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# Effect of preoperative small dose of tirofiban on PCI treatment in patients with acute coronary syndrome

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ABSTRACT

**Objective:** To analyze the effect of preoperative small dose of tirofiban on PCI treatment prognosis in patients with acute coronary syndrome. **Methods:** A total of 108 cases with acute coronary syndrome who received PCI treatment in our hospital from August 2011 to May 2014 were included for study and randomly divided into observation group and control group by half according to different treatment methods. Control group received PCI treatment alone, observation group received small dose of tirofiban combined with PCI treatment, and then differences in hemorheology indicators, platelet function, left ventricular systolic function and left ventricular diastolic function parameters, serum indicators and so on were compared between two groups after treatment. **Results:** Whole blood high shear viscosity, whole blood low shear viscosity, reduced high shear viscosity, reduced low shear viscosity, plasma ratio viscosity, erythrocyte aggregation index and erythrocyte deformability index of observation group after treatment were all less than those of control group ($P$<0.05); PAdT, PAgT, CD62p, CD40L and P-selectin values of observation group after treatment were all lower than those of control group ($P$<0.05); LPER and LPFR values of observation group 1 week after treatment were higher than those of control group while LTPER and LTPFR values were lower than those of control group ($P$<0.05); serum GA, MCP-1, PAI-1, NT-proBNP, PAC-1, VCAM-1 and ICAM-1 values of observation group after treatment were all lower than those of control group ($P$<0.05). **Conclusions:** Small dose of tirofiban combined with PCI treatment for patients with acute coronary syndrome can effectively enhance therapeutic effect, inhibit platelet activity while protect heart function and optimize long-term treatment outcome.

## 1. Introduction

Acute coronary syndrome (ACS) belong to the clinical severe cardiovascular illness caused by the unstable atherosclerotic plaque, secondary intraplaque hemorrhage or fibrous cap rupture, and the local activation and aggregation of platelets plays an important role in the development process of ACS[1]. Coronary artery balloon expansion stent implantation (PCI) is the main way for the treatment of ACS that can early recover coronary perfusion and avoid the heart failure caused by excessive myocardial ischemia[2]. Tirofiban is platelet membrane glycoprotein Ⅱb/Ⅲa receptor antagonist that can block the combination of glycoprotein Ⅱb/Ⅲa receptor with fibrinogen and inhibit platelet aggregation, blocking the final pathway of thrombosis. In the research, the improvement of preoperative small dose of tirofiban on PCI treatment prognosis in patients with acute coronary syndrome was mainly analyzed, hereby reported as follows.

## 2. Materials and methods

### 2.1. General information

A total of 108 cases with acute coronary syndrome who received PCI treatment in our hospital from August 2011 to May 2014 were

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included for study and randomly divided into observation group 54 cases and control group 54 cases according to different treatment methods. Control group included 30 male cases and 24 female cases, they were 56-72 years old and the average was (65.28±5.93) years; observation group included 29 male cases and 25 female cases, they were 53-71 years old and the average was (63.98±5.76) years. All included patients and their families learned about the research process and then signed informed consent forms, and differences in gender, age and other information were without statistical significance between two groups ($P$>0.05).

### 2.2. Treatment methods

Both groups received oral administration of aspirin and clopidogrel as well as subcutaneous injection of low molecular weight heparin. Control group received PCI treatment, which was as follows: femoral artery puncture was conducted, thrombus aspiration catheter was used at first for coronary artery with preoperative TIMI staging lower than 3 stage, then semi-compliant balloon was used to pre-dilated the lesions and insert stent (rapamycin drug-eluting stent), and the success of surgery was confirmed by coronary angiography. Observation group received small dose of tirofiban before PCI treatment, intravenous infusion at 0.4 μg/(kg·min) for 30 min, and then it was infused with micro-pump at the velocity of 0.1 μg/(kg·min) for continuous 48 h. After that, they received PCI treatment and the specific methods were the same as those of control group.

### 2.3. Observation indicators

Peripheral venous blood was drawn from patients, rotating glass ball method was used to detect platelet adhesion (PAdT), turbidimetry was used to detect platelet aggregation rate (PAgT) and enzyme-linked immunosorbent assay (ELISA) was used to detect platelet CD62p, CD40L and P-selectin levels.

