Correlation of serum PCT levels with target organ damage and inflammatory reaction degree in patients with severe acute pancreatitis

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Objective: To study the correlation of serum procalcitonin (PCT) levels with target organ damage and inflammatory reaction degree in patients with severe acute pancreatitis. Methods: 146 patients who were diagnosed with acute pancreatitis in our hospital between May 2014 and September 2016 were selected, the patients with mild acute pancreatitis and severe acute pancreatitis were selected as the mild group (n=48) and severe group (n=98) respectively, and healthy subjects who received physical examination during the same period were selected as the control group (n=50). Serum was collected to determine the contents of PCT, liver and kidney function indexes as well as inflammatory reaction indexes. Results: Serum PCT, soluble triggering receptor expressed on myeloid cells-1 (sTREM-1), interleukin-1β (IL-1β), IL-6, IL-8, IL-18 and tumor necrosis factor-α (TNF-α) contents of severe group and mild group were significantly higher than those of control group (P<0.05), and serum PCT, sTREM-1, IL-1β, IL-6, IL-8, IL-18 and TNF-α contents of severe group were significantly higher than those of mild group (P<0.05); serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), total bilirubin (TBIL), blood urea nitrogen (BUN) and serum creatinine (Scr) contents of severe group were significantly higher than those of mild group and control group (P<0.05), and serum ALT, AST, TBIL, BUN and Scr contents of mild group were not significantly different from those of control group; serum ALT, AST, BIL, Scr, sTREM-1, IL-1β, IL-6, IL-8, IL-18 and TNF-α contents of severe group of patients with high PCT content were significantly higher than those of patients with low PCT content (P<0.05). Conclusion: Serum PCT levels significantly increase in patients with severe acute pancreatitis and on liver and have evaluation value for liver and kidney function damage as well as inflammatory reaction degree.

1. Introduction

Acute pancreatitis is the clinical common acute abdominal disease, including two different pathological types: mild acute pancreatitis and severe acute pancreatitis. Mild acute pancreatitis is self-limiting, its main pathological feature is pancreatic edema, and the prognosis is high; severe acute pancreatitis is critical, its main pathological characteristics are the pancreatic hemorrhage and necrosis, it is mostly accompanied by the activation of systemic inflammatory response syndrome and multiple organ damage, the prognosis is poor and the mortality is high[1,2]. In clinical practice, the accurate diagnose of the severity of acute pancreatitis and the early detection of severe acute pancreatitis is helpful for early intervention and disease outcome improvement. Procalcitonin (PCT) is the precursor of calcitonin, it is synthesized in thyroid C cells, and the PCT content is extremely low in blood circulation under physiological conditions; severe infections can stimulate the extra-thyroid tissue and cells to massively synthesize PCT and release it into the blood circulation, which is characterized by a dramatic increase in serum PCT levels[3]. In recent years, PCT is increasingly used in the
diagnosis and assessment of infectious diseases. In the following study, the correlation of serum PCT levels with target organ damage and inflammatory reaction degree in patients with severe acute pancreatitis was analyzed.

2. Materials and methods

2.1. Research subjects

146 patients who were diagnosed with acute pancreatitis in our hospital between May 2014 and September 2016 were selected as the research subjects, all the patients were in accordance with the diagnostic criteria for acute pancreatitis in China Guide for Diagnosis and Treatment of Acute Pancreatitis, and according to the disease classification standard, the patients with acute pancreatitis were divided into those with mild acute pancreatitis and severe acute pancreatitis, and included in mild group and severe group respectively. Mild group, a total of 98 cases, included 62 male cases and 36 female cases that were 33–65 years old; severe group, a total of 48 cases, included 32 male cases and 16 female cases that were 31–66 years old. 50 healthy subjects who received physical examination in hour hospital during the same period were selected as the control group, including 32 male cases and 18 female cases that were 31–66 years old. The general data were not significantly different among three groups of subjects (P>0.05).”

2.2. Research methods

2.2.1. Serum sample separating and storing methods

5 mL of peripheral venous blood was collected from the mild group and severe group after admission, 5 mL of peripheral venous blood was collected from the control group during physical examination, and the blood was centrifuged at 3 000 r/min to separate serum, move it into the new EP tubes and place it at -80℃.

2.2.2. Serum index detecting methods

Serum specimens were taken and thawed at room temperature, microplate reader and the matched enzyme-linked immunosorbent assay kits were used to determine PCT, soluble triggering receptor expressed on myeloid cells-1 (sTREM-1), interleukin-1β (IL-1β), IL-6, IL-8, IL-18 and tumor necrosis factor-α (TNF-α) levels, and the automatic biochemical analyzer and auxiliary reagent were used to determine alanine aminotransferase (ALT), aspartate aminotransferase (AST), total bilirubin (TBIL), blood urea nitrogen (BUN) and serum creatinine (Scr) levels.

2.3. Statistical analysis

SPSS21.0 software was used to statistically process and input data, the differences among three groups of measurement data were by variance analysis, the differences between two groups of measurement data were by t test and P<0.05 indicated statistical significance in differences.

