Expression of fatty acid synthase and inflammation severity evaluation in peripheral blood of patients with ACS and intervention effect of sEHi

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ABSTRACT

Objective: To analyze fatty acid synthase expression and inflammation degree evaluation in peripheral blood of patients with ACS and intervention effect of sEHi. Methods: Inclusion time of all research subjects was from January 2013 to February 2015, 132 cases of patients with acute coronary syndrome included 68 cases of patients with acute ST segment elevation myocardial infarction (STEMI) and 64 cases of patients with non-ST segment elevation acute coronary syndrome (NSTE-ACS), 78 cases of healthy subjects who received physical examination in our hospital were selected as healthy control group, fatty acid synthase expression and inflammation degree in peripheral blood of three groups were detected, and differences in levels of fatty acid synthase, inflammatory factors and blood lipid in patients with ACS before and after sEHi intervention were compared. Results: Serum FASN, CRP, IL-6, IL-12, IL-18 and IL-23 levels of STEMI group were higher than those of NSTE-ACS group and healthy control group; serum FASN level of patients with ACS after sEHi intervention was lower than that before intervention, and values of inflammatory factors CRP, IL-6, IL-12, IL-18 and IL-23 were also dramatically lower than those before intervention; TC, TG and LDL-C levels of patients with ACS after sEHi intervention were lower than those before intervention, and HDL-C levels were higher than those before intervention. Conclusion: Fatty acid synthase expression and inflammation degree increase in peripheral blood of patients with ACS, levels of fatty acid synthase, inflammation and blood lipid are optimized after sEHi intervention, and it is an effective way to treat ACS.

1. Introduction

Acute coronary syndrome (ACS) is with main pathological change of coronary atherosclerosis plaque rupture and can cause secondary complete or incomplete occlusive thrombosis. ACS is a serious cardiovascular disease that is more common in the elderly, especially populations with smoking, hypertension, hyperlipidemia and other high risks[1,2]. In addition to active symptomatic treatment for patients with ACS, early monitoring disease progression and preventing disease attack are the more ideal ways. Content of saturated fatty acid around atherosclerotic plaque dramatically increases in patients with ACS, this is the sign of active mononuclear macrophages in the plaque and also the prelude to plaque rupture, fatty acid synthase (FASN) is the key enzyme in the formation of saturated fatty acids, and FASN level can accurately reflect the activity and stability of atheromatous plaque[3]. Soluble epoxide hydrolase inhibitor (sEHi) is a new type of anti-atherosclerosis drug, it is known to be able to dilate coronary artery and be anti-inflammatory, and it has an active role in stabilizing plaque, which may be related to its inhibition of FASN activity. In the research, fatty acid synthase expression and inflammation degree evaluation
in peripheral blood of patients with ACS and intervention effect of sEHi were mainly analyzed, hereby reported as follows.

2. Information and methods

2.1. Case information

Inclusion time of all research subjects was from January 2013 to February 2015, 132 cases of patients with acute coronary syndrome included 68 cases of patients with ST segment elevation myocardial infarction (STEMI) and 64 cases of patients with non-ST segment elevation acute coronary syndrome (NSTE-ACS), 78 cases of healthy subjects who received physical examination in our hospital were selected as healthy control group, and baseline information of subjects was shown in Table 1.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Gender (male/female)</th>
<th>Age</th>
<th>BMI (kg/cm²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>STEMI</td>
<td>68</td>
<td>35/33</td>
<td>63±5</td>
<td>23.17±2.03</td>
</tr>
<tr>
<td>NSTE-ACS</td>
<td>64</td>
<td>34/30</td>
<td>63±6</td>
<td>22.86±2.41</td>
</tr>
<tr>
<td>Healthy control</td>
<td>78</td>
<td>40/38</td>
<td>63±5</td>
<td>23.43±2.37</td>
</tr>
<tr>
<td>F</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>P</td>
<td>&gt;0.05</td>
<td>&gt;0.05</td>
<td>&gt;0.05</td>
<td></td>
</tr>
</tbody>
</table>

2.2. Specimen collection and detecting items

Subjects were fasting for 12 h, 5 mL of fasting venous blood was drawn from cubital vein in the morning, enzyme-linked immunosorbent assay (ELISA) was used to detect serum fatty acid synthase (FASN), interleukin-6 (IL-6), interleukin-12 (IL-12), interleukin-18 (IL-18) and interleukin-23 (IL-23), liquid immunoprecipitation scatter turbidimetry was used to detect C-reactive protein (CRP) and enzymatic method was used to detect serum total cholesterol (TC), triglyceride (TG), low density lipoprotein cholesterol (LDL-C) and high density lipoprotein cholesterol (HDL-C) levels.

