Effect of Atorvastatin intensive therapy on the serum inflammatory factors, platelet activity and fibrinolytic activity in patients with acute coronary syndrome

Xiao-Li Zhu, Yun Zhou, Fang Liu

Department of Cardiology, The Xinjiang Uyghur Autonomous Region Traditional Chinese Medicine Hospital, Xinjiang, Urumqi 830000, China

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ABSTRACT

Objective: To observe the effect of Atorvastatin intensive therapy on the serum inflammatory factors, platelet activity and fibrinolytic activity in patients with acute coronary syndrome (ACS). Methods: A total of 92 patients with ACS were randomly divided into observation group (47 cases) and control group (45 cases). The control group was given Atorvastatin (10 mg/d) based on the conventional therapy, while the observation group was given Atorvastatin at an intensive dose (40 mg/d) based on the conventional therapy. Half a month later, the changes of IL-6, IL-8, hs-CRP, TNF-α, TXB2, GMP-140, PAI-1 and t-PA were observed and compared between the two groups. Results: After treatment, the inflammatory factors (IL-6, IL-8, hs-CRP and TNF-α) and the indicators of platelet activity (TXB2, GMP-140 and PAI-1) were obviously decreased, while the indicator of fibrinolytic activity (t-PA) was apparently increased in the two groups. Besides, the amplitudes of change referring to these indicators in the observation group were bigger than those in the control group after treatment, and the differences were statistically significant. Conclusion: The intensive therapy with the administration of Atorvastatin at a dose of 40 mg/d was better than the conventional therapy (Atorvastatin 10 mg/d) in aspects of reducing inflammatory factors, inhibiting platelet activity and correcting the high coagulation state of fibrinolytic system.

1. Introduction

The erosion of atherosclerotic plaque is the main pathogenesis of acute coronary syndrome (ACS), and the secondary thrombosis due to the rupture or erosion induces the acute cardiac ischemia. At this very moment, the stabilization of atherosclerotic plaque and the inhibition of thrombosis are particularly important. Due to the features of anti-inflammation and anti-oxidation as well as the ability to improve the activity of platelet and fibrinolysis, statins has been greatly emphasized in clinical. However, the clinical results are far from the desired therapeutic effects, which result from the low-dose administration of drugs because of the concern of their safety. In recent years, among the ACS patients treated in our department, many cases adopted the Atorvastatin intensive therapy, which showed a beneficial effect on the serum inflammatory factor and the activity of platelet and fibrinolysis for ACS patients. Details are as follows.

2. Materials and methods

2.1. General data

From January 2014 to September 2015, a total of 92 patients with ACS were chosen as research objects. All patients had paroxysmal or persistent precordial region pain, and they were confirmed by the combination of electrocardiogram and laboratory examination, and they met the diagnostic standards for ACS established by the American College of Cardiology (ACC) and American Heart Association (AHA). Exclusion criteria: (1) patients with severe brain, liver, kidney, lung, hematopoietic system or endocrine system disease, uncontrolled high blood pressure, peripheral vascular disease or cancer; (2) patients with acute myocardial infarction.
receiving thrombolysis or coronary intervention treatment, or orally taking statins, non-steroidal drugs or anticoagulant drugs within 2 months; (3) patients with uncontrolled infection or allergic constitution; (4) patients without signed informed consent form. All patients were randomly divided into observation group and control group. In the observation group (47 cases), there were 29 males and 18 females, who were 43-76 (63.23 ± 13.35) years old; the duration from onset to admission was 0.5-6 (2.42 ± 1.27) h; complications: 16 cases with hypertension, 19 cases with diabetes mellitus and 16 cases with hyperlipidemia. In the control group (45 cases), there were 28 males and 17 females, who were 40.77 (62.85 ± 14.38) years old; the duration from onset to admission was 0.5-6 (2.42 ± 1.27) h; complications: 25 cases with hypertension, 20 cases with diabetes mellitus and 14 cases with hyperlipidemia. Referring to gender, age, duration from onset to admission and complication, there were no significant differences between the two groups (P>0.05), indicating they were comparable.

2.2 Therapeutic methods

All patients received the conventional therapy, mainly including anti-myocardial ischemia and anticoagulation. The administration of drugs were -receptor blocker, calcium channel blocker, angiotensin converting-enzyme inhibitor, nitrate, low molecular heparin, aspirin and clopidogrel. On the basis of conventional therapy, the control group was given Atorvastatin at a conventional dose (Lipitor, from Pfizer Inc., approved by the state: H20051407), and the dose of Atorvastatin was 10 mg/d taken once a day at a draught at night; on the basis of conventional therapy, the observation group was given Atorvastatin at a dose of 40 mg/d taken once a day at a draught at night. Both groups received continuous treatment for half a month.

