Effects of preoperative trimetazidine application on myocardial injury indexes and oxidative stress indexes in patients with AMI after PCI

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1. Introduction

Acute myocardial infarction (AMI) is one of the most serious clinical cardiovascular diseases caused by coronary acute and persistent ischemia hypoxia, and patients can be complicated with cardiac arrhythmia, shock, etc., which can directly endanger the life[1,2]. Percutaneous coronary intervention (PCI) is a kind of technique that dredges stenotic/occluded coronary vascular cavity and improves myocardial perfusion, it is one of the most reliable means for current treatment of AMI, and it can rapidly improve the myocardial ischemia hypoxia and avoid the irreversible myocardial cell necrosis caused by continuous hypoxia[3,4]. But along with the popularity of clinical PCI treatment, more and more cases have shown that there are different degrees of myocardial ischemia-reperfusion injury after PCI, which may affect the PCI treatment effect and even result in serious consequences. Trimetazidine is a kind of antianginal drug, the current cytological studies have confirmed that it has positive effect on myocardial cell protection, and therefore, some scholars suggest it be applied in perioperative treatment of PCI in order to optimize the myocardial function after PCI[5,6]. In this study, trimetazidine was used for combined treatment before PCI, and the effects of this treatment on myocardial injury and oxidative stress response of AMI patients after PCI were discussed.

2. Information and methods

2.1 Inclusion criteria

(1) In accordance with the clinical diagnostic criteria for AMI; (2) in accordance with the indications of emergency PCI; (3) 80 years old; (4) without the history of trimetazidine application; (5) whose family members signed the informed consent.
2.2 Exclusion criteria

(1) Combined with infective endocarditis and other heart diseases;
(2) combined with systemic infectious diseases; (3) combined with severe cardiac, hepatic or renal insufficiency; (4) severe allergic reactions after the use of trimetazidine; (5) dropping out of the treatment without the doctor’s consent, and with the clinical data missing.

2.3 Case information and grouping

A total of 70 patients with AMI received emergency PCI in our hospital between January 2015 and January 2018, and were divided into the control group (n=35) (received no trimetazidine) and the trimetazidine group (n=35) (received trimetazidine) according to the application of trimetazidine before PCI or not. There were 20 males and 15 females in the control group, and they were 51–77 years old; there were 21 males and 14 females in the trimetazidine group, and they were 51–77 years old. There was no statistically significant difference in the distribution of basic data between groups (P>0.05), and the research proposal was submitted to and approved by the ethics committee of the hospital.

2.4 Therapy

Control group received routine emergency PCI treatment, which was as follows: Judikin’s catheter was used for femoral artery puncture, angiography was conducted to confirm the infarction scope and extent, and the contrast agent was injected for coronary angiography. 100 mg of aspirin and 75 mg of clopidogrel bisulfate were provided before stent implantation, the patients’ specific vascular conditions were referred to choose the right types of stent and balloon, the balloon pressure was controlled between 4–16 atm, the dilatation lasted for 10–20 s, and the dilatation degree should be greater than 20% of the stenotic blood vessels. The drug-eluting stents were implanted, and they were given subcutaneous injection of low molecular heparin after operation, took 100 mg of aspirin orally, 1 time/d, and continuously took clopidogrel tablets for 9–12 months.

Trimetazidine group received trimetazidine treatment before PCI, which was as follows: they took loading dose of trimetazidine 60 mg at draught 2 h before PCI, and took 20 mg at draught after operation, 3 timesiday for 12 consecutive weeks.

2.5 Observation indexes

Peripheral venous blood samples were collected from the patients immediately after admission and 24 h after PCI, and the serum was isolated and cryopreserved for test. Immunofluorescence quantitative method was used to determine the serum levels of myocardial injury markers creatine kinase isoenzyme (CK-MB), troponin I (cTn I), myoglobin (Myo) and heart-type fatty acid-binding protein (h-FABP); ELISA was used to determine the serum levels of inflammatory factors high-sensitive C-reactive protein (hs-CRP), Neopterin and interleukin-1β (IL-1β); the ELISA was adopted to determine the serum levels of oxidative stress indexes superoxide dismutase (SOD), malondialdehyde (MDA) and lipid hydroperoxide (LHP).

2.6 Statistical methods

The myocardial injury markers, inflammatory factors and oxidative stress indexes involved in the study were measurement data, expressed as mean ± standard deviation and calculated by software SPSS 24.0, and the obtained statistic P<0.05 indicated that the difference was statistically significant.

