Myocardium-protective effect of ticagrelor combined with emergency PCI treatment of acute myocardial infarction

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1. Introduction

Acute ST-segment elevation myocardial infarction (STEMI) is an important cardiovascular disease threatening people’s life health and safety, it develops rapidly and both mortality and morbidity are high. The pathological basis of STEMI is coronary artery atherosclerotic plaque rupture and thrombosis as well as the resulting coronary vascular obstruction, and the platelet activation and aggregation are the key links in the process of thrombosis. Recanalizing coronary artery, restoring myocardial perfusion and implementing necessary anti-platelet therapy as soon as possible are the key to clinical treatment. Percutaneous coronary intervention (PCI) is an effective method for clinical emergency treatment of STEMI, and the dual anti-platelet drugs based on aspirin are the common anti-platelet therapy[1,2]. Combined therapy of clopidogrel and aspirin has the most wide clinical application, but under the influence of CYP2C19 gene polymorphisms, the responsiveness of some patients to clopidogrel is poor, and therefore, the anti-platelet effect is not ideal[3,4]. Ticagrelor is a new type of anti-platelet medicine, it has anti-platelet activity and can exert anti-platelet effect in the body without the metabolism and activation by cytochrome P450 in the liver, and it has the advantages of quicker and stronger action[5]. In the following study, the myocardium-protective effect of ticagrelor combined with emergency PCI treatment of acute myocardial infarction was analyzed and the possible molecular mechanisms were explored.

2. Materials and methods

Objective: To study the myocardium-protective effect of ticagrelor combined with emergency PCI treatment of acute myocardial infarction and explore the possible molecular mechanisms. Methods: A total of 84 patients with acute myocardial infarction who received emergency PCI treatment in our hospital from February 2014 to October 2015 were selected for study and randomly divided into and ticagrelor group and clopidogrel group that received different perioperative anti-platelet therapy. Degree of myocardial cell damage, cardiac pump function as well as blood perfusion and platelet aggregation function of two groups were evaluated. Results: Before as well as 10 min and 24 h after PCI, plasma CK-MB and cTnI levels as well as maximum platelet aggregation rate and P2Y12 reaction unit of ticagrelor group were significantly lower than those of clopidogrel group, and ADP-way platelet inhibition rate were higher than those of clopidogrel group; after PCI, TIMI blood flow grade, TMP myocardial perfusion grade and LVEF of ticagrelor group were significantly higher than those of clopidogrel group, LVEDD was significantly lower than that of clopidogrel group and the number of cases with no reflow/slow flow was less than that of clopidogrel group. Conclusions: The myocardium-protective effect of ticagrelor combined with emergency PCI treatment of acute myocardial infarction is better than that of clopidogrel, and ticagrelor can enhance the anti-platelet aggregation effect to exert myocardium-protective effect.
2.1. Subjects

A total of 84 patients with acute myocardial infarction who received emergency PCI treatment in our hospital from February 2014 to October 2015 were selected for study, all patients were admitted to hospital within 8h after the onset and diagnosed with ST-elevation myocardial infarction by ECG examination, and emergency PCI therapy was proposed. According to different perioperative anti-platelet therapy, they were randomly divided into ticagrelor group and clopidogrel group: (1) ticagrelor group: 42 cases included 27 male cases and 15 female cases, they were (62.1±7.9) years old, 12 cases were complicated with type 2 diabetes and 17 cases were complicated with hyperlipidemia; (2) clopidogrel group: 42 patients included 29 male cases and 13 female cases, they were (61.3±8.1) years old, 14 cases were complicated with type 2 diabetes and 16 cases were complicated with hyperlipidemia. The comparison of general data between two groups showed no significant difference.

2.2. Treatment methods

Clopidogrel group were treated by 600 mg of clopidogrel sulfate tablets, 300 mg of aspirin enteric-coated tablets before operation, and ticagrelor group were treated by 180 mg of ticagrelor and 300 mg of aspirin enteric-coated tablets before operation. After the examination was completed, PCI treatment was conducted, and stent implantation or stent implantation after balloon dilation was conducted according to the radiography. Anti-platelet therapy was continued after operation, clopidogrel group received oral administration of clopidogrel sulfate tablets 75 mg/d and aspirin enteric-coated tablets 100 mg/d, and ticagrelor group received oral administration of ticagrelor 90mg/bid and aspirin enteric-coated tablets 100 mg/d, which was changed to oral administration of clopidogrel sulfate tablets 75 mg/d and aspirin enteric-coated tablets 100 mg/d.

