The value of serum procalcitonin content for assessing the inflammation and organ injury in neonatal septicemia

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Objective: To study the value of serum procalcitonin content for assessing the inflammation and organ injury in neonatal septicemia. Methods: 48 children with neonatal septicemia who were treated in our hospital between April 2014 and May 2016 were selected as the observation group, 50 healthy newborns who were delivered in our hospital during the same period were selected as the normal control group, and the observation group were further divided into high PCT group and low PCT group (n=24) according to the median of serum PCT content. Enzyme-linked immunosorbent assay (ELISA) was used to detect the serum contents of inflammatory mediators, and color Doppler diasonograph was used to measure heart injury index levels. Results: Peripheral blood PCT content of observation group was significantly higher than that of control group (P<0.05); serum inflammatory mediators IL-1β, IL-6, IL-8 and TNF-α contents of high PCT group and low PCT group were significantly higher than those of normal control group, and as the PCT content increased, serum inflammatory mediators interleukin-1β (IL-1β), interleukin-6 (IL-6), interleukin-8 (IL-8) and tumor necrosis factor-α (TNF-α) contents increased (P<0.05); routine ultrasound parameters cardiac output (CO) and left ventricular ejection fraction (LVEF) levels as well as the absolute value of two-dimensional speckle tracking imaging parameters left ventricular global longitudinal strain rate (GLSr) and left ventricular global circumferential strain rate (GCSr) of high PCT group and low PCT group were lower than those of normal control group while serum myocardial injury indexes cardiac troponin I (cTnI), heart-type fatty acid-binding protein (H-FABP) and α-hydroxybutyric dehydrogenase (HBDH) contents were higher than those of normal control group, and as the PCT content increased, CO and LVEF levels as well as the absolute value of GLSr and GCSr decreased while the indexes cTnI, H-FABP and HBDH contents increased (P<0.05). Conclusion: Serum PCT content is positively correlated with the degree of inflammation and heart injury in neonatal septicemia, and can be used as a reliability index to early judge the disease severity and the target organ damage.

1. Introduction

Neonatal septicemia is one of the most serious infectious diseases in infants, it progresses fast and is short of early typical clinical manifestations, and it is currently one of the main causes of neonatal death[1,2]. Blood culture shows that pathogens is the gold standard for the diagnosis of neonatal septicemia, but the inspection is quite time-consuming and cannot be used as the routine method in early disease diagnosis. At present, more and more researches are committed to exploring the early sensitive clinical indicators of neonatal septicemia, procalcitonin (PCT) is a sensitive parameter to monitor inflammatory disease bacteria infection, and its value for the diagnosis and treatment of neonatal septicemia has received much concern[3,4]. In the study, serum PCT level change in neonatal septicemia was detected, and the inner link between the specific PCT content and the disease severity was discussed, hereby reported as follows.
2. Materials and methods

2.1. Case information

48 children with neonatal septicemia who were treated in our hospital between April 2014 and May 2016 were selected as the observation group, 50 healthy newborns who were delivered in our hospital during the same period were selected as the normal control group, and the families of research subjects signed informed consent. Observation group included 25 male cases and 23 female cases with gestational age at delivery 39–41 weeks and (39.51±0.47) weeks in average; control group included 25 male cases and 25 female cases with gestational age at delivery 38–41 weeks and (39.71±0.53) weeks in average. Two groups of subjects were not statistically different in the distribution of gender and gestational age at delivery (P>0.05), and the hospital ethics committee discussed and then approved the research.

2.2. Inclusion and exclusion criteria

Inclusion criteria: (1) in accordance with the diagnostic criteria for neonatal septicemia by Pediatrics Branch of Chinese Medical Association; (2) ≤28 d years old; (3) blood specimens were collected for inspection immediately after admission (≤2 h); (4) gestational age ≥38 weeks. Exclusion criteria: (1) complicated by intrauterine infection; (2) associated with congenital disorders of brain, heart, liver and other important organs; (3) without antimicrobial therapy prior to admission.

2.3. Peripheral blood procalcitonin levels

Immediately after admission, 0.5 mL of peripheral venous blood was collected from the newborns, solid-phase immunochromatography was used to detect the levels of procalcitonin (PCT), and PCT > 2.0 ng/mL was the standard of clinical value.

2.4. Serum inflammatory mediators

Immediately after admission, 0.5 mL of peripheral venous blood was collected from the newborns in the same way, anti-coagulated with heparin, then let stand at room temperature for 24 h and centrifuged for 10min in low-temperature centrifuge at 2,500 r/min to get the supernatant, and enzyme-linked immunosorbent assay (ELISA) was used to determine the inflammatory mediator levels in it, including interleukin-1β (IL-1β), interleukin-6 (IL-6), interleukin-8 (IL-8) and tumor necrosis factor-α (TNF-α).