3. Results

3.1 Myocardial injury markers

Comparison of serum myocardial injury markers CK-MB, cTn I, Myo and h-FABP levels of two groups of patients at different points in time was as follows: immediately after admission, serum CK-MB, cTn I, Myo and h-FABP levels were not significantly different between the two groups of patients (P>0.05); 24 h after surgery, serum CK-MB, cTn I, Myo and h-FABP levels of both groups showed a significant difference (P<0.05).

Table 2.

Comparison of serum inflammatory factor levels.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Immediately after admission</th>
<th>24 h after surgery</th>
<th>Immediately after admission</th>
<th>24 h after surgery</th>
<th>Immediately after admission</th>
<th>24 h after surgery</th>
<th>Immediately after admission</th>
<th>24 h after surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>35</td>
<td>12.38±1.79</td>
<td>7.01±0.78</td>
<td>8.21±0.95</td>
<td>5.09±0.54</td>
<td>23.47±2.68</td>
<td>17.09±2.16</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tratamentidine</td>
<td>35</td>
<td>12.56±1.68</td>
<td>3.96±0.45</td>
<td>8.17±0.92</td>
<td>3.18±0.35</td>
<td>23.95±2.74</td>
<td>11.24±1.85</td>
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<tr>
<td>t</td>
<td></td>
<td>0.284</td>
<td>10.495</td>
<td>0.195</td>
<td>7.596</td>
<td>0.361</td>
<td>8.264</td>
<td></td>
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<tr>
<td>P</td>
<td></td>
<td>&gt;0.05</td>
<td>&lt;0.05</td>
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<td>&gt;0.05</td>
<td>&lt;0.05</td>
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<td></td>
</tr>
</tbody>
</table>

Note: compared with same group immediately after admission, P<0.05.
were lower than those immediately after admission ($P<0.05$). 24 h after surgery, serum CK-MB, cTn I, Myo and h-FABP levels of trimetazidine group were lower than those of control group ($P<0.05$), shown in Table 1.

### 3.2 Inflammatory factors

Comparison of serum inflammatory factors hs-CRP (mg/L), Neopterin (nmol/L) and IL-1 β (pg/mL) levels of two groups of patients at different points in time was as follows: immediately after admission, serum hs-CRP, Neopterin and IL-1 β levels were not significantly different between the two groups of patients ($P>0.05$), 24 h after surgery, serum hs-CRP, Neopterin and IL-1 β levels of both groups were lower than those immediately after admission ($P<0.05$). 24 h after surgery, serum hs-CRP, Neopterin and IL-1 β levels of trimetazidine group were lower than those of control group ($P<0.05$), shown in Table 2.

### 3.3 Oxidative stress indexes

Comparison of serum oxidative stress indexes SOD (U/L), MDA (μmol/L) and LHP (μmol/L) levels of two groups of patients at different points in time was as follows: immediately after admission, serum SOD, MDA and LHP levels were not significantly different between the two groups of patients ($P>0.05$); 24 h after surgery, serum SOD levels of both groups were higher than those immediately after admission whereas MDA and LHP levels were lower than those immediately after admission ($P<0.05$). 24 h after surgery, serum SOD level of trimetazidine group was higher than that of control group whereas MDA and LHP levels were lower than those of control group ($P<0.05$), shown in Table 3.

### 4. Discussion

The early mortality rate of AMI is extremely high if the patients were not treated in time. PCI is one of the most reliable methods for current treatment of AMI. It can directly dilate the stenotic coronary arteries, increase myocardial blood supply and reduce the myocardial injury caused by ischemia hypoxia. However, PCI not only recovers myocardial blood supply, but also brings another difficult problem - ischemia reperfusion injury. At present, many studies have shown that there is significant myocardial injury again in patients with AMI within a short period of time after PCI, which directly affects the therapeutic effect of PCI and can even lead to the occurrence of secondary AMI[7,8]. How to effectively reduce or avoid the occurrence of myocardial injury after PCI is the focus of current clinical research. Trimetazidine is a new drug against myocardial ischemia, and it inhibits myocardial fatty acid β oxidation to improve glycolysis and glucose oxidation coupling and finally achieve the goal of optimizing the myocardial cell energy metabolism[9,10]. At the same time, trimetazidine has neither obvious effect on hemodynamics, nor negative inotropic effect. In this study, trimetazidine was applied before PCI in order to determine whether its preventive use could alleviate the myocardial ischemia reperfusion injury after PCI.

