Effect of prostaglandin E1 combined with Xuebijing on the inflammatory response process and target organ function in patients with sepsis

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ABSTRACT

Objective: To explore the effect of prostaglandin E1 combined with Xuebijing on the inflammatory response process and target organ function in patients with sepsis. Methods: A total of 78 patients with sepsis who were treated in our hospital between February 2014 and July 2017 were divided into control group (n=39) and study group (n=39) by random number table method. Control group received Xuebijing therapy on the basis of routine treatment, and study group received prostaglandin E1 combined with Xuebijing therapy on the basis of routine treatment. The differences in serum levels of inflammatory mediators and target organ function indexes were compared between the two groups before treatment (T0), after 1 week of treatment (T1) and after 2 weeks of treatment (T2). Results: At T0, there was no statistically significant difference in the serum levels of inflammatory mediators, myocardial enzyme spectrum indexes as well as liver and kidney function indexes between the two groups. At T1 and T2, serum inflammatory mediators IL-6, IL-10, PCT and CRP levels of study group were lower than those of control group; serum myocardial enzyme spectrum indexes CK-MB, hs-cTnT and LDH contents were lower than those of control group; serum liver and kidney function indexes BUN, Cr, TBIL and TBA contents were lower than those of control group. Conclusion: Prostaglandin E1 combined with Xuebijing can effectively reduce the systemic inflammatory response and actively protect the liver and kidney function of patients with sepsis.

1. Introduction

Sepsis is a disease with a high clinical mortality rate and is induced after the bacteria and its toxic products enter the blood. In essence, the disease is the body’s reaction to infectious factors[1,2]. According to the current relevant statistics, about 14 000 people die from the complications of sepsis each year in the world, its mortality rate has exceeded that of myocardial infarction, and rescue is needed to save patient’s life once diagnosed. Early fluid resuscitation and infection control by sensitive antibiotics is the conventional way to treat sepsis, and Xuebijing is a drug to antagonize endotoxin, can improve the microcirculation, reduce inflammatory exudation and so on, and has been widely applied in current treatment of sepsis. Prostaglandin E1 is the active substance widely existing in the body, it can improve hemodynamics, inhibit platelet activation, stimulate tissue fibrinolysis substance generation and so on[3,4], it has been confirmed that it can improve the condition of sepsis rat models, but it is less applied and studied in human body. In this research, prostaglandin E1 and Xuebijing were used together for clinical treatment of patients with sepsis, and the effects of the therapeutic regimen on the systemic inflammatory response and target organ damage were explored in order to provide reference for subsequent treatment establishment for similar patients.

2. Information and methods

2.1 Case information

A total of 78 patients with sepsis who were treated in our hospital between February 2014 and July 2017 were selected as the research subjects and divided into control group (n=39) and study group
by random number table method. Control group included 21 males and 18 females who were 42-70 years old; study group included 20 males and 19 females who were 39-71. There was no statistically significant difference in the distribution of above basic information between the two groups, and the follow-up research plan was reviewed and approved by the ethics committee of the hospital.

Inclusion criteria: (1) clinically diagnosed with sepsis; (2) with sepsis attack for the first time and receiving no relevant treatment out of hospital before admission; (3) whose family members signed the informed consent. Exclusion criteria: (1) with basic severe heart, liver and kidney insufficiency before sepsis attack; (2) combined with severe autoimmune dysfunction; (3) pregnant or breast-feeding women.

2.2 Therapy

Both groups of patients received clinical routine therapy for sepsis, including fluid resuscitation, anti-infection, water-electrolyte balance regulation, nutritional support, etc. On the basis of the above routine treatment, control group received Xuebijing therapy, which was as follows: 100 mL of Xuebijing injection in 200 mL of 5% glucose liquid, by intravenous drip, 2 times/d for continuous 14 d.

On the basis of the above routine treatment, study group received prostaglandin E1 combined with Xuebijing treatment, which was specifically as follows: 20 μg of prostaglandin E1 in 100 mL of saline, by intravenous drip, 1 time/d for continuous 14 d.

2.3 Observation indexes

Before treatment (T0), after 1 week of treatment (T1) and after 2 weeks treatment (T2), cubital venous blood samples were obtained from the two groups and anti-coagulated to separate serum for test. Enzyme-linked immunosorbent assay was adopted to determine the serum levels of inflammatory mediators interleukin-6 (IL-6), interleukin-10 (IL-10), procalcitonin (PCT) and C-reactive protein (CRP); RIA method was used to detect the serum levels of myocardial enzyme spectrum indexes creatine kinase isoenzyme (CK-MB), hypersensitive cardiac troponin (hs-cTnT) and lactate dehydrogenase (LDH), liver function indexes total bilirubin (TBIL), and total bile acid (hs-cTnT) as well as kidney function indexes blood urea nitrogen (BUN) and serum creatinine (Cr).