2.3. Statistical methods

SPSS 21.0 software was used to process data, measurement data comparison was by variance analysis and pair wise comparison was by LSD test. Differences were considered to be statistically significant at a level of P<0.05.

<table>
<thead>
<tr>
<th>Groups</th>
<th>CRP (mg/L)</th>
<th>IL-6 (ng/L)</th>
<th>IL-12 (ng/L)</th>
<th>IL-18 (ng/L)</th>
<th>IL-23 (ng/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>STEMI</td>
<td>58.73±3.56</td>
<td>172.93±11.67</td>
<td>98.27±7.63</td>
<td>83.61±8.05</td>
<td>74.28±7.23</td>
</tr>
<tr>
<td>NSTE-ACS</td>
<td>41.68±3.42</td>
<td>116.77±9.95</td>
<td>83.17±7.03</td>
<td>72.15±6.93</td>
<td>63.56±6.11</td>
</tr>
<tr>
<td>Control</td>
<td>2.87±0.16</td>
<td>65.28±5.93</td>
<td>34.81±5.32</td>
<td>39.72±3.56</td>
<td>25.87±2.07</td>
</tr>
<tr>
<td>P</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. Results

3.1. Fatty acid synthase expression

Serum FASN level of STEMI group was (47.38±4.77) μg/L, serum FASN level of NSTE-ACS group was (38.27±3.39) μg/L, serum FASN level of healthy control group was (7.79±0.68) μg/L, there were statistically significant differences among three groups (P<0.05), and pair wise comparison through LSD showed that serum FASN level of NSTE-ACS group was higher than that of healthy control group and serum FASN level of STEMI group was higher than that of NSTE-ACS group (P<0.05).

3.2. Degree of inflammation

ELISA was used to detect serum inflammatory factor levels of three groups, and it was found out that differences in levels of serum inflammatory factors such as CRP, IL-6, IL-12, IL-18 and IL-23 among three groups were statistically significant (P<0.05), and pair wise comparison through LSD showed that serum CRP, IL-6, IL-12, IL-18 and IL-23 levels of NSTE-ACS group were higher than those of healthy control group and serum CRP, IL-6, IL-12, IL-18 and IL-23 levels of STEMI group were higher than those of NSTE-ACS group (P<0.05), shown in Table 2.

3.3. Fatty acid synthase and inflammatory factor levels before and after intervention

Serum fatty acid synthase and inflammatory factor levels of patients with ACS before and after sEHi intervention were compared, and the results were as follows: compared with related values before intervention, serum FASN level of patients with ACS after sEHi intervention was lower than that before intervention, and values of inflammatory factors CRP, IL-6, IL-12, IL-18 and IL-23 were also dramatically lower than those before intervention (P<0.05), shown in Figure 1.

3.4. Blood lipid index levels

Blood lipid index levels of patients with ACS before and after sEHi intervention were compared, and the results were as follows: compared with the values before intervention, TC, TG and LDL-C levels 2 weeks and 4 weeks after intervention were significantly
lower than those before intervention, and HDL-C levels were higher than those before intervention ($P<0.05$), shown in Figure 2.

