP before and after treatment (ng/mL, $\bar{x} \pm sd$)

Group	Before treatment	After treatment	Difference before and after treatment	t	P
Observation group	278.35±26.09	95.50±11.78	182.55±19.86	49.847	0.000
Control group	275.80±16.00	113.72±15.34	162.43±15.09	43.800	0.000
t	0.567	-6.368	5.512		
P	0.572	0.000	0.000		

Note: BNP, brain natriuretic peptide.

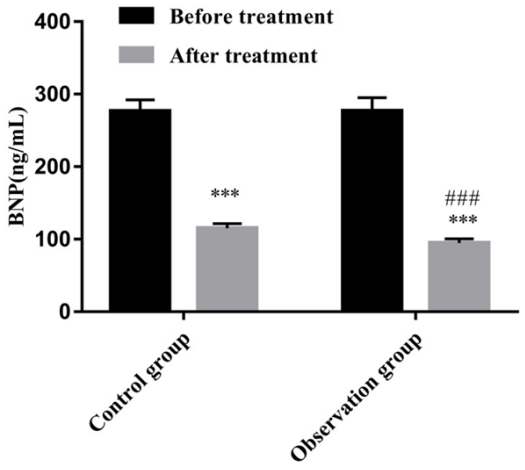

Figure 2. Comparison of BNP before and after treatment between the two groups. ***, relative to before treatment, the observation group: t=49.847, P=0.000; the control group: t=43.800, P=0.000. ###, differences before and after treatment in the observation group relative to the control group: t=5.512, P=0.000. BNP, brain natriuretic peptide.

decreases in reinfarction and mortality after MI. Clinical studies have found that the combination of betaloc and tirofiban can provide superior efficacy as a means of managing blood pressure and preventing MI. Tirofiban is a GPIIb/IIIa receptor antagonist that inhibits the platelet aggregation pathway, improves myocardial perfusion by promoting the release of nitric oxide, reduces myocardial reperfusion injury, and significantly improves cardiac function [16, 17]. This study therefore combined tirofiban with betaloc after PCI in patients with AMI in order to explore the therapeutic efficacy of the combined application of these agents.

BNP is a cardiac neurohormone produced by ventricular myocytes. In patients with heart failure, the ventricular wall pressure is elevated, leading to release of this hormone which serves as an indicator that cardiac function is seriously damaged. Clinically, this hormone is primarily used to evaluate the left ventricular systolic and diastolic function. BNP is cleared by neutral endopeptidases and receptors, with some limited clearance in the kidney. The half-life of this hormone is only 20 minutes, indicating that it is readily decomposed [18]. P-selectin is a cell adhesion molecule of the selectin family. P-selectin levels in healthy individuals are low, but they increase after inflammation, apoptosis, or myocardial injury [19, 20].

In the present study, the improved hemodynamics in the observation group was superior to those in the control group; heart function was similarly improved. The LVEDD and LVESD values in the observation group were significantly lower than those in the control group; the LVEF was significantly higher than that of the control group following treatment. These results indicate that the hemodynamics of patients treated with tirofiban were improved significantly; the blood flow rate was accelerated; blood vessel clogging was avoided. At the same time, the BNP and P-selectin levels in the observation group were significantly lower than those in the control group after treatment, which further validated the above results. These results suggest that Tirofiban inhibited platelet aggregation and platelet adhesion by reducing the expression and secretion of BNP and P-selectin, thus reducing the myocardial injury and protecting the vascular endothelium, ultimately improving cardiac function and blood flow. The results of this study are similar to those of Huang et al., which have shown that perioperative tirofiban injection in patients with AMI yields a good short-term prognosis, improving coronary blood flow and cardiac function [21]. One limitation of this study is that the molecular mechanisms of tirofiban activity have not been studied in depth, and as such warrant further research. In addition, a control

Table 6. Comparison of LVEF before and after treatment (%, $\bar{x}$ ± sd)

Group	Before treatment	After treatment	Difference before and after treatment	t	P
Observation group	48.29±5.65	65.20±6.88	-17.87±2.98	-14.42	0.000
Control group	49.03±5.09	53.25±5.77	-4.54±0.65	-4.054	0.000
t	-0.668	9.117	-29.370		
P	0.506	0.000	0.000		

Note: LVEF, left ventricular ejection fraction.

Table 7. Comparison of LVEDD before and after treatment (mm, $\bar{x}$ ± sd)

Group	Before treatment	After treatment	Difference before and after treatment	t	P
Observation group	58.29±6.09	40.01±4.65	18.89±2.09	17.130	0.000
Control group	59.20±5.99	46.73±5.03	12.09±1.99	11.505	0.000
t	-0.733	-6.766	16.196		
P	0.465	0.000	0.000		

Note: LVEDD, left ventricular end-diastolic diameter.

Table 8. Comparison of LVESD before and after treatment (mm, $\bar{x}$ ± sd)

Group	Before treatment	After treatment	Difference before and after treatment	t	P
Observation group	42.34±4.97	29.42±3.21	12.90±1.76	16.107	0.000
Control group	41.98±5.09	35.67±4.09	5.98±0.54	7.413	0.000
t	0.349	-8.327	24.582		
P	0.728	0.000	0.000		

Note: LVESD, left ventricular end-systolic diameter.

Table 9. Comparison of hs-CRP before and after treatment (mg/L)

Group	Before treatment	After treatment	Difference before and after treatment	t	P
Observation group	62.34±6.32	24.23±3.21	38.65±4.76	39.121	0.000
Control group	61.98±5.99	48.43±4.09	15.98±1.76	13.918	0.000
t	0.284	-32.241	30.135		
P	0.777	0.000	0.000		

Note: hs-CRP, high-sensitivity C-reactive protein.

Table 10. Comparison of TNT before and after treatment (ng/mL, $\bar{x}$ ± sd)

Group	Before treatment	After treatment	Difference before and after treatment	t	P
Observation group	3.39±0.32	0.98±0.07	2.56±0.32	48.913	0.000
Control group	3.45±0.43	1.92±0.11	1.50±0.11	24.991	0.000
t	-0.776	-50.194	21.117		
P	0.439	0.000	0.000		

Note: TNT, troponin T.

group of patients receiving tirofiban alone was not included in this study, and may warrant inclusion in a subsequent study.

In conclusion, the treatment of AMI with a combination of tirofiban and betaloc after PCI can clearly improve cardiac function and hemodynamics, and the therapeutic efficacy is good and has the potential for wide application.

Disclosure of conflict of interest

None.

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