2.4 Statistical methods

The numerical values of inflammatory mediators, myocardial enzyme spectrum indexes as well as liver and kidney function indexes were all input in SPSS 25.0, the t test was used to calculate the statistic P and P<0.05 was set as the standard of statistical significance in differences.

3. Results

3.1 Inflammatory mediators

Comparison of serum inflammatory mediators IL-6 (pg/mL), IL-10 (pg/mL), PCT (μg/L) and CRP (mg/L) levels between two groups of patients was as follows: at T0, the differences in serum IL-6, IL-10, PCT and CRP levels were not statistically significant between the two groups of patients (P>0.05). At T1 and T2, serum IL-6, IL-10, PCT and CRP levels of both groups were lower than those at T0; serum IL-6, IL-10, PCT and CRP levels of study group were lower than those of control group (P<0.05), shown in Table 1.

3.2 Myocardial enzyme spectrum indexes

Comparison of serum myocardial enzyme spectrum indexes CK-MB (U/L), hs-cTnT (mg/L) and LDH (U/L) levels between two groups of patients was as follows: at T0, differences in serum CK-MB, hs-cTnT, and LDH levels of both groups were not statistically significant (P>0.05). At T1 and T2, serum CK-MB, hs-cTnT, and LDH levels of both groups were lower than those at T0; serum CK-MB, hs-cTnT, and LDH levels of study group were lower than those of control group (P<0.05), shown in Table 2.

Table 1.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Time point</th>
<th>IL-6</th>
<th>IL-10</th>
<th>PCT</th>
<th>CRP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>39</td>
<td>T0</td>
<td>45.39±5.12</td>
<td>103.18±14.27</td>
<td>8.33±0.91</td>
<td>10.28±1.64</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T1</td>
<td>30.17±3.42</td>
<td>75.32±8.15</td>
<td>5.17±0.58</td>
<td>7.13±0.94</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T2</td>
<td>14.29±1.73</td>
<td>32.77±4.83</td>
<td>2.16±0.23</td>
<td>3.88±0.42</td>
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<tr>
<td>Study group</td>
<td>39</td>
<td>T0</td>
<td>45.42±5.48</td>
<td>103.21±13.58</td>
<td>8.19±0.92</td>
<td>10.31±1.59</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T1</td>
<td>21.33±2.75</td>
<td>50.48±5.41</td>
<td>3.41±0.38</td>
<td>5.06±0.54</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T2</td>
<td>8.05±0.89</td>
<td>14.39±1.61</td>
<td>0.91±0.12</td>
<td>1.85±0.21</td>
</tr>
</tbody>
</table>

Note: compared with same group at T0, P<0.05.

Table 2.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Time point</th>
<th>CK-MB</th>
<th>hs-cTnT</th>
<th>LDH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>39</td>
<td>T0</td>
<td>74.28±9.13</td>
<td>29.47±3.51</td>
<td>294.57±34.12</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T1</td>
<td>41.53±5.42</td>
<td>21.09±2.45</td>
<td>180.45±21.36</td>
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<tr>
<td></td>
<td></td>
<td>T2</td>
<td>18.45±2.31</td>
<td>10.35±1.61</td>
<td>113.74±13.29</td>
</tr>
<tr>
<td>Study group</td>
<td>39</td>
<td>T0</td>
<td>74.37±9.33</td>
<td>29.51±3.47</td>
<td>293.48±32.64</td>
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<tr>
<td></td>
<td></td>
<td>T1</td>
<td>29.74±3.51</td>
<td>14.88±1.62</td>
<td>120.39±14.71</td>
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<tr>
<td></td>
<td></td>
<td>T2</td>
<td>11.19±1.63</td>
<td>5.48±0.61</td>
<td>65.48±7.12</td>
</tr>
</tbody>
</table>

Note: compared with same group at T0; P<0.05.
MB, hs-cTnT and LDH levels were not statistically significant between the two groups of patients \((P > 0.05)\). At T1 and T2, serum CK-MB, hs-cTnT and LDH levels of both groups were lower than those at T0; serum CK-MB, hs-cTnT and LDH levels of study group were lower than those of control group \((P < 0.05)\), shown in Table 2.

### 3.3 Liver and kidney function indexes

Comparison of serum liver and kidney function indexes BUN (mmol/L), Cr (μmol/L), TBIL (μmol/L) and TBA (μmol/L) levels between two groups of patients was as follows: at T0, the differences in serum BUN, Cr, TBIL and TBA levels were not statistically significant between the two groups of patients \((P > 0.05)\). At T1 and T2, serum BUN, Cr, TBIL and TBA levels of both groups were lower than those at T0; serum BUN, Cr, TBIL and TBA levels of study group were lower than those of control group \((P < 0.05)\), shown in Table 3.

