Research on predictive value of cytokine changes for athermanous plaque instability among ACS patients

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Objective: To analyze the correlation between serum IL-6, IL-10, IL-6/IL-10, TNF-α, hsCRP level and athermanous plaque instability among Acute Coronary Syndrome (ACS) patients, as well as discuss its clinical predictive value. Method: 240 patients admitted into our hospital from August 2011 to July 2013 for coronary angiography (CAG) were chosen, among which 188 cases were diagnosed with ACS. Patients were divided into acute myocardial infarction (AMI) group (106 cases), unstable angina (UA) group (82 cases) and control group of 52 cases of negative patients according to diagnosis. Serum IL-6, IL-10, IL-6/IL-10, TNF-α and hsCRP level were tested by ELISA and analyzed statistically. Results: Serum IL-6, IL-10, IL-6/IL-10 and TNF-α levels in observation groups were significantly higher than those of control group (P<0.05). Positive correlations between IL-6 and hsCRP were observed in observation groups (r=0.385, P<0.05). There was positive correlation between IL-6 and TNF-α (r=0.259, P<0.05). Conclusions: A certain degree of correlation was observed between serum IL-6/IL-10, TNF-α, hsCRP and ACS symptoms among ACS patients, and it is valuable for the clinical prediction of athermanous plaque instability.

1. Introduction

Acute coronary syndrome (ACS) is a clinical syndrome of secondary complete or incomplete occlusion thrombus resulted from coronary rupture due to its athermanous plaque instability[1]. ACS could be categorized into unstable angina (UA), ST elevation myocardial infarction (STEMI) and non ST elevation myocardial infarction (NSTEMI)[2]. In recent years, it was found that serum IL-6, TNF-α or hsCRP levels were higher than normal levels among ACS patients, thus it was conjectured that IL-6 could be regarded as a marker of unstable athermanous plaque or ACS[4]. Meanwhile, IL-10 was found to prevent the formation of athermanous plaque or strengthen the stability of athermanous plaque already formed[5]. In this research, the correlation between serum IL-6, IL-10, IL-6/IL-10, TNF-α, hsCRP level and athermanous plaque instability among ACS patients was analyzed to discuss its clinical predictive value. The results are as follows:

2. Materials and methods

2.1. Clinical information

A total of 240 patients admitted into our hospital from August, 2011 to July, 2013 for coronary angiography (CAG) were chosen, including 122 male and 66 female, aging between 48 and 86 years with the average age of (63.4±10.9). Of all patients, 188 cases were diagnosed with ACS. 240 patients were divided into acute myocardial infarction (AMI) group (106 cases), unstable angina (UA) group (82 cases) and control group of 52 cases of negative patients. Inclusion criteria for AMI and UA patients in this research were made according to the textbook of Internal Medicine. AMI patients should possess typical AMI clinical symptoms with chest pain duration over 5 hours, the ECG must show new ST elevation...
in two or more adjacent ECG leads, positive troponin T (cTnT), CK-MB in myocardial enzymes over two times reference value. UA patients possessed typical repeated pain in precordium and ST-segment arose in attack time while they were resting. CAG showed at least one vascular stenosis degree over 50% among left main, left anterior descending, circumflex artery or right coronary artery. Patients with complicated infection, or patients taking steroid or non-steroid type anti-inflammatory analgesic or taking opium type inflammation inhibition drugs before diagnosis and those with tumors or with immune system disorder were excluded.

2.2. Treatment method

5 mL venous bloods were collected in the morning from all patients before breakfast. Enzyme-linked immunosorbent assay (ELISA) was used for the determination of TNF-α, IL-6, IL-10 levels.

2.3. Statistical analysis

Data were analyzed by using SPSS 17.0 software and expressed as (mean SD). Single factor in multiple groups was tested by LSD, correlation of interclass variance was analyzed by nonparametric Spearman, while statistical difference was set at P<0.05.

3. Results

3.1. Comparison of cytokine content among patients in each group

Serum IL-6, IL-10, IL-6/IL-10, TNF-α and hsCRP level of two ACS subgroups were significantly higher than those of control group (P<0.05). IL-6, TNF-α and hsCRP level of AMI group were significantly higher than that of control group, and positive correlation was observed between serum IL-6 level and hsCRP level. By humoral immunity and cell immunity, IL-6 could initiate inflammatory response to spare host the invasion of foreign bodies and spare tissues the damage[11]. As central regulation factor, IL-6 played a significant role in vascular injury and acute myocardial ischemia. IL-6 could enable liver secretes hsCRP and plasma fibrinogen as well. The expression of IL-6 in atheroma of ACS patients was much more, which impelled the formation of thrombus, induced secretory expression of adhesion molecule in myocardial cells, and enhanced adhesive action of myocardial cells, so that the damage of myocardial cells became worse. As a result, if serum IL-6 level elevates, it could be predicted that the occurrence of inflammatory response, then the instability of athermanous plaque. In terms of IL-10, it also has anti-inflammatory effect, and it can inhibit the generation of other cytokines with anti-inflammatory effect, the apoptosis of cells, and the rupture of coronary athermanous plaque and the formation of thrombus. IL-10 is generated by Th0, Th2 and mononuclear macrophage. It can inhibit immune response of Th1 cells, and infiltration effect of inflammatory cells, down-regulates the expression of cytokines such as IL-1, IL-6, TNF-α, etc., and reduces monocyte adhesion to vessels inter wall, decreases lipid accumulation in artery vascular, at last, prevents the formation of artery athermanous plaque.