![Figure 1. Comparison of serum fatty acid synthase and inflammatory factor levels of patients with ACS before and after sEHi intervention.](image1)

![Figure 2. Comparison of blood lipid levels of patients with ACS before and after sEHi intervention.](image2)

4. Discussion

Acute coronary syndrome (ACS) is mostly caused by unstable plaque activities, and studies have shown that mononuclear macrophages increase in ruptured plaque and proportion of saturated fatty acid content also increases in plaque edge area while there are no above changes in stable plaque\(^4,5\). It is speculated that increased synthesis of saturated fatty acid in plaque edge is the sign of metabolic activity of mononuclear macrophages within plaque, and monitoring saturated fatty acid level is expected to become an effective index for judging the severity and prognosis of patients with ACS. Fatty acid synthase (FASN) is the key enzyme in the synthesis of saturated fatty acid in the body and the key enzyme in the differentiation of monocytes into macrophages, and in the research, serum FASN level of patients with ACS was dramatically higher than that of normal subjects, which confirmed that FASN played an important role in the occurrence and development process of ACS and intervention of FASN level was expected to become a new target for the treatment of ACS\(^6\).

Many studies confirm that levels of inflammatory factors increase in patients with ACS, and among them C-reactive protein (CRP) level can accurately reflect the severity of body’s inflammatory state and is closely related to the prognosis. In the research, serum CRP, IL-6, IL-12, IL-18 and IL-23 levels of patients with ACS were dramatically higher than those of normal subjects, and levels of above inflammatory factors of patients with acute ST segment elevation myocardial infarction (STEMI) were higher, which were consistent with previous research results\(^7,8\). Current study has shown that FASN level is positively correlated with levels of inflammatory factors in patients with ACS, and therefore if FASN can be effectively intervened, it may simultaneously optimize patients’ systemic inflammatory state.

Soluble epoxide hydrolase inhibitor (sEHi) has anti-atherosclerosis effect and it has been confirmed in animal model of mice that application of sEHi can reduce aorta atheromatous plaque area, study of Gonzalez-Pacheco\(^10\) shows that sEHi can inhibit monocyte secretion of inflammatory factors such as IL-6 and TNF-\(\alpha\), and it is speculated that the anti-atherosclerosis effect of sEHi may be associated with its anti-inflammation effect\(^9\). Above research results showed that after patients with ACS received sEHi intervention, serum FASN level decreased and values of inflammatory factors CRP, IL-6, IL-12, IL-18 and IL-23 decreased, indicating that sEHi might inhibit FASN expression in peripheral blood mononuclear cells (PBMC) to inhibit the synthesis of saturated fatty acids, reduce lipid metabolism disorder in the plaque and decrease the activity of unstable plaque. Inflammatory factors can stimulate macrophages and increase cholesterol accumulation in cells, sEHi inhibits FASN to lessen cholesterol pool in macrophages and significantly reduce triglyceride and cholesterol contents, and it also indicates that inhibiting the synthesis of saturated fatty acids can reduce the systemic inflammatory state in patients, further reduce lipid accumulation in cells induced by inflammatory response and inhibit the synthesis and development of foam cells, and fundamentally inhibit ACS progression and improve the prognosis\(^11,12\).

Formation of atheromatous plaque in patients with ACS is mostly because of abnormal blood lipid levels in patients, mostly manifested as increased levels of total cholesterol (TC) and low density lipoprotein cholesterol (LDL-C) and decreased level of high density lipoprotein cholesterol (HDL-C)\(^13\). Fundamental way to inhibit further accumulation of atheromatous plaque is to optimize blood lipid levels in patients and reduce the destructive effect on endangium. sEHi acts on sEH, has the effect of dilating coronary artery, inhibiting vascular smooth muscle cell locomotion, inhibiting platelet aggregation and reducing adhesion factor expression, and
is a new type of anti-atherosclerosis drug[14,15]. Above research has confirmed that sEHi can inhibit the synthesis of saturated fatty acid in plaque edge, and its effect on patients’ systemic blood lipid state was further studied in the research. Detection of blood lipid levels in patients before and after intervention showed that TC, TG and LDL-C levels in patients with ACS decreased after sEHi intervention and HDL-C levels increased, it indicated that sEHi could optimize patients’ systemic blood lipid state and increase levels of blood lipid lowering-related indexes, and it could not only reduce lipid accumulation in atheromatous plaque, but also reduce systemic high blood lipid state in patients.

To sum up, it is concluded that fatty acid synthase expression and inflammation degree increase in peripheral blood of patients with ACS, levels of fatty acid synthase, inflammation and blood lipid are optimized after sEHi intervention, and it is an effective way to treat ACS and worth popularization in clinical practice in the future.

References