2.5. Myocardial injury

Immediately after admission, color Doppler diasonograph (Wuhan Kaijin Medical Technology Co., Ltd., kai-x6) was used to determine the cardiac output (CO) and left ventricular ejection fraction (LVEF) of each group, MyLab Desk workstation was further used for two-dimensional speckle-tracking imaging, and the left ventricular global longitudinal strain rate (GLSr) and left ventricular global circumferential strain rate (GCSr) were analyzed and calculated. At the same time, peripheral blood serum was obtained from each group in the same way, and the conditioned immunity was used to detect myocardial injury index content, including cardiac troponin I (cTnI), heart-type fatty acid-binding protein (H-FABP) and α-hydroxybutyric dehydrogenase (HBDH).

2.6. Statistical analysis

One person with professional statistical qualification was selected to calculate and record the data obtained in the study, measurement data was in terms of mean ± standard deviation, comparison between two groups was by paired t test, comparison among three groups was by variance analysis of repeated measures and P<0.05 was set as the standard of statistical significance in differences.

3. Results

3.1. Peripheral blood procalcitonin levels

Immediately after admission, peripheral blood PCT content of observation group was (10.23±2.17) ng/mL, and the peripheral blood PCT content of control group was (0.73±0.09) ng/mL. Peripheral blood PCT content of observation group was significantly higher than that of control group, differences between groups were statistically significant (P<0.05). The median of peripheral blood PCT content was referred to further divide the observation group into high PCT group and low PCT group, 24 cases in each group.

3.2. Serum inflammatory mediators

Differences in serum inflammatory mediators IL-1β, IL-6, IL-8 and TNF-α contents were statistically significant among the three groups (P<0.05). Serum inflammatory mediators IL-1β, IL-6, IL-8 and TNF-α contents of high PCT group and low PCT group were significantly higher than that of control group, differences between groups were statistically significant (P<0.05). The median of peripheral blood PCT content was referred to further divide the observation group into high PCT group and low PCT group, 24 cases in each group.
3.3. Left ventricular systolic function indexes

Differences in left routine ultrasound parameters CO and LVEF as well as two-dimensional speckle-tracking imaging parameters GLSr and GCSR were statistically significant among the three groups ($P<0.05$). CO and LVEF levels as well as the absolute value of GLSr and GCSR of high PCT group and low PCT group were lower than those of normal control group, CO and LVEF levels as well as the absolute value of GLSr and GCSR of high PCT group were lower than those of low PCT group, and differences between groups were statistically significant ($P<0.05$), shown in Table 2.

### Table 2

Comparison of left ventricular systolic function index levels among groups (mean ± SD).

<table>
<thead>
<tr>
<th>Groups</th>
<th>$n$</th>
<th>Routine ultrasound parameters</th>
<th>Two-dimensional speckle-tracking imaging parameters</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>CO (L/min)</td>
<td>LVEF (%)</td>
</tr>
<tr>
<td>High PCT group</td>
<td>28</td>
<td>0.31±0.04$^a$</td>
<td>0.51±0.06$^a$</td>
</tr>
<tr>
<td>Low PCT group</td>
<td>28</td>
<td>0.34±0.04$^a$</td>
<td>0.55±0.07$^a$</td>
</tr>
<tr>
<td>Normal control group</td>
<td>50</td>
<td>0.39±0.05</td>
<td>0.63±0.08</td>
</tr>
<tr>
<td>$F$</td>
<td></td>
<td>6.29</td>
<td>7.12</td>
</tr>
<tr>
<td>$P$</td>
<td></td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

Compared with normal control group, $^aP<0.05$; compared with low PCT group, $^bP<0.05$.

3.4. Serum myocardial injury indexes

Differences in serum myocardial injury indexes cTnl, H-FABP and HBDH contents were statistically significant among the three groups ($P<0.05$). Serum myocardial injury indexes cTnl, H-FABP and HBDH contents of high PCT group and low PCT group were significantly higher than those of normal control group, serum myocardial injury indexes cTnl, H-FABP and HBDH contents of high PCT group were significantly higher than those of low PCT group, and differences between groups were statistically significant ($P<0.05$), shown in Table 3.

### Table 3

Comparison of serum myocardial injury index contents among groups (mean ± SD).

<table>
<thead>
<tr>
<th>Groups</th>
<th>$n$</th>
<th>cTnl (ng/mL)</th>
<th>H-FABP (ng/mL)</th>
<th>HBDH (U/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>High PCT group</td>
<td>28</td>
<td>0.34±0.05$^b$</td>
<td>16.34±2.85$^a$</td>
<td>341.28±45.79$^a$</td>
</tr>
<tr>
<td>Low PCT group</td>
<td>28</td>
<td>0.19±0.03$^a$</td>
<td>9.17±0.98$^a$</td>
<td>173.28±20.95$^a$</td>
</tr>
<tr>
<td>Normal control group</td>
<td>50</td>
<td>0.08±0.01</td>
<td>5.93±0.72</td>
<td>150.28</td>
</tr>
<tr>
<td>$F$</td>
<td></td>
<td>7.23</td>
<td>12.19</td>
<td>18.56</td>
</tr>
<tr>
<td>$P$</td>
<td></td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

Compared with normal control group, $^aP<0.05$; compared with low PCT group, $^bP<0.05$.