2.3 Observation indicators

1) Inflammatory factors: IL-6, IL-8, hs-CRP and TNF-. The level of hs-CRP was detected by immunoturbidimetry using the SHIMADZU CL-7200 Biochemical Analyzer, and kit was from ANDOX; the levels of IL-6, IL-8 and TNF- were measured by enzyme-linked immunosorbent assay (ELISA), and kits were from Jing mei (Beijing) biotechnology co., LTD; 2) Indicators of platelet activity and fibrinolytic activity: TXB2, GMP-140, PAI-1 and t-PA. ELISA was adopted to measure the levels of these indicators, and kits for TXB2 and GMP-140 were from Shanghai Yadu biotechnology research institute, while kits for PAI-1 and t-PA were from Sumbio (Shanghai).

2.4 Statistics

Data were analyzed using SPSS 17.0 medical statistical software. Measurement data were described as mean ± standard deviation, and the inter-group comparison was conducted by t test. The values of P<0.05 were considered to be statistically significant.

3. Results

3.1 The comparison of the levels of inflammatory factors before and after treatment

Before treatment, there were no significant differences with respect to the levels of IL-6, IL-8, hs-CRP and TNF- between the two groups (P>0.05), which were comparable; after half a month of therapy, the levels of the above-mentioned factors were significantly decreased (P<0.05). Besides, bigger decreases were observed in the observation group, with the corresponding figures (8.75 ± 2.25) ng/mL for IL-6, (142.37 ± 51.45) pg/mL for IL-8, (64.12 ± 2.18) ng/mL for hs-CRP and (5.12 ± 3.35) ng/mL for TNF-, respectively, and the differences were significantly different compared with the control group (P<0.05). See table 1.

3.2 The comparison of the levels of indicators regarding platelet activity and fibrinolytic activity

Before treatment, there were no significant differences with respect to the levels of TXB2, GMP-140, PAI-1 and t-PA between the two groups (P>0.05), which were comparable; after half a month of therapy, the levels of TXB2, GMP-140 and PAI-1 were significantly decreased, while the level of t-PA was obviously increased (P<0.05). Besides, the amplitudes of change referring to these indicators in the observation group were bigger than those in the control group, with the corresponding figures (63.57 ± 5.57) pg/mL for TXB2, (11.25 ± 2.26) ng/mL for GMP-140, (8.31 ± 1.15) ng/mL for PAI-1 and (2.66 ± 0.48) IU/L for t-PA, respectively, and the differences were significantly different compared with the control group (P<0.05). See table 2.

Table 1

Comparison of the levels of inflammatory factors before and after treatment.

<table>
<thead>
<tr>
<th>Group (n=47)</th>
<th>Time points</th>
<th>IL-6 (ng/mL)</th>
<th>IL-8 (ng/mL)</th>
<th>hs-CRP (mg/L)</th>
<th>TNF- (ng/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>Before treatment</td>
<td>8.75 ± 2.25</td>
<td>142.37 ± 51.45</td>
<td>4.12 ± 2.18</td>
<td>5.12 ± 3.35</td>
</tr>
<tr>
<td></td>
<td>After treatment</td>
<td>8.75 ± 2.25</td>
<td>142.37 ± 51.45</td>
<td>4.12 ± 2.18</td>
<td>5.12 ± 3.35</td>
</tr>
<tr>
<td>Control (n=45)</td>
<td>Before treatment</td>
<td>35.32 ± 7.54</td>
<td>474.48 ± 70.35</td>
<td>17.12 ± 5.06</td>
<td>15.98 ± 7.52</td>
</tr>
<tr>
<td></td>
<td>After treatment</td>
<td>15.60 ± 4.13</td>
<td>185.48 ± 54.76</td>
<td>8.73 ± 4.45</td>
<td>8.85 ± 3.73</td>
</tr>
</tbody>
</table>

Note: intra-group comparison with before treatment, *P<0.05, inter-group comparison with the control group, **P<0.05.
Table 2
Comparison of the levels of indicators regarding platelet activity and fibrinolytic activity.