One week after patients received PCI treatment, SPECT imager was used to calculate left ventricular systolic function (LVSF) and left ventricular diastolic function (LVDF) parameters according to cardiac cycle, including left ventricular peak ejection rate (LPER), left ventricular time to peak ejection rate (LTPER), left ventricular peak filling rate (LPFR) and left ventricular time to peak filling rate (LTPFR).

Glycated albumin (GA), monocyte/macrophage chemoattractant protein-1 (MCP-1), plasminogen activator inhibitor-1(PAI-1), N-terminal pro-brain natriuretic peptide (NT-proBNP), platelet membrane glycoprotein Ⅱb/Ⅲa complex fibrinogen receptor (PAC-1), vascular cell adhesion molecule-1 (VCAM-1) and intercellular adhesion molecule-1 (ICAM-1) levels were detected.

### 2.4. Statistical methods

Data obtained in the research was analyzed by SPSS23.0 software, measurement data was in terms ofmean±sd, comparison between two groups was performed by $t$ test and $P$<0.05 was set as the standard of statistical significant differences.

## 3.Results

### 3.1. Hemorheology indicators

Results showed that after observation group received small dose of tirofiban and PCI treatment, whole blood high shear viscosity, whole blood low shear viscosity, reduced high shear viscosity, reduced low shear viscosity, plasma ratio viscosity, erythrocyte aggregation index and erythrocyte deformability index were all lower than those of control group ($P$<0.05), shown in Table 1.

### 3.2. Platelet function

Results showed that PAdT, PAgT, CD62p, CD40L and P-selectin values of observation group after treatment were all lower than those of control group ($P$<0.05), shown in Table 2.

### 3.3. Left ventricular systolic function and left ventricular diastolic function parameters

Results showed that LPER and LPFR values of observation group 1 week after treatment were higher than those of control group while LTPER and LTPFR values were lower than those of control group ($P$<0.05), shown in Table 3.

### 3.4. Serum indicators

Results showed that serum GA, MCP-1, PAI-1, NT-proBNP, PAC-1, VCAM-1 and ICAM-1 values of observation group after treatment were all lower than those of control group ($P$<0.05), shown in Table 4.

**Table 1**

Comparison of hemorheology indicator values after different treatment.

| Groups | Plasma ratio viscosity (mPa/s) | Whole blood viscosity | | Reduced viscosity | | Erythrocyte aggregation index | Erythrocyte deformability index |
|---|---|---|---|---|---|---|---|
| | | High shear (mPa/s) | Low shear (mPa/s) | High shear (mPa/s) | Low shear (mPa/s) | | |
| Observation group | 1.27±0.12 | 3.17±0.29 | 10.62±1.05 | 6.13±0.45 | 21.15±1.87 | 3.27±0.29 | 0.43±0.03 |
| Control group | 1.38±0.13 | 3.98±0.34 | 11.78±1.56 | 6.57±0.58 | 22.67±1.96 | 3.68±0.31 | 0.51±0.04 |
| $t$ | 5.485 | 6.493 | 5.883 | 5.728 | 7.182 | 5.093 | 6.182 |
| $P$ | <0.05 | <0.05 | <0.05 | <0.05 | <0.05 | <0.05 | <0.05 |

**Table 2**

Comparison of platelet function levels between two groups after treatment.

| Groups | PAdT (%) | PAgT (%) | CD62p (μg/L) | CD40L (μg/L) | P-selectin (μg/L) |
|---|---|---|---|---|---|
| Observation group | 34.28±2.79 | 27.54±2.35 | 2.17±0.21 | 8.12±0.76 | 9.27±0.85 |
| Control group | 38.16±2.48 | 33.61±2.98 | 2.96±0.24 | 12.36±1.56 | 14.15±1.39 |
| *t* | 5.394 | 8.293 | 7.263 | 8.485 | 9.182 |
| *P* | <0.05 | <0.05 | <0.05 | <0.05 | <0.05 |

**Table 3**

Comparison of left ventricular systolic function and left ventricular diastolic function parameters after different treatment.

| Groups | LPER (EDV/S) | LPFR (EDV/S) | LTPER (ms) | LTPFR (ms) |
|---|---|---|---|---|
| Observation group | 2.91±0.23 | 2.48±0.21 | 153.28±13.26 | 158.81±12.07 |
| Control group | 2.25±0.19 | 2.03±0.16 | 191.55±15.86 | 198.73±1.86 |
| *t* | 5.182 | 5.893 | 8.293 | 9.162 |
| *P* | <0.05 | <0.05 | <0.05 | <0.05 |

