Effects of atorvastatin combined with trimetazidine on cardiac function, inflammatory factors and endothelial function in patients with coronary artery disease

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ABSTRACT

Objective: To investigate the effects of atorvastatin combined with trimetazidine on cardiac function, inflammatory factors and endothelial function in patients with coronary artery disease. Method: A total of 164 patients with coronary artery disease were collected and randomly divided into observation group (n=83) and control group (n=81). Control group were given trimetazidine with conventional symptomatic treatments, and observation group were given atorvastatin on the basis of control group. The cardiac function, inflammatory factors and endothelial function were compared between two groups. Result: No significantly differences were found in all indexes before treatment between two groups. After different treatments, left ventricular ejection fraction (LVEF) in both group increased significantly. The left ventricular diastolic dimension (LVDD), total cholesterol (TC) and low densith lipoprotein cholesterol (LDL-C) decreased significantly. LVEF in observation group was significantly higher, while TC and LDL-C were significantly lower than that in control group. High sensitive C reactive protein (hsCRP), tumornecrosis factor-α (TNF-α), matrix metalloproteinase-9 (MMP-9) and malondialdehyde (MDA) decreased significantly after treatment. All inflammatory factors in observation group were lower than that in control group. Endothelin-1 (ET-1) decreased significantly after treatment, but nitrie oxide (NO) and circulating endothelial microparticles (cEMPs) increased significantly. ET-1 in observation group was lower, while NO and cEMPs were significantly higher than that in control group. Conclusion: Atorvastatin combined with trimetazidine can effectively improve the cardiac function, reduce the level of inflammatory factors and improve the endothelial function in patients with coronary artery disease.

1. Introduction

Coronary heart disease is mainly caused by vascular narrowing or obstruction in atherosclerosis of coronary artery, ultimately results in myocardial ischemia and hypoxia or even necrosis disease[1], and can cause a series of changes in cardiac function, inflammatory factors and endothelial function[2-4]. Atorvastatin and trimetazidine are clinical commonly used drugs for treatment of ischemic cardiomyopathy. In order to further clarify the role of atorvastatin in treatment of coronary heart disease, this study adopted different treatments by randomization and compared the differences between the two groups before and after treatment, and investigated the effects of atorvastatin combined with trimetazidine on cardiac function, inflammatory factors and endothelial function in patients with coronary artery disease, aimed to provide laboratory basis for the effective treatment of coronary heart disease.

2. Clinical data and methods

2.1. General data

From March 2014 to September 2015, 164 cases of patients...
with coronary artery disease from The First Affiliated Hospital of Xi'an Medical University were collected and randomly divided into observation group (83 cases) and control group (81 cases). In the observation group, total of 83 cases were composed of 47 male and 36 female, who were 46-78 (62.31±5.39) years old. In the control group, total of 81 cases were composed of 46 male and 35 female, who were 45-78 (62.98±7.27) years old. The gender and age of the two groups were not statistically different ($P>0.05$). All patients were diagnosed with naming and diagnostic standard of ischemic heart disease enacted by WHO in 1979, and exclusion of patients with severe heart failure, hepatic and renal dysfunction, cancer patients, patients with acute or chronic infectious diseases, patients with severe illness of other organs. This study was approved by the Ethics Committee, all patients volunteered for the study and signed the informed consent.

2.2. Methods

2.2.1. Drug-delivery method

The two groups were treated based on conventional therapy of giving oxygen, diuretics, vascular medicine and calcium antagonists. Atorvastatin (10 mg/once, once a day) combined with trimetazidine (20 mg/once, 3 times a day) were adopted in the observation group, and trimetazidine (20 mg/once, 3 times a day) was adopted in the control group. The courses of the two groups were 30 d.

2.2.2. Assay method

Left ventricular ejection fraction (LVEF) and left ventricular diastolic dimension (LVDD) were detected by color Doppler ultrasonography (Philips HD15000). Cholesterol (TC) and low densith lipoprotein cholesterol (LDL-C) were detected by enzyme method, the level of hypersensitive c-reactive protein (hs-CRP) was detected by immunity transmission turbidity with automatic biochemical analyzer (Hitachi 7060 type) and related reagents. Tumornecrosis factor-$\alpha$ (TNF-$\alpha$ ), matrix metalloproteinase-9 (MMP-9), malondialdehyde (MDA), Endothelin-1 (ET-1) and nitrie oxide (NO) were detected by enzyme linked immunosorbent assay (ELISA), TNF-$\alpha$ reagent was purchased from Beijing Dependend Biomedical co., LTD, MMP-9 reagent was purchased from R&D company (USA), MDA reagent was purchased from ELIXIR company (Canada), ET-1 and NO reagents were purchased from Shanghai tai biotechnology company (China). All operations were followed the instructions carefully. The detecting method of circulating endothelial microparticles (cEMPs) refers to the reference[5].