<table>
<thead>
<tr>
<th>Group</th>
<th>Time points</th>
<th>TXB2 (ng/mL)</th>
<th>GMP-140 (ng/mL)</th>
<th>PAI-1 (ng/mL)</th>
<th>t-PA (IU/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>Before treatment</td>
<td>123.39 ± 18.77</td>
<td>28.14 ± 2.81</td>
<td>13.71 ± 3.31</td>
<td>1.52 ± 0.25</td>
</tr>
<tr>
<td>(n=47)</td>
<td>After treatment</td>
<td>63.57 ± 5.57*</td>
<td>11.25 ± 2.76*</td>
<td>8.31 ± 1.15*</td>
<td>2.66 ± 0.46*</td>
</tr>
<tr>
<td>Control</td>
<td>Before treatment</td>
<td>132.87 ± 19.82</td>
<td>27.75 ± 2.79</td>
<td>13.44 ± 3.37</td>
<td>1.53 ± 0.29</td>
</tr>
<tr>
<td>(n=45)</td>
<td>After treatment</td>
<td>82.32 ± 6.01*</td>
<td>18.45 ± 2.80*</td>
<td>11.44 ± 2.29*</td>
<td>1.93 ± 0.31*</td>
</tr>
</tbody>
</table>

Note: intra-group comparison with before treatment, *P<0.05; inter-group comparison with the control group, †P<0.05.

4. Discussion

ACS is a critical illness in clinical, which requires cautious treatment. At present, it is well acknowledged that the abnormal lipid metabolism, inflammatory reaction and thrombus formation are quite important in the occurrence and development of the disease. Statins are greatly emphasized in clinical because they act on all the above-mentioned aspects. As for their role in the lipid regulation, there is no need to spell out. In this study, we focused on the inhibitory effect of Atorvastatin intensive therapy on the inflammation and thrombosis so as to provide reference data for better administration of this drug in clinical.

It is well known that the correlation research between the chosen inflammatory factors in this study (IL-6, IL-8, hs-CRP and TNF-α) and ACS is already very profound. When inflammatory factors destroy the stability of atherosclerotic plaque, the progress of ACS occurs. After that, the levels of pro-inflammatory cytokines are increased rapidly, which in turn results in the progressive severity of ACS. Studies have demonstrated that these indicators could be used to assess the prognosis of coronary heart disease, especially ACS. The higher the expression level and the longer the duration, the worse the prognosis, as a matter of fact, it is key to control the levels of these indicators timely and effectively in order to recover the stabilization of atherosclerotic plaque for the prognosis of ACS. The activation of fibrinolysis is directly related to platelet activation and thrombosis. As a result of atherosclerotic plaque erosion, endothelial injury induced by rupture, and dysfunction, platelets are activated. The following formation of thrombus because of platelet activation not only leads to the occurrence of ACS, but also stimulates the injury of endothelium, provoking the expansion of inflammatory response and the severity of ACS. The reduced activity of fibrinolysis not only accelerates the formation of atherosclerotic plaque by the deposition of collagen and matrix protein, but also delays the lysis due to the tendency of thrombus formation induced by blood hypercoagulability, which is also a reason for the aggravation of ACS. In this study, the expression of GMP140 and TXB2 reflects the activity of platelet, and their higher expression levels means larger extent of platelet activation; PAI-1 and t-PA are indicators for the fibrinolytic status, and they are antagonistic to each other. The former promotes thrombus formation, while the latter stimulates thrombolysis, and the balance between them determines the activity of fibrinolysis. The results in the present study show that the levels of inflammatory factors were more decreased when Atorvastatin was used at an intensive dose of 40 mg/d instead of a conventional dose of 20 mg/d, besides, a stronger inhibition of platelet activity and a greater correction of high coagulation fibrinolytic status were achieved.

Atorvastatin is the kind most used among statins in clinical application with the most proofs in evidence-based medicine. From all clinical considerations, such as lipid regulation, tolerance and even economical benefit, it is why Atorvastatin is chosen in the present study. The existing literatures showed the clinical dose of Atorvastatin is generally quite conservative, mainly 10-40 mg/d, and 40 mg/d is already regarded as the high-dose administration in domestic. Therefore, this very dose was selected in the current study for the Atorvastatin intensive therapy, expecting to achieve the optimal effect at an appropriate dose. The more important thing to verify the Atorvastatin intensive therapy for ACS lies in its possibility to change the traditional conservative ideas about administration of drugs, which turned out to be true in this study. The administration of Atorvastatin at a dose of 40 mg/d was effective for the stabilization of atherosclerotic plaque and the inhibition of thrombosis, indicating great benefits for ACS patients, which was consistent with the previous findings. However, it is not yet definitive whether the dose of 40 mg/d is the optimal dose for native patients. Internationally, the use of Atorvastatin at a dose of 80 mg/d was not rare, and it is possible that there are differences in the optimal dose of drug for different ethnic groups. However, this point should not be excessively exaggerated, and further studies are expected in the future.

References