**Table 4**

Comparison of serum indicator values after different treatment.

| Groups | GA (mmol/L) | MCP-1 (pg/mL) | PAI-1 (ng/L) | NT-proBNP (pg/Ml) | PAC-1 (μg/L) | VCAM-1 (μg/L) | ICAM-1 (μg/L) |
|---|---|---|---|---|---|---|---|
| Observation group | 1.28±0.11 | 39.82±3.46 | 38.29±3.13 | 187.29±15.73 | 3.27±0.23 | 502.72±39.72 | 231.73±20.58 |
| Control group | 1.61±0.14 | 48.71±4.35 | 51.67±4.98 | 269.85±23.66 | 9.56±0.85 | 702.85±68.61 | 372.95±30.81 |
| *t* | 5.834 | 8.293 | 7.823 | 11.284 | 6.486 | 8.294 | 9.832 |
| *P* | <0.05 | <0.05 | <0.05 | <0.05 | <0.05 | <0.05 | <0.05 |

## 4. Discussion

ACS has the main pathological changes of coronary atherosclerotic plaque rupture, completely or incompletely stimulated vascular occlusion, belongs to the clinical serious cardiovascular disease, and must be treated within the prescribed time window after admission. Coronary artery balloon expansion stent implantation (PCI) is commonly used and effective way for the treatment of ACS, but recent studies have found many cases of coronary artery re-embolism events after PCI, and indicate that they are related to platelet activation[3,4]. Adding platelet function-inhibitory drug before PCI is considered to be a more reasonable treatment, and tirofiban is the highly praised drug by scholars at present. Tirofiban is highly selective platelet inhibitor, belongs to the non-peptide platelet glycoprotein GP Ⅱ b/Ⅲa receptor antagonist, acts on the final pathway of platelet aggregation, and can occupy platelet GP Ⅱ b/Ⅲa crosslinking sites and competitively inhibit platelet aggregation mediated by fibrinogen. In the research, small dose of tirofiban was applied in observation group and specifically studied from the aspects such as hemorheology indicators, platelet function, left ventricular systolic function and left ventricular diastolic function parameters and serum indicators[5].

In coronary atherosclerotic conditions, ACS patients are with elevated blood adhesion, decreased cardiac output and increased peripheral resistance, and basic vascular stenosis can seriously affect coronary blood flow and cause myocardial ischemia. Hemorheology includes whole blood contrast viscosity, whole blood reduced viscosity, plasma viscosity, and so on, and mainly reflects the changes of blood fluidity, stagnation, viscosity, and so on caused by the changes of blood components[6]. When the blood adhesion increases, blood fluidity deteriorates, it is prone to thromboembolic events, and this is also one of the direct causes of ACS. Blood rheological property can change with the treatment of diseases, and for ACS patients, one of the purposes of appropriate treatment is to optimize patients' hemorheology indexes and lower blood viscosity, which removes existing thrombosis while avoids the recurrence of long-term coronary thromboembolic event[7,8]. In the research, hemorheology indicator levels were compared at first after patients received treatment, and results showed that whole blood high shear viscosity, whole blood low shear viscosity, reduced high shear viscosity, reduced low shear viscosity, plasma ratio viscosity, erythrocyte aggregation index and erythrocyte deformability index of observation group after treatment were less, indicating that small dose of tirofiban therapy before PCI treatment could effectively improve high blood viscosity and RBC aggregation state and directly reduce the risk of coronary thrombosis and embolism, and its specific mechanism of action is to be further studied.

Platelet function is throughout the development of ACS, and when the platelet activation or platelet adhesion and aggregation is activated, a large number of platelets aggregate in coronary artery and form thrombus, further aggravating coronary stenosis and even blocking coronary artery, and resulting in myocardial blood supply decrease and ischemia degeneration necrosis. Platelet function state plays an important role in ACS, and a study shows that the level of platelet function has a direct correlation with ACS outcome[9]. PAdT, PAgT, CD62p, CD40L and P-selectin are all closely associated with platelet function. CD40L is involved in the whole process of plaque development and rupture, more than 95% of CD40L in cycle

