Effect of tirofiban combined with PCI on myocardial damage and platelet activation in patients with STEMI

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ABSTRACT

Objective: To study the effect of tirofiban combined with PCI on myocardial damage and platelet activation in patients with STEMI. Methods: Patients with STEMI who were treated and underwent PCI in Wujiang First People's Hospital in Suzhou between March 2015 and February 2017 were selected as the research subjects and randomly divided into two groups, intervention group received tirofiban combined with PCI therapy, control group received routine PCI therapy, and the myocardial damage indexes and platelet activation indexes of two groups of patients were detected. Results: 24 h after PCI treatment, serum S100A/B, H-FABP, GDF-15, cTnT, FKN, MDA, sFas, sTWEAK and 8-OHdG levels of intervention group were obviously lower than those of control group; before PCI treatment and 24 h after PCI treatment, peripheral blood CD62p and PAC-1 expression intensity as well as serum P-selectin, thrombospondin and CD40 ligand levels of intervention group were obviously lower than those of control group. Conclusion: Tirofiban therapy before PCI can help alleviate myocardial damage and inhibit platelet activation.

1. Introduction

ST segment elevation myocardial infarction (STEMI) is a clinical common cardiovascular system disease and belongs to the category of acute coronary syndrome, and the coronary occlusion and myocardial cell ischemia hypoxia are the basic pathological characteristics of the disease. STEMI had high mortality and poor prognosis. In recent years, percutaneous coronary intervention (PCI) has been increasingly used for the emergency treatment of acute myocardial infarction, which can effectively recanalize the coronary artery and restore myocardial perfusion, and has exact and positive clinical value. However, there is widespread excessive platelet activation in patients with acute myocardial infarction, and the in-stent thrombosis will occur after PCI and influence myocardial perfusion[1,2]. Therefore, antiplatelet therapy should be performed in the perioperative period of PCI. Tirofiban is an antagonist of the glycoprotein IIb/IIIa receptor on the platelet membrane[3]. The effect of tirofiban combined with PCI on myocardial damage and platelet activation in patients with STEMI was specifically analyzed in the following studies.

2. Clinical information and research methods

2.1 Clinical information of enrolled patients

Patients with STEMI who were treated and underwent PCI in Wujiang First People’s Hospital in Suzhou between March 2015 and February 2017 were selected as the research subjects, all patients were with STEMI confirmed by myocardial injury biochemical indexes and electrocardiogram examination, onset time was ≤12 h, and the patients with cardiac Killip IV, those combined with cardiogenic shock and those with contraindications to antiplatelet therapy were excluded. A total of 152 patients were enrolled and divided into the intervention group and control group according to the tirofiban application before PCI. There were 69 cases in the intervention group, including 42 male cases and 27 female cases.
that were 47-71 years old; control group included 83 cases, including 54 male cases and 29 female cases that were 45-70 years old. There was no significant difference in general information between the two groups of patients.

2.2 Therapy

Both groups of patients chewed 300 mg of Aspirin Enteric-coated Tablets and 300 mg of Clopidogrel Hydrogen Sulphate Tablets immediately after admission, and then received PCI treatment according to the following method: the catheter was inserted after radial artery or femoral artery puncture, coronary angiography was done after cathetering, the area with coronary artery infarction was judged according to the angiography results, thrombus suction or intravascular drug injection was selected according to the situation of vascular infarction, and the stent was placed at last. Intervention group received tirofiban before PCI, and the method was as follows: continuous micropump injection of 5 mg of tirofiban sodium chloride injection at 0.2 mg/kg/min.

2.3 Myocardial injury index detection

24 h after PCI, 1-2 mL of cubital venous blood was collected from two groups of patients and centrifuged to separate serum, and then enzyme-linked immunosorbent assay kit was used to determine S100A/B, H-FABP, GDF-15, cTnT, FKN, MDA, sFas, sTWEAK and 8-OHdG levels.

2.4 Platelet activation index detection

Before PCI and 24 h after PCI, 3 mL of cubital venous blood was collected from two groups of patients and divided into two, one was centrifuged to separate serum and determine the P-selectin, thrombospondin and CD40 ligand contents by enzyme-linked immunosorbent kit, and the other was anti-coagulated to determine the expression intensity of CD62p and PAC-1 with flow cytometer.

2.5 Statistical methods

SPSS 18.0 software was used to input data, the measurement data between the two groups were by \( t \) test, and \( P < 0.05 \) indicated statistical significance in differences.