3. Results

3.1. Serum PCT levels of three groups of subjects

Serum PCT levels of severe group, mild group and control group were (4.63±0.65), (2.42±0.31) and (0.52±0.07) ng/mL respectively. Method analysis was as follows: serum PCT levels of severe group and mild group were significantly higher than that of control group, and serum PCT level of severe group was significantly higher than that of mild group. Differences in pair-wise comparison of serum PCT levels were statistically significant among three groups of subjects (P<0.05).

3.2. Serum liver and kidney function index contents in three groups of subjects and their correlation with PCT levels

Analysis of serum liver function indexes ALT, AST and TBIL as well as kidney function indexes BUN and Scr contents among severe group, mild group and control group was shown in Table 1: serum ALT, AST, TBIL, BUN and Scr contents of severe group were significantly higher than those of mild group and control group (P<0.05), and serum ALT, AST, TBIL, BUN and Scr contents of mild group were not significantly different from those of control group (P>0.05); analysis of serum ALT, AST, TBIL, BUN and Scr contents between severe group of patients with high PCT level and low PCT level was shown in Table 2: serum ALT, AST, TBIL, BUN and Scr contents of severe group of patients with high PCT content were significantly higher than those of patients with low PCT content, and differences in serum ALT, AST, TBIL, BUN and Scr contents were statistically significant between severe group of patients with high and low PCT level (P<0.05).

3.3. Serum inflammatory factor contents in three groups of subjects and their correlation with PCT levels

Analysis of inflammatory factors sTREM-1, IL-1β, IL-6, IL-8, IL-18 and TNF-α contents among severe group, mild group and control group was shown in Table 3: serum sTREM-1, IL-1β, IL-6, IL-8, IL-18 and TNF-α contents of severe group were significantly higher than those of mild group and control group, and serum sTREM-1, IL-1β, IL-6, IL-8, IL-18 and TNF-α contents of mild group were significantly higher than those of control group (P<0.05); analysis of serum inflammatory factors sTREM-1, IL-1β, IL-6, IL-8, IL-18 and TNF-α contents between severe group of patients with high PCT level and low PCT level was shown in Table 4: serum sTREM-1, IL-1β, IL-6, IL-8, IL-18 and TNF-α contents of severe group of patients with high PCT content were significantly higher than those of patients with low PCT content, and differences in serum sTREM-1, IL-1β, IL-6, IL-8, IL-18 and TNF-α contents were statistically significant between severe group of patients with high and low PCT level (P<0.05).
Comparison of serum inflammatory factor contents among three groups of subjects (Table 3).

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>PCT (ng/mL)</th>
<th>sTREM-1 (ng/mL)</th>
<th>IL-1β (pg/mL)</th>
<th>IL-6 (pg/mL)</th>
<th>IL-8 (pg/mL)</th>
<th>IL-18 (pg/mL)</th>
<th>TNF-α (ng/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe group</td>
<td>48</td>
<td>15.2±0.05</td>
<td>36.7±4.62</td>
<td>17.65±2.03</td>
<td>26.78±3.25</td>
<td>9.27±1.04</td>
<td>15.25±1.87</td>
<td></td>
</tr>
<tr>
<td>Mild group</td>
<td>98</td>
<td>0.35±0.05</td>
<td>21.57±3.04</td>
<td>11.24±1.42</td>
<td>17.47±1.97</td>
<td>5.68±0.73</td>
<td>9.38±1.03</td>
<td></td>
</tr>
<tr>
<td>Control group</td>
<td>50</td>
<td>0.2±0.03</td>
<td>13.24±1.76</td>
<td>6.87±0.89</td>
<td>12.23±1.57</td>
<td>3.25±0.36</td>
<td>6.23±0.78</td>
<td></td>
</tr>
</tbody>
</table>

*: compared with control group, P<0.05; #: compared with mild group, P<0.05.

Table 2
Comparison of serum liver and kidney function indexes between severe group of patients with high PCT level and low PCT level (Table 2).

4. Discussion

The main pathological change of severe acute pancreatitis is the pancreatic hemorrhage and necrosis, it is mostly associated with the activation of systemic inflammatory response syndrome and with high occurrence risk of multiple organ dysfunction syndrome, and it is with rapid development, poor prognosis and outcome as well as high mortality[4]. In clinical practice, early identification and intervention of severe acute pancreatitis can significantly improve the prognosis and reduce the mortality[5,6]. The occurrence of severe acute pancreatitis will activate the systemic inflammatory response, and inflammation indexes can be used to assess the illness development. PCT is the calcitonin precursor synthesized by thyroid C cells, and it splits into calcitonin and is released into the blood circulation; under physiological conditions, PCT is hardly released into the circulation, so the serum PCT content is extremely low. Under the pathological condition of severe infection, extra-thyroid viscera tissues and cells can massively synthesize and secrete PCT, leading to higher serum PCT levels[7,8]. In order to define the value of serum PCT levels for assessing severe acute pancreatitis, serum PCT levels in patients with severe acute pancreatitis and mild acute pancreatitis were analyzed, and the results showed that serum PCT contents of severe group and mild group were significantly higher than that of control group (P<0.05), and serum PCT content of severe group was significantly higher than that of mild group (P<0.05). This means that serum PCT levels increase significantly during the occurrence of acute pancreatitis; with the development of mild acute pancreatitis into severe acute pancreatitis, serum PCT levels further increase, and serum PCT content has assessment value for the development and changes of acute pancreatitis.