### 4. Discussion

Sepsis is one of the diseases with the highest mortality rates in the world. After routine treatment, such as anti-shock and anti-infection, a large number of patients still die from multiple organ dysfunction. To seek more efficient and reliable treatment, the focus is on the current study of sepsis, and Xuebijing has anti-endotoxin effect, can effectively reduce the endotoxin release after bacteria infection, and helps relieve the illness in sepsis patients. Alprostadil E1 is a vasoactive drug, and pharmacological studies have confirmed that it can (1) inhibit platelet aggregation, reduce platelet hyperresponsiveness and improve erythrocyte deformability; (2) activate lipoprotein lipase and reduce blood viscosity; (3) activate the tissue-type plasminogen activator substances produced by vascular endothelial cells and have certain drim, mm mb ect thrombolytic effect; (4) inhibit calcium influx in vascular smooth muscle cells, improve microcirculation, and so on, its efficacy is significant in protecting the blood supply in tissue vessels and other aspects, so it was introduced into the treatment of patients with sepsis in the research, and the effects of combined treatment on patients’ conditions were discussed.

Systemic inflammatory response syndrome (SIRS) is the most typical symptom in patients with sepsis, the body releases pro-inflammatory mediators IL-6, CRP and so on in early stage of the disease to activate white blood cells and blood coagulation system, and prevent further spread of the pathogen. Anti-inflammatory cytokines IL-10 and so on are often produced together with pro-inflammatory factors to prevent excessive inflammatory response. When the pathogenic bacteria persist and secrete endotoxin and so on to aggravate systemic vascular and tissue organ damage, and the inflammatory response gradually expands and forms SIRS. PCT content is stable in patients with mild infection, the PCT content increases rapidly when severe infection occurs, and the specific content is highly consistent with the severity of sepsis. The study results showed that serum inflammatory mediators IL-6, IL-10, PCT and CRP levels of both groups at different time points after treatment were lower than those before treatment, and the decrease in serum levels of above indexes in study group was more significant, indicating that prostaglandin E1 combined with Xuebijing therapy can effectively reduce the systemic inflammatory response in the patients with sepsis.

The myocardial injury rate is high in patients with sepsis, and the specific mechanisms include the followings: (1) the endotoxin and other pathogenic bacteria directly injure the myocardial cells; (2) the body’s immunity declines and the systemic inflammatory reaction causes myocardial cell injury; (3) under shock state, myocardial blood supply decreases and myocardial ischemic hypoxic injury occurs. Myocardial cells are rich in enzymes, the cytokines specifically existing in the cells are released into the blood after injury occurs, and they can be used as the specific indicators to diagnose and determine the degree of myocardial injury. The study results showed that serum myocardial enzyme spectrum indexes CK-MB, hs-cTnT and LDH levels of both groups at different time points after treatment were lower than those before treatment, and the decrease in serum levels of above indexes in study group was more significant, it indicates that prostaglandin E1 combined with Xuebijing therapy can effectively protect the myocardial cells in patients with sepsis, and this is directly related to the effects of prostaglandin E1 on expanding blood vessels and optimizing microcirculation.

Both liver and kidney tissues are the important organs with large blood volume, and the patients with sepsis show different levels of shock state, which results in target organ ischemia as well as dysfunction in severe cases. At the same time, latest studies have shown that ATPase activity decreases in the mitochondrial
membrane of liver cells in the rats with sepsis, showing that energy metabolism disorder also plays an important role in target organ damage. BUN and Cr are the most typical renal function indexes, and when the renal blood flow reduces or there is renal parenchyma dysfunction, the glomerular ability to filtrate above substances declines, and the BUN and Cr contents in the circulating blood increase. TBIL and TBA contents represent the liver function, and when there is liver dysfunction, the liver cells cannot effectively metabolize intrahepatic bile, so its contents rises in the circulating blood, and the specific increase is consistent with the degree of liver dysfunction. The study results showed that serum liver and kidney function indexes BUN, Cr, TBIL, and hs-cTnT levels of both groups decreased at different time points after treatment, and the decrease in the levels of above indexes in study group was more significant, indicating that prostaglandin E1 combined with Xuebijing treatment can effectively protect the liver and kidney function.

To sum up, it is concluded that prostaglandin E1 combined with Xuebijing can effectively reduce the systemic inflammatory response and protect the heart, liver and kidney function in patients with sepsis, and it is of positive clinical significance and is worth popularization and application in clinical practice in the future.

References


