Influence of continuous blood purification on inflammation and target organ damage in patients with severe acute pancreatitis complicated by MODS

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Objective: To study the influence of continuous blood purification on inflammation and target organ damage in patients with severe acute pancreatitis accompanied by MODS. Methods: A total of 78 patients with severe acute pancreatitis complicated by MODS who were treated in our hospital between June 2012 and March 2016 were selected and divided into control group (n=39) and observation group (n=39) according to random number table. Control group were treated with routine treatment, observation group were treated with conventional treatment plus continuous blood purification, and serum inflammatory factors, liver function indexes and renal function indexes were compared between two groups of patients before and after treatment. Results: Before treatment, differences in serum levels of inflammatory factors, liver function indexes and renal function indexes were not statistically significant between two groups of patients. After treatment, serum inflammatory factors IL-6, IL-8, MCP-1 and HMGB1 levels of observation group were lower than those of control group, liver function indexes ALT, AST, TBIL and ALP levels of observation group were lower than those of control group, and renal function indexes Scr and BUN levels of observation group were lower than those of control group. Conclusion: Continuous blood purification can reduce the systemic inflammatory response as well as liver and kidney injury in patients with severe acute pancreatitis complicated by MODS.

1. Introduction

Severe acute pancreatitis is a clinical critical disease with extremely high case fatality rate, and the trypsin autodigestion leads to pancreatic congestion necrosis, which can cause secondary abdominal and respiratory infections, and multiple organ function failure[1,2]. Multiple organ dysfunction syndrome (MODS) is a severe complication of severe acute pancreatitis, pancreatitis patients with MODS are with high mortality rate, and early positive rescue measures need to be taken. Fasting, gastrointestinal decompression, resolving tetany and relieving pain, etc are the most common means for acute pancreatitis treatment, but their effect on severe acute pancreatitis patients with MODS is weak, and they are unable to effectively prevent disease progression. Continuous blood purification is a reliable method to remove the abundant toxins and inflammatory factors in the body, which helps to reduce systemic inflammatory response and stabilize the internal environment, and is expected to become the new way for severe acute pancreatitis treatment[3,4]. In the study, continuous blood purification was added in the treatment of patients with severe acute pancreatitis complicated by MODS, and its curative effect was analyzed from inflammatory response, target organ injury and other aspects.

2. Information and methods

2.1 Case information

A total of 78 patients with severe acute pancreatitis complicated by MODS who were treated in our hospital between June 2012 and March 2016 were selected as the research subjects, and the families of the patients signed the consent form. Inclusion criteria: (1) in accordance with the clinical and laboratory diagnostic criteria for severe acute pancreatitis and MODS; (2) without prior history of
acute pancreatitis; (3) with normal liver and kidney function before the pancreatitis attack. Exclusion criteria: (1) dead shortly after admission; (2) refusing to cooperate with the treatment and related examination, and with incomplete clinical data. The 78 patients were divided into control group (n=39) and observation group (n=39) according to random number table. Control group included 20 male cases and 19 female cases that were 32-71 years old; observation group included 21 male cases and 18 female cases that were 30-73 years old. The two groups of patients were not significantly different in gender and age (P>0.05), and the research was approved by the hospital ethics committee.

2.2 Therapy

Control group were treated with conventional clinical treatment for severe acute pancreatitis complicated by MODS, including fasting, gastrointestinal decompression, resolving tetany and relieving pain, inhibiting trypsin secretion, anti-infection, etc. Observation group of patients, on the basis of conventional treatment, received continuous blood purification therapy, specifically as follows: conducting femoral vein intubation to establish effective venous pathway, adopting continuous blood purification system, setting substitution fluid velocity to 3 L/h, and conducting continuous blood purification for 5 d in a row.

2.3 Observation indexes

Immediately after admission and 1 week after treatment, 2.0 mL of peripheral venous blood was extracted from two groups of patients respectively, intervened with anticoagulant, then let stand at room temperature for stratification, and centrifuged at 4 ℃ and low speed to get supernatant and freeze it in the deep cryogenic refrigerator for testing. ELISA kits were used to determine serum levels of inflammatory factors, including interleukin-6 (IL-6), interleukin 8 (IL-8), monocyte chemotactant protein 1 (MCP-1) and high mobility group box 1 (HMGB1). Automatic biochemical analyzer (Wuhan Shengshida Medical Equipment Co., Ltd., bs-330e) was used to determine serum levels of liver function and renal function indexes: alanine aminotransferase (ALT), aspartate aminotransferase (AST), total bilirubin (TBIL) and alkaline phosphatase (ALP) as well as renal function indexes: serum creatinine (Scr) and blood urea nitrogen (BUN).

2.4 Statistical methods

Statistical software was SPSS 21.0, and the statisticians were with professional statistical knowledge and researcher qualification. Inflammatory indexes, liver and renal function indexes and other measurement data were in terms of mean ± standard deviation, comparison within group before and after treatment was by paired t test and comparison between groups after treatment was by grouping t test. P<0.05 was the standard of statistical significance in differences in the study.

3. Results

3.1 Inflammatory factors

Analysis of serum inflammatory factors IL-6 (ng/L), IL-8 (ng/L), MCP-1 (ng/mL) and HMGB1 (ng/mL) levels between two groups of patients was as follows: before treatment, serum IL-6, IL-8, MCP-1 and HMGB1 levels were not significantly different between two groups of patients (P>0.05); after treatment, serum IL-6, IL-8, MCP-1 and HMGB1 levels of both groups were significantly lower than those before treatment (P<0.05), and serum IL-6, IL-8, MCP-1 and HMGB1 levels of observation group were significantly lower than those of control group (P<0.05), shown in Table 1.

3.2 Liver function

Analysis of serum liver function indexes ALT (IU/L), AST (IU/L), TBIL (μmol/L) and ALP (IU/L) between two groups of patients was as follows: before treatment, serum ALT, AST, TBIL and ALP levels were not significantly different between two groups of patients (P>0.05); after treatment, serum ALT, AST, TBIL and ALP levels of both groups were significantly lower than those before treatment (P<0.05), and serum ALT, AST, TBIL and ALP levels of observation group were significantly lower than those of control group (P<0.05), shown in Table 2.

Table 1.
Comparison of serum inflammatory factor levels between two groups before and after treatment.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Time</th>
<th>IL-6</th>
<th>IL-8</th>
<th>MCP-1</th>
<th>HMGB1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>39</td>
<td>Before treatment</td>
<td>121.38±15.79</td>
<td>148.26±17.83</td>
<td>56.38±7.19</td>
<td>19.27±2.64</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>82.64±9.13  *</td>
<td>92.17±10.53 *</td>
<td>40.17±5.28 *</td>
<td>10.85±2.14 *</td>
</tr>
<tr>
<td>Observation</td>
<td>39</td>
<td>Before treatment</td>
<td>122.16±14.85</td>
<td>147.58±17.66</td>
<td>56.19±6.73</td>
<td>19.31±2.58</td>
</tr>
<tr>
<td>group</td>
<td></td>
<td>After treatment</td>
<td>45.92±6.16 *</td>
<td>57.52±7.15 *</td>
<td>24.68±3.17 *</td>
<td>6.11±0.73 *</td>
</tr>
</tbody>
</table>

Note: compared with same group before treatment, \*P<0.05; compared with control group after treatment, \#P<0.05.

Table 2.
Comparison of serum liver function index levels between two groups before and after treatment.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Time</th>
<th>ALT</th>
<th>AST</th>
<th>TBIL</th>