2.3. Statistics

SPSS 19.0 statistical software was adopted for data analysis. Measurement data were described as mean ± standard deviation (mean ± sd) after normality test, comparison between the different groups used independent sample $t$ test, comparison between the same patients before and after treatment used paired $t$ test. Values of $P<0.05$ were considered to be statistically significant.

3. Results

3.1. Comparison of cardiac function and lipid indexes before and after treatment

The indexes in both groups were not statistically significant before treatment ($P>0.05$). After different treatments, LVEF in both group increased significantly ($P<0.05$), while LVDD, TC and LDL-C decreased significantly ($P<0.05$). LVEF in the observation group was (43.66±6.53)% after treatment, which was significantly higher than that in the control group. TC and LDL-C in the observation group were (5.32±0.81) mmol/L and (2.18±0.39) mmol/L, which were significantly lower than that in the control group, and considered to be statistically significant ($P<0.05$). See Table 1.

3.2. Comparison of inflammatory factor levels before and after treatment

The indexes in both groups were not statistically significant before treatment ($P>0.05$). After different treatments, hsCRP, TNF-$\alpha$ , MMP-9 and MDA in both groups decreased significantly ($P<0.05$). hsCRP, TNF-$\alpha$ , MMP-9 and MDA in the observation group were (2.33±0.98) mg/L, (96.73±21.05) ng/mL, (32.58±9.60) ng/L and (8.63±0.96) $\mu$mol/L, respectively, which were significantly lower than that in the control group, and considered to be statistically significant ($P<0.05$). See Table 2.

Table 1.
Comparison of cardiac function and lipid indexes before and after treatment.

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Time</th>
<th>LVEF (%)</th>
<th>LVDD (mm)</th>
<th>TC (mmol/L)</th>
<th>LDL-C (mmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>83</td>
<td>Before treatment</td>
<td>36.48±5.74</td>
<td>62.37±9.64</td>
<td>5.33±0.83</td>
<td>3.16±0.48</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>36.48±5.74</td>
<td>52.10±8.35</td>
<td>3.92±0.58</td>
<td>2.18±0.39</td>
</tr>
<tr>
<td>Control</td>
<td>81</td>
<td>Before treatment</td>
<td>37.09±5.82</td>
<td>60.47±11.30</td>
<td>5.05±0.76</td>
<td>2.78±0.42</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>39.48±6.17</td>
<td>51.66±8.74</td>
<td>5.32±0.81</td>
<td>3.14±0.47</td>
</tr>
</tbody>
</table>

Note: compared with before treatment, $^aP<0.05$; compared with control group, $^bP<0.05$. 
3.3. Comparison of endothelial function before and after treatment

The indexes in both groups were not statistically significant before treatment ($P>0.05$). After different treatments, ET-1 in both groups decreased significantly ($P<0.05$), NO and cEMPs increased significantly ($P<0.05$). ET-1 in the observation group was $(61.02\pm13.58)$ μg/L, which was significantly lower than that in the control group. NO and cEMPs in the observation group were $(382.34\pm69.03)$ μmol/L and $(1\ 686.17\pm412.82)\times10^7$/L, respectively, which were significantly higher than that in the control group, and considered to be statistically significant ($P<0.05$). See Table 3.

4. Discussion

Coronary heart disease is mainly caused by atherosclerosis of coronary artery, results in local tissue fibrosis of heart, thickening of heart’s left ventricle and LVDD increase, affects the systolic and diastolic function of heart, so the patients with coronary heart disease have cardiac function changes[6,7]. In addition, the results showed that inflammation played an important role in the occurrence and development of coronary heart disease, including neutrophile granulocyte, mononuclear macrophage and lymphocyte which played promoting roles in the occurrence of coronary heart disease[8,9], increase of inflammatory factor levels also played promoting roles in the development of coronary heart disease[10,12]. The relationship between vascular endothelial function and cardiovascular disease is more and more clear with the deepening of the research on coronary heart disease. Researches suggested that impaired endothelial function is the prime core of cardiovascular disease, reduced arterial elasticity and atherosclerosis occur gradually with the endothelial function damage added[13,14].