During the development from mild acute pancreatitis to severe acute pancreatitis, a variety of inflammatory factors and vasoactive molecules will be released into the blood circulation, and the inflammatory factors and vasoactive molecules that enter into the liver and kidney with the blood circulation will further cause liver and kidney function damage[9-11]. The direct sign of liver damage is liver cell rupture, the ALT, AST and other transaminases in the cytoplasm are released into the blood circulation, liver injury can also affect the bilirubin metabolism and lead to a rise in serum bilirubin content. The characteristics of renal injury are that the side metabolites in the body cannot be discharged and they accumulate in the body, creatinine and urea nitrogen are the products of protein catabolism, they are mainly excreted through the kidney, and the secondary renal damage of severe acute pancreatitis will cause the elevated BUN and Scr contents. In the study, analysis of serum liver and kidney damage indexes of patients with severe acute pancreatitis...
and mild acute pancreatitis showed that serum ALT, AST, TBIL, BUN and Scr contents of severe group were significantly higher than those of mild group and control group ($P<0.05$), and serum ALT, AST, TBIL, BUN and Scr contents of mild group were not significantly different from those of control group. This means that when the acute pancreatitis is in mild stage, liver and kidney function are without obvious damage; when it develops into severe stage, liver and kidney function are with obvious damage, and ALT, AST, TBIL, BUN and Scr levels increase significantly. In order to further clarify the assessment value of PCT levels for visceral function damage of severe acute pancreatitis, the liver and kidney damage in severe acute pancreatitis patients with different PCT contents were analyzed in the study, and the results showed that serum ALT, AST, TBIL, BUN and Scr contents of severe group with high PCT content were significantly higher than those of patients with low PCT content ($P<0.05$). This means that the increased serum PCT levels in patients with severe acute pancreatitis are correlated with the increased ALT, AST, TBIL, BUN and Scr contents, and serum PCT levels have assessment and prediction value for liver and kidney function damage in patients with severe acute pancreatitis.

Systemic inflammatory response syndrome is an important characteristic of acute severe pancreatitis, and the cascade activation of inflammatory reaction as well as the massive release of sTREM-1, IL-1β, IL-6, IL-8, IL-18, TNF-α and other inflammatory factors are the important causes of multiple organ dysfunction[12,13]. sTREM-1 is the soluble form of TREM-1, and it has promoting effect on the differentiation of mononuclear macrophages and neutrophils as well as the secretion of inflammatory mediators[14], IL-1β, IL-6, IL-8 and IL-18 are the interleukin family members with pro-inflammatory activity, and they have promoting effect on the cascade amplification of inflammatory response[15,16]; TNF-α is the inflammatory factor that first changes during inflammation cascade activation, and it can not only mediate inflammatory tissue damage, but also can promote the inflammation activation in the form of positive feedback. In the study, analysis of serum inflammatory response-related indexes in patients with severe acute pancreatitis and mild acute pancreatitis showed that serum sTREM-1, IL-1β, IL-6, IL-8, IL-18 and TNF-α contents of severe group and mild group were significantly higher than those of control group ($P<0.05$), and serum sTREM-1, IL-1β, IL-6, IL-8, IL-18 and TNF-α contents of severe group were significantly higher than those of mild group ($P<0.05$). This means that during the development and change of acute pancreatitis, inflammation is apparently activated, and a variety of inflammatory cytokines are released into the blood circulation. In order to further clarify the assessment value of PCT levels for the inflammation in patients with severe acute pancreatitis, serum inflammatory response-related indexes in severe acute pancreatitis patients with different PCT contents were analyzed in the study, and the results showed that serum TREM-1, IL-1β, IL-6, IL-8, IL-18 and TNF-α contents of severe group of patients with high PCT content were significantly higher than those of patients with low PCT content ($P<0.05$). This means that the increased serum PCT levels in patients with severe acute pancreatitis are correlated with the increased sTREM-1, IL-1β, IL-6, IL 8 and IL-18 contents, and serum PCT levels have assessment and prediction value for the inflammation degree in patients with severe acute pancreatitis.

To sum up, it is believed that serum PCT levels significantly increase during the development of acute pancreatitis; the normally elevated serum PCT has good correlation with the degree of liver and kidney damage as well as inflammatory reaction, and can be used to assess the degree of liver and kidney damage as well as inflammatory reaction in patients with severe acute pancreatitis.

References