In this research, serum IL-6/IL-10 in ACS patients was obvious higher than that of control group, suggesting that the imbalance of IL-6 and IL-10 secretion might influence the metabolism of blood lipid and plays a critical role in the formation and ulceration of artery athermanous plaque. In normal condition, there is dynamic equilibrium between inflammatory factors and anti-inflammatory factors. The balance would be broken down when myocardial ischemia occurs, which would increase the content of inflammatory factors and decrease that of anti-inflammatory factors. It is concluded that serum IL-6/IL-10 is with clinical value for the prediction of athermanous plaque instability. Moreover, results showed that there was positive correlation between serum TNF-α and IL-6 of ACS patients, so there was cascade enlarge effect of internal inflammatory cytokines. The expression of serum IL-6, IL-8 and TNF-α of ACS patients impels myocardial damage and apoptosis, which degrades liver function and leads to heart failure. TNF-α could increase the permeability of micro vessel and formation of thrombus. Moreover, it can also accelerate matrix degradation of vascular cell then increase the instability of athermanous plaque. HsCRP, secreted from liver cells, reflects arterial athermanous inflammatory and predicts plaque instability. It could stimulate lymphocytes and monocytes generate oxygen free radicals[17,18], which plays a significant role

4. Discussion

Results showed that serum IL-6 level of ACS patients was significantly higher than that of control group, and positive correlation was observed between serum IL-6 level and hsCRP level. The expression of IL-6 and IL-10 secretion might influence the metabolism of blood lipid and plays a critical role in the formation and ulceration of artery athermanous plaque. In normal condition, there is dynamic equilibrium between inflammatory factors and anti-inflammatory factors. The balance would be broken down when myocardial ischemia occurs, which would increase the content of inflammatory factors and decrease that of anti-inflammatory factors. It is concluded that serum IL-6/IL-10 is with clinical value for the prediction of athermanous plaque instability. Moreover, results showed that there was positive correlation between serum TNF-α and IL-6 of ACS patients, so there was cascade enlarge effect of internal inflammatory cytokines. The expression of serum IL-6, IL-8 and TNF-α of ACS patients impels myocardial damage and apoptosis, which degrades liver function and leads to heart failure. TNF-α could increase the permeability of micro vessel and formation of thrombus. Moreover, it can also accelerate matrix degradation of vascular cell then increase the instability of athermanous plaque. HsCRP, secreted from liver cells, reflects arterial athermanous inflammatory and predicts plaque instability. It could stimulate lymphocytes and monocytes generate oxygen free radicals[17,18], which plays a significant role

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>IL-6</th>
<th>IL-10</th>
<th>TNF-α</th>
<th>hsCRP</th>
<th>IL-6/IL-10</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMI</td>
<td>106</td>
<td>4.85±8.75*</td>
<td>17.57±2.09*</td>
<td>56.34±30.63*</td>
<td>25.54±29.51*</td>
<td>0.28±0.49*</td>
</tr>
<tr>
<td>UA</td>
<td>82</td>
<td>2.58±2.88*</td>
<td>16.85±2.75*</td>
<td>41.13±24.35*</td>
<td>9.94±11.06*</td>
<td>0.23±0.18*</td>
</tr>
<tr>
<td>Control</td>
<td>52</td>
<td>1.63±1.72</td>
<td>15.70±1.79</td>
<td>28.62±17.53</td>
<td>4.03±4.30</td>
<td>0.11±0.10</td>
</tr>
</tbody>
</table>

Compare with middle dose group, *P<0.05; Compare with high dose group, #P<0.05.

3.2. Correlation analysis

Positive correlations were observed between serum IL-6 content and hsCRP content in two ACS subgroups (r=0.385, P<0.05). So as the content of IL-6 and TNF-α (r=0.259, P<0.05)
in inflammatory response. This result demonstrated that there was correlation between hsCRP and IL-6 in serum of patients and consequently hsCRP level could be regarded as a clinical index to predict the instability of arterial athermanous plaque.

Study results suggested that serum IL-6, IL-10, IL-6/IL-10, TNF-α, hsCRP in ACS patients were much higher than those of control group, and positive correlation was observed between IL-6 and TNF-α. Thus, all these cytokines could be regarded as biochemical indexes for the prediction of athermanous plaque instability.

References