2.3. Clinical index evaluation

Before as well as 10 min and 24 h after PCI, 10ml of peripheral blood was extracted from two groups and centrifuged to separate serum, then enzyme-linked immunosorbent assay was used to determine creatine kinase isoenzyme (CK-MB) and troponin I (cTnI) levels, platelet aggregation separator and matched reagent were used to get maximum platelet aggregation rate and ADP-way platelet inhibition rate, and anti-platelet therapy detection system and supporting light path quality control plate were used to detect P2U12 reaction unit. After operation, myocardial and coronary blood perfusion was judged according to the TIMI blood flow grade and TMP myocardial perfusion grade. On the very day after operation, color Doppler ultrasonography was conducted to determine left ventricular ejection fraction (LVEF) and left ventricular end-diastolic dimension (LVEDD).

2.4. Statistical methods

SPSS20.0 software was used to input and analyze data, measurement data analysis was performed by t test, count data analysis by chi-square test and P<0.05 indicated statistical significant differences.

3. Results

3.1. Myocardial damage molecules

Plasma CK-MB levels as well as cTnI levels of ticagrelor group were significantly lower than those of clopidogrel group (Table 1).

### Table 1

<table>
<thead>
<tr>
<th>Groups</th>
<th>Points in time</th>
<th>CK-MB (IU/L)</th>
<th>cTnI (ng/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ticagrelor group</td>
<td>Before PCI</td>
<td>178.42±22.62</td>
<td>52.23±7.85</td>
</tr>
<tr>
<td>(n=42)</td>
<td>10 min after PCI</td>
<td>205.61±31.57</td>
<td>67.45±9.14</td>
</tr>
<tr>
<td></td>
<td>24 h after PCI</td>
<td>124.52±23.03</td>
<td>40.28±5.73</td>
</tr>
<tr>
<td>Clopidogrel group</td>
<td>Before PCI</td>
<td>258.89±31.47</td>
<td>89.36±11.36</td>
</tr>
<tr>
<td>(n=42)</td>
<td>10 min after PCI</td>
<td>331.25±42.74</td>
<td>110.33±16.69</td>
</tr>
<tr>
<td></td>
<td>24 h after PCI</td>
<td>190.41±27.54</td>
<td>70.29±8.76</td>
</tr>
</tbody>
</table>

*: compared with clopidogrel group at the same point in time, P<0.05; **: compared with clopidogrel group at the same point in time, P<0.01.

3.2. Myocardial function and blood flow

TIMI blood flow grade and TMP myocardial perfusion grade of ticagrelor group were significantly higher than those of clopidogrel group, and the number of cases with no reflow/slow flow was less than that of clopidogrel group; heart color Doppler ultrasound spectrum was shown in Figure 1. LVEF of ticagrelor group was significantly higher than that of clopidogrel group, and LVEDD was significantly lower than that of clopidogrel group (Table 2).

### Table 2

Myocardial function and blood flow of two groups.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Case No.</th>
<th>TIMI grade</th>
<th>TMP grade</th>
<th>No reflow/slow flow</th>
<th>LVEF (%)</th>
<th>LVEDD (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ticagrelor group</td>
<td>42</td>
<td>2.89±0.36</td>
<td>2.92±0.37</td>
<td>0</td>
<td>56.97±9.26</td>
<td>45.29±6.12</td>
</tr>
<tr>
<td>Clopidogrel group</td>
<td>42</td>
<td>2.21±0.28</td>
<td>2.19±0.38</td>
<td>6†</td>
<td>48.28±6.71</td>
<td>51.29±7.29</td>
</tr>
</tbody>
</table>

*: compared with clopidogrel group at the same point in time, P<0.05; †: compared with clopidogrel group at the same point in time, P<0.01.
3.3. Platelet aggregation function

ADP-way platelet inhibition index of Ticagrelor group were higher than those of clopidogrel group, and both maximum platelet aggregation index and P2Y12 reaction unit were lower than those of clopidogrel group (Table 3).