exists in platelets, and when platelets are activated, it can be quickly expressed on the membrane surface, and the expression level rises significantly. CD62p is also called platelet A granule membrane protein-140, it can be rapidly fused with its membrane and released after platelet activation to start and expand the thrombosis, and it is the currently accepted gold standard to reflect platelet activation[10]. P-selectin is the standard of particle release after platelet activation, belongs to the platelet-specific active molecule, and can directly reflect the degree of platelet activation. PAdT mainly reflects the function of platelet adhesion on foreign body surface, and the increase of its level is mostly found in myocardial infarction, angina pectoris, cerebrovascular disease and other thromboembolic diseases[11]. PAgT mainly reflects platelet aggregation function, refers to the adhesion ability between platelets, and when diabetes, acute myocardial infarction, varicose vein of lower limb and other high blood viscosity diseases occur, its value rises. Results of above research showed that platelet function-related indicators such as PAdT, PAgT, CD62p, CD40L and P-selectin values of observation group after treatment were all lower, indicating that application of small dose of tirofiban therapy before PCI treatment could inhibit platelet activity and reduce platelet adhesion and aggregation as well as reduce PCI treatment difficulty and also avoid the occurrence of re-embolism events after coronary recanalization.

There is myocardial ischemia after ACS, and severe ischemic myocardium will lead to normal cardiac vasomotor dysfunction. PCI is an effective means of reperfusion therapy that opens coronary artery to restore myocardial blood supply and improve ventricular remodeling. Cardiac systolic and diastolic function is another objective indicator to examine the therapeutic effects of ACS, and also the gold standard to evaluate whether PCI therapy is effective. (LPER, LTPER, LPFR and LTPFR are the objective indexes to reflect left ventricular function, the values of above parameters may be abnormal in ACS patients with cardiac dysfunction, and the detection sensitivity and accuracy are both higher[12]. Results of above research showed that LPER and LPFR values of observation group after treatment were higher while LTPER and LTPFR values were lower, indicating that small dose of tirofiban therapy before PCI treatment could effectively improve left ventricular systolic and diastolic function, which was mainly because that tirofiban not only maintained unobstructed epicardial vessels, but could also prevent platelet aggregation-induced distal embolism, microcirculation disorder and so on, and it could effectively improve myocardial tissue perfusion.

CAM participates in the development of atherosclerosis, is a kind of membrane surface glycoprotein mediating the adhesion and interaction between cell and cell or cell and extracellular matrix, and can mediate monocyte and lymphocyte adhesion to endothelial cell and promote mononuclear cells to migrate into the endothelium, take in lipid and transformed into foam cells[13]. Both VCAM-1 and ICAM-1 are important members of CAM family and the most studied adhesion molecules, and research has confirmed that VCAM-1 and ICAM-1 expression increases in patients with ACS. PAI-1, the inhibitor of the main physiological activator t-PA in fibrinolytic system, is involved in the maintenance of body's anticoagulant and pro-coagulant balance, and PAI-1 level increases in patients with ACS so as to make the body in hypercoagulable state[14]. GA is the Schiff base formed by serum protein amidogen and glucose aldehyde group, its content is abundant in blood circulation, and can activate nuclear factor κ B (NF- κ B) to promote inflammation-related gene expression, up-regulate inducible nitric oxide synthase expression, increase the body's oxidative stress and induce mononuclear cell differentiation into foam cell. MCP-1 is an important factor of the chemotaxis of monocytes that can specifically act on the mononuclear cells in the blood and attract them to inner endothelium, which is the important mechanism of atherosclerosis. NT-proBNP is the other half product when proBNP split into BNP and is extremely sensitive to myocardial ischemia, and NT-proBNP level can reflect the scope and severity of ischemic injury, and has important significance in the early diagnosis and risk classification of patients with ACS[15]. PAC-1 is an important part of the platelet activation aggregation, its level can rise early when ACS occurs, and it is an effective indicator to judge the ACS severity. Results of above research showed that serum GA, MCP-1, PAI-1, NT-proBNP, PAC-1, VCAM-1 and ICAM-1 values of observation group after treatment were lower, indicating that small dose of tirofiban therapy before PCI treatment could effectively optimize the illness in patients.

To sum up, it is concluded as follows: small dose of tirofiban combined with PCI treatment for patients with acute coronary syndrome can effectively enhance therapeutic effect, inhibit platelet activity while protect heart function, and it's worth popularization in clinical practice in the future.

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