4. Discussion

The diagnosis of neonatal septicemia mostly depends on the risk factors and clinical symptoms in medical history as well as peripheral hemogram change, the definite diagnosis depends on pathogen detection, but the early clinical symptoms of the disease are not obvious, the rise of white blood cell levels appears late, the pathogenic bacteria culture is time-consuming, and all of them cannot become the reliable means for early diagnosis of disease[5,6].

Looking for the quantitative indicators with high sensitivity and specificity is the focus of the current research on neonatal septicemia, and PCT, as a new type of infection index, has attracted much attention at the moment. PCT, as a protein, can be early highly expressed in plasma in the case of severe bacterial infections and septicemia, but its level does not rise in the case of autoimmune diseases, allergies, virus infection or mild local infection[7,8].

Current research has confirmed that the PCT mRNA is highly expressed in septicemia rat model, and the detection of serum PCT contents in newborns with neonatal septicemia and normal newborns in the study showed that serum PCT content of observation group was lower than that of normal control group, it indicates that PCT is highly expressed in neonatal septicemia, and it macroscopically confirms that high levels of PCT is a sensitive indicator to identify
the occurrence of neonatal septicemia, and can be used for early diagnosis and identification of the disease.

Systemic inflammatory response is one of the specific manifestations of the pathophysiological process of septicemia, the pro-inflammatory factors are massively secreted in the body and form the inflammatory cascade reaction, which weakens the autoimmune function, attacks the important tissue and viscera, and lead to further damage[9]. IL-1β, IL-6, IL-8 and TNF-α are all pro-inflammatory factors, the fluctuation of their contents can quantifiably reflect the extent of the body's inflammatory response, the above indicators keep dynamic balance within a certain scope under physiological state, and the pathogen infection and the above indicators keep dynamic balance within a certain scope under physiological state, and the pathogen infection and massive toxin secretion into the blood can stimulation the massive generation of IL-1β, IL-6, IL-8, TNF-α and other pro-inflammatory mediators[10,11]. The body's inflammatory response extent is directly related to the septicemia severity, and comparison of serum inflammatory mediator contents among groups in the study showed that serum IL-1β, IL-6, IL-8 and TNF-α contents of observation group were higher than those of control group, serum IL-1β, IL-6, IL-8 and TNF-α contents of high PCT group were higher than those of low PCT group, it indicates that the existence of massive pro-inflammatory mediators is an important characteristic of neonatal septicemia, PCT levels are positively correlated with the degree of systemic inflammatory response, and it directly shows its value for judging the disease severity.

Existence of a large amount of pro-inflammatory mediators can lead to important viscera function injury in newborns, the heart is the most affected viscera, and the main manifestation is the damaged myocardial function and the reduced left ventricular systolic capacity[12,13]. Ultrasound is the preferred noninvasive method to determine cardiac damage degree, conventional ultrasound can detect the cardiac dynamics change, two-dimensional speckle tracking imaging can detect tiny heart damage, and the large application value is great in the early disease[14]. In the study, it was found after all groups of subjects received conventional ultrasound and two-dimensional speckle tracking imaging that CO and LVEF levels as well as the absolute value of GLSr and GCSr of observation group were lower than those of control group, and CO and LVEF levels as well as the absolute value of GLSr and GCSr of high PCT group were lower than those of low PCT group, it indicates that there are myocardial injury and left ventricular systolic capacity reduction in newborns with septicemia, PCT content is positively correlated with cardiac damage degree, and it can be used to indirectly judge the target organ damage.

Ultrasoundography can reflect the macroscopic damage of the cardiac function, it mostly shows abnormality in more serious conditions, and the myocardial enzyme spectrum index levels in circulating blood may change in early septicemia, and are more advantageous in the sensitivity to reflect the occurrence of heart damage or not/heart injury severity[15,16]. cTnI, H-FABP and HBDH are the myocardial enzyme spectrum indexes covered in many clinical reports, cTnI is the regulatory protein of cardiac muscle contraction, its serum content is little under physiological condition, and it can be released into the blood by myocardial cells in the case of myocardial injury; H-FABP specifically exists in the myocardial cells, and peripheral blood H-FABP content may increase in early myocardial infarction, heart failure and other diseases; HBDH can reflect the activity of lactate dehydrogenase isozyme, it is of great significance to diagnosing myocardial diseases, and it is mostly used together with other myocardial injury markers to early diagnose myocardial dysfunction[17]. In the study, comparison of serum myocardial enzyme spectrum index contents among groups showed that serum cTnI, H-FABP and HBDH contents of observation group were higher than those of control group, and serum cTnI, H-FABP and HBDH contents of high PCT group were higher than those of low PCT group, which further illustrates that there is myocardial injury in neonatal septicemia, and also confirms that serum PCT levels in children with septicemia are positively correlated with the severity of myocardial injury.

Serum PCT content can be used as an auxiliary index to early diagnose neonatal septicemia, PCT content is positively correlated with the degree of systemic inflammatory response and heart injury, and it is of great value for judgment of disease severity, establishment of treatment solution and other aspects. The heart injury is mainly discussed in the study, and the value of PCT content for assessing other tissue viscera injury is to be confirmed in subsequent study.

References