There is obvious myocardial ischemic hypoxic injury in patients with AMI. PCI relieves coronary artery stenosis and recovers myocardial blood supply in infarcted area to a certain extent, so it can reverse myocardial damage, but the existence of postoperative ischemia-reperfusion injury can inhibit the self-healing function of myocardial cells, which is serologically manifested in the fluctuations of a variety of myocardial injury markers. CK-MB is the most common and typical clinical myocardial enzyme spectrum index, it is released from the inside to the outside of the cells early after myocardial injury, and the abnormal increase of CK-MB content in the circulating blood is visual sign of myocardial injury in the body[11,12]. cTn I belongs to myocardin complexes, it specifically exists within myocardial cells under physiological condition, and the change in serum cTn I content has good directivity to myocardial damage[13]. Myo is a protein that specifically exists in the striated muscle, its content is very little in normal human serum, but when the myocardium is damaged, the striated muscle will produce a large number of Myo and release them into the blood[14,15]. h-FABP is the myocardial injury marker with the smallest molecular weight, which is released into the blood immediately after myocardial injury and has a high specificity and sensitivity to the diagnosis of myocardial injury[16]. In this study, serum levels of above myocardial injury markers of trimetazidine group 24 h after surgery were significantly lower than those of control group, which shows that preoperative preventive use of trimetazidine has played a positive role in myocardial protection.

Inflammation is one of the important causes of myocardial injury, the metal stents, balloon, etc. can all cause coronary mechanical expansion during PCI, vascular intima can be damaged to different extent, and a large number of inflammatory cytokines will be released. All kinds of inflammatory cytokines released can increase the overall inflammatory state of the body through the inflammatory cascade, and further participate in the development of myocardial injury. hs-CRP is an inflammatory factor with the highest sensitivity, the increase of serum hs-CRP levels could be detection almost at the same time after myocardial injury, and the degree of increase is positively correlated with the severity of myocardial injury[17]. Neopterin is a soluble marker released during the activation of macrophages and is also a risk indicator for ischemic heart disease. The increase in serum content is a sign of plaque rupture[18]. IL-1 β is also a typical pro-inflammatory factor, and its content change is basically consistent with that of hs-CRP. The results of the study showed that serum levels of above inflammatory markers of trimetazidine group 24 h after PCI were significantly lower than those of control group, it shows that the preventive use of trimetazidine before PCI could help reduce the synthesis of

### Table 3.

Comparison of serum oxidative stress index levels.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>SOD Immediately after admission (μmol/L)</th>
<th>24 h after surgery (μmol/L)</th>
<th>MDA Immediately after admission (μmol/L)</th>
<th>24 h after surgery (μmol/L)</th>
<th>LHP Immediately after admission (μmol/L)</th>
<th>24 h after surgery (μmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>35</td>
<td>9.48±1.05</td>
<td>14.32±1.61</td>
<td>15.48±1.39</td>
<td>9.77±0.94</td>
<td>20.45±2.78</td>
<td>13.18±1.69</td>
</tr>
<tr>
<td>Trimetazidine</td>
<td>35</td>
<td>9.37±0.97</td>
<td>18.64±2.09</td>
<td>15.57±1.41</td>
<td>6.12±0.68</td>
<td>20.31±2.66</td>
<td>9.42±0.98</td>
</tr>
</tbody>
</table>

Note: compared with same group immediately after admission, $P<0.05$.
inflammatory factors in the PCI, and this is also one of the important links of it to reduce postoperative myocardial injury.

The core mechanism of ischemia-reperfusion injury is oxidative stress reaction. When PCI dilates stenotic coronary artery and increase myocardial blood perfusion in local infarction, phospholipase A2 is activated and leads to the mass generation of ROS, and a large number of ROS can directly cause myocardial injury and even apoptosis, and can also cause myocardial apoptosis by mitochondrial pathway, endoplasmic reticulum pathway, DNA repair enzyme pathway, and so on[9,20]. The degree of oxidative stress reaction in the body is highly consistent with the degree of myocardial injury[21,22], the contents of oxidation and anti-oxidation factors of the two groups were detected in the study, and it was found that serum anti-oxidation factor SOD level of trimetazidine group 24 h after PCI was higher whereas oxidation factors MDA and LHP levels were was lower, it indicates that preoperative application trimetazidine before PCI can effectively suppress the oxidative stress reaction in patients with AMI, and this is the core mechanism of it to protect myocardial cells and reduce myocardial injury. Preventive use of trimetazidine in patients with AMI before PCI can effectively reduce the postoperative myocardial injury, and the realization of the myocardial protective effect is directly related to the inhibiting effect of trimetazidine on the systemic oxidative stress reaction.

References


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