Atorvastatin and trimetazidine are clinical commonly used drugs for treatment of ischemic cardiomyopathy. Atorvastatin belongs to the cholesterol-lowering drugs and can make the cholesterol synthesis decreased significantly, accelerates the remove of LDL-C, has the effects of inhibiting synthesis of low density lipoprotein cholesterol (VLDL-C) and reducing the concentration of triglyceride (TG) [15]. Researches suggested that atorvastatin can obviously reduce the incidence of coronary heart disease, its main mechanism is not only related to antihyperlipidemic effect, but also cardiovascular protective effects including anti-inflammatory effect and reducing serum fibrinogen concentration, which can effectively protect blood vessels and prevent atherosclerosis[16,18]. Trimetazidine belongs to pipеразине derivatives, is a new drug of myocardial cell for metabolism regulation, can effectively improve the myocardial and fatty acid metabolism, inhibit free radical generation, improve sugar metabolism and myocardial efficiency, and maintain the normal function of myocardium[19]. This study adopted atorvastatin combined with trimetazidine to treat the patients with coronary heart disease and compared the effects with trimetazidine treatment, and investigated the effects of the two treatments on cardiac function, inflammatory factors and endothelial function in patients with coronary artery disease.

The patients with coronary artery disease in this study were collected and randomly divided into observation group and control group, the results indicated that the indexes in both groups were not statistically significant before treatment, and the two groups were comparable. After different treatments for 30 d, the cardiac function and endothelial function in both groups have different degrees of improvement, and the improvement in the observation group which was adopted by atorvastatin combined with trimetazidine treatment was significantly better than that in the control group, showed that LVEF, NO and cEMPs were significantly higher than that in the

### Table 2
Comparison of inflammatory factor levels before and after treatment.

<table>
<thead>
<tr>
<th>Group</th>
<th>Time</th>
<th>hsCRP (mg/L)</th>
<th>TNF-$\alpha$ (ng/mL)</th>
<th>MMP-9 (ng/mL)</th>
<th>MDA (μmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>83</td>
<td>Before treatment</td>
<td>5.62±1.67</td>
<td>261.48±77.65</td>
<td>98.66±13.51</td>
</tr>
<tr>
<td>Control</td>
<td>81</td>
<td>After treatment</td>
<td>2.33±0.98$^a$</td>
<td>96.73±2.10$^a$</td>
<td>32.58±9.60$^a$</td>
</tr>
<tr>
<td></td>
<td>Before treatment</td>
<td>5.67±1.69</td>
<td>261.53±76.49</td>
<td>98.91±13.56</td>
<td>14.63±1.41</td>
</tr>
<tr>
<td></td>
<td>After treatment</td>
<td>4.01±1.08$^a$</td>
<td>178.32±38.4$^a$</td>
<td>42.41±11.11$^a$</td>
<td>9.81±1.01$^a$</td>
</tr>
</tbody>
</table>

Note: compared with before treatment, $^aP<0.05$; compared with control group, $^bP<0.05$.

### Table 3
Comparison of endothelial function before and after treatment.

<table>
<thead>
<tr>
<th>Group</th>
<th>Time</th>
<th>ET-1 (μg/L)</th>
<th>NO (μmol/L)</th>
<th>CEMPs ($\times10^7$/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>83</td>
<td>Before treatment</td>
<td>118.59±28.14</td>
<td>218.69±44.10</td>
</tr>
<tr>
<td></td>
<td>After treatment</td>
<td>61.02±13.58$^a$</td>
<td>382.34±69.03$^a$</td>
<td>1 686.17±412.82$^a$</td>
</tr>
<tr>
<td>Control</td>
<td>81</td>
<td>Before treatment</td>
<td>120.05±28.91</td>
<td>217.04±45.31</td>
</tr>
<tr>
<td></td>
<td>After treatment</td>
<td>70.61±15.67$^a$</td>
<td>330.78±56.50$^a$</td>
<td>1 300.14±333.54$^a$</td>
</tr>
</tbody>
</table>

Note: compared with before treatment, $^aP<0.05$; compared with control group, $^bP<0.05$. 
control group, while LVDD, lipid levels, inflammatory factor levels and ET-1 were significantly lower than that in the control group. The results indicated that combined with atorvastatin therapy can more effectively improve cardiac function and endothelial function in the patients with coronary heart disease compared with trimetazidine treatment, also further confirmed atorvastatin has strong anti-inflammatory effects at the same time, which was identical with those reported in literature[20,21].

In a word, atorvastatin combined with trimetazidine can effectively improve the cardiac function, reduce the level of inflammatory factors and improve the endothelial function in patients with coronary artery disease, and it is beneficial to the postoperative recovery and worthwhile for spreading in clinical practice.

References