4. Discussion

Routine clopidogrel combined with aspirin is needed for peri-PCI anti-platelet therapy, and the use of anti-platelet drugs can improve hypercoagulable state, increase myocardial perfusion and protect myocardial cells. Aspirin is a cyclooxygenase inhibitor that can block the production of thromboxane A2 and exert anti-platelet effect, and it has to be combined with ADP receptor antagonist clopidogrel to obtain the exact anti-platelet effect[6]. The clinical practice and studies in recent years have found that inadequate anti-platelet therapy can increase the risk of stent thrombosis and influence the prognosis of patients[7,8]. In anti-platelet therapy with clopidogrel, there is CYP2C19 gene polymorphisms in different crowds, the drug responsiveness is different, and there is clopidogrel resistance in about 5%–44% of the patients in the treatment, which will affect the recovery of myocardial perfusion and overall prognosis after PCI[9,10]. Therefore, exploring more effective peri-PCI anti-platelet therapy has received more and more attention.

Ticagrelor is a new type of P2Y12 receptor antagonist used for clinical anti-platelet therapy in recent years, it has rapid onset and strong function and its activity is not affected by CYP2C19 gene polymorphisms, which makes up for the defects of clopidogrel for anti-platelet therapy[11,12]. In the study, Ticagrelor combined with aspirin was used for peri-PCI anti-platelet therapy, aiming at exerting the anti-platelet effect of Ticagrelor. First of all, myocardial damage molecules CK-MB and cTnI levels in plasma were analyzed, and the results showed that before as well as 10 min and 24 h after PCI, plasma CK-MB and cTnI levels of Ticagrelor group were significantly lower than those of clopidogrel group. This means that the effect of Ticagrelor on alleviating myocardial cell damage is better than that of clopidogrel. Really effective anti-platelet therapy can improve myocardial perfusion and help the recovery of cardiac function, and analysis of myocardial function and blood flow after PCI in the study confirmed that TIMI blood flow grade, TMP myocardial perfusion grade and LVEF of Ticagrelor group were significantly higher than those of clopidogrel group, and the number of cases with no reflow/slow flow and LVEDD were lower than those of clopidogrel group. This means that perioperative anti-platelet therapy with Ticagrelor could reduce myocardial cell injury, improve myocardial perfusion and enhance cardiac systolic and diastolic function.

Both clopidogrel and ticagrelor belong to ADP receptor antagonists, and can antagonize platelet aggregation by ADP way and exert anti-platelet aggregation effect. After entering the body, clopidogrel needs to be metabolized by cytochrome P450 isoenzyme so as to be converted into active metabolites, and CYP2C19 gene polymorphism in patients can affect the activity of cytochrome P450 isoenzyme, resulting in the different responsiveness of patients to clopidogrel, and influencing the effect of peri-PCI anti-platelet therapy[13,14]. Ticagrelor is the antagonist that can be reversibly combined with P2Y12 receptor, has the anti-platelet biological activity itself, and doesn't need the bioconversion of hepatic metabolic enzyme to exert the anti-platelet effect. Ticagrelor, therefore, can more quickly exert anti-platelet activity after oral administration and lasts longer[15-17]. So it was speculated that ticagrelor could inhibit platelet aggregation to protect the myocardial cells and enhance myocardial perfusion.

Analysis of the platelet aggregation function in the study confirmed that before as well as 10 min and 24 h after PCI, ADP-way platelet inhibition rate of ticagrelor group was higher than that of clopidogrel group.
group, and the maximum platelet aggregation rate and P2Y12 reaction unit were lower than those of clopidogrel group. It confirms that the anti-platelet aggregation effect of ticagrelor is better than that of clopidogrel.

To sum up, the myocardium-protective effect of ticagrelor combined with emergency PCI treatment of acute myocardial infarction is better than that of clopidogrel, and ticagrelor can enhance the anti-platelet aggregation effect to exert myocardium-protective effect.

References