3. Results

3.1 Myocardial injury indexes

24 h after PCI treatment, analysis of serum myocardial injury markers S100A/B (ng/L), H-FABP (pg/L), GDF-15 (μg/L), cTnT (μg/L) and FKN (ng/L) as well as myocardial oxidative injury indexes MDA (μmol/L), sFas (μg/L), sTWEAK (ng/L) and 8-OHdG (μg/L) between two groups of patients was as follows: serum S100A/B, H-FABP, GDF-15, cTnT, FKN, MDA, sFas, sTWEAK and 8-OHdG levels of intervention group were obviously lower than those of control group. Differences in serum S100A/B, H-FABP, GDF-15, cTnT, FKN, MDA, sFas, sTWEAK and 8-OHdG levels were statistically significant between two groups of patients 24 hours after treatment (\( P < 0.05 \)).

Table 1.
Comparison of serum myocardial injury markers between two groups of patients.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>S100A/B (ng/L)</th>
<th>H-FABP (pg/L)</th>
<th>GDF-15 (μg/L)</th>
<th>cTnT (μg/L)</th>
<th>FKN (ng/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention</td>
<td>69</td>
<td>125.2±15.9</td>
<td>29.3±4.6</td>
<td>0.52±0.08</td>
<td>2.41±0.35</td>
<td>0.61±0.08</td>
</tr>
<tr>
<td>Control</td>
<td>83</td>
<td>194.5±25.2</td>
<td>40.2±5.9</td>
<td>0.93±0.14</td>
<td>3.77±0.51</td>
<td>1.24±0.18</td>
</tr>
<tr>
<td>( t )</td>
<td></td>
<td>8.109</td>
<td>7.428</td>
<td>9.338</td>
<td>7.139</td>
<td>10.948</td>
</tr>
<tr>
<td>( P )</td>
<td></td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

3.2 Platelet activation indexes

Before PCI and 24 h after PCI treatment, analysis of platelet activation indexes CD62p, PAC-1, P-selectin, thrombospondin and CD40 ligand between two groups of patients was as follows: peripheral blood CD62p and PAC-1 expression intensity as well as serum P-selectin, thrombospondin and CD40 ligand levels of intervention group were obviously lower than those of control group. Differences in serum CD62p, PAC-1, P-selectin, thrombospondin and CD40 ligand levels of intervention group were statistically significant between two groups of patients before PCI treatment and 24 hours after PCI treatment (\( P < 0.05 \)).

Table 3.
Comparison of platelet activation indexes between two groups of patients.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Time</th>
<th>CD62p</th>
<th>PAC-1</th>
<th>P-selectin</th>
<th>Thrombospondin</th>
<th>CD40 ligand</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention</td>
<td>69</td>
<td>Before PCI</td>
<td>24.61±3.52</td>
<td>18.45±2.75</td>
<td>6.59±0.93</td>
<td>26.59±3.48</td>
<td>15.41±1.98</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After PCI</td>
<td>19.39±2.36</td>
<td>13.59±1.76</td>
<td>4.52±0.68</td>
<td>19.39±2.14</td>
<td>12.15±1.58</td>
</tr>
<tr>
<td>Control</td>
<td>83</td>
<td>Before PCI</td>
<td>33.78±5.29</td>
<td>25.53±3.29</td>
<td>9.49±1.13</td>
<td>40.28±5.85</td>
<td>23.59±3.29</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After PCI</td>
<td>26.51±3.52</td>
<td>21.38±2.93</td>
<td>8.49±1.09</td>
<td>33.58±4.57</td>
<td>19.29±2.35</td>
</tr>
</tbody>
</table>

* comparison between intervention group and control group, \( P < 0.05 \).
4. Discussion

PCI is the first choice of clinical treatment of acute myocardial infarction, which can reconnect the occluded coronary artery and restore the myocardial perfusion in time. PCI is significantly valuable for myocardial infarction, but under the influence of persistent platelet activation in the patients, there is the risk of in-stent thrombosis after PCI, which will affect myocardial perfusion and cause myocardial no-reflow. Excessive platelet activation is an important factor affecting blood perfusion after PCI, so it is necessary to perform antiplatelet therapy in perioperative period of PCI. Tirofiban is a kind of high-selective platelet glycoprotein IIb/IIIa receptor antagonist that has the characteristics of rapid onset, strong effect and fast metabolism[4]. 5 minutes after it enters the body, the drug can make the platelet inhibition rate reach 98% and it has strong anti-platelet effect; at the same time, the half-life of the drug is only 2, and the function of platelets can be restored 2-4 hours after the drug was taken, which can reduce the risk of bleeding[5,6]. At present, the value of intra-coronary administration of tirofiban during PCI is accurate, but it is not clear about the value of its intravenous administration before PCI.

The myocardial cell damage in patients with myocardial infarction can cause many marker molecules in cells to be released into the blood circulation, and the changes in corresponding marker molecules can reflect the degree of myocardial injury. S100A/B is a calcium-containing protein synthesized by neutrophils and macrophages, which infiltrates in the infarcted lesion and causes the S100A/B secretion to increase in the process of myocardial infarction; H-FABP is a fatty acid binding protein rich in myocardium, and involved in the transport of fatty acids and the process of oxidative energy supply[7]; GDF-15 is a type of protective cytokine expressed in myocardial cells, it belongs to the TGF-β superfamily, and it is increasingly expressed as compensation and released into the blood circulation in the process of myocardial infarction[8]; cTnT is a specific protein that regulates the calcium ion transport and myocardial contraction in myocardial cells, which can sensitively reflect the myocardial injury[9]; FKN is a kind of adhesion molecule, which can promote the deposition of macrophage-derived foam cells in coronary arteries and participate in coronary artery infarction after it identifies receptor CX3CR1[10]. In the research, the analysis of the changes in above myocardial injury markers in serum after PCI treatment showed that serum S100A/B, H-FABP, GDF-15, cTnT and FKN levels of intervention group were obviously lower than those of control group. This indicates that tirofiban application before PCI can significantly reduce the degree of myocardial injury.

In the process of coronary artery infarction and myocardial ischemia hypoxia, the massive generation of oxygen free radicals is the important pathological process that causes myocardial cell injury. The massively generated oxygen free radicals can on the one hand, damage the structure of myocardial cells by oxidative stress, and on the other hand, cause myocardial cell death by apoptosis activation. In the process of oxidative stress reaction, the lipid and nucleic acid in myocardial cells will have oxidation reaction and generate the corresponding oxidation products MDA and 8-OHdG, and can also cause the cellular structure damage[11,12]. In the process of myocardial cell apoptosis, Fas and TWEAK are important molecules that mediate apoptosis, and sFas and sTWEAK are their soluble forms respectively. sFas can identify the ligand FasL to initiate the cascade reaction mediated by Caspase8 and then cause apoptosis; sTWEAK induces apoptosis and can enhance the activity of various caspase molecules and induce cell apoptosis[13,14]. In the study, the analysis of the changes in above serum myocardial oxidative injury indexes after PCI treatment showed that serum MDA, sFas, sTWEAK and 8-OHdG levels of intervention group were obviously lower than those of control group. This indicates that tirofiban application before PCI can significantly reduce the myocardial injury caused by oxidative stress response.

The value of tirofiban for myocardial infarction is to inhibit the platelet activation and adhesion mediated by GPIIb/IIIa on platelet surface. In the process of platelet activation, a variety of molecules on the platelet surface and granule surface in platelet plasma are exposed and mediate the continuous thrombosis. CD62p is the glycoprotein on granule surface in platelet plasma. When platelets are activated, the CD62p can be released and fused with platelet membrane to activate the process of thrombosis; PAC-1 is the binding site of platelet surface fibrin, and the changes in GPIIb/IIIa conformation during platelet activation can lead to PAC-1 exposure and promote the fibrin aggregation and thrombosis[15]. At the same time, in the activation of platelet, p-selectin, thrombospondin, CD40 ligand and other molecules are increasingly released, and can mediate platelet chemotaxis and adhesion during the process[16]. In the study, analysis of the changes in above platelet activation indexes after PCI treatment showed that peripheral blood CD62p and PAC-1 expression intensity as well as serum P-selectin, thrombospondin and CD40 ligand levels of intervention group were obviously lower than those of control group. This indicates that tirofiban application before PCI can significantly reduce the activation of platelets.

Based on the analysis of above clinical indexes, it shows that tirofiban application before PCI can alleviate the myocardial damage degree, and can also inhibit the activation of oxidative stress reaction and apoptosis as well as the platelet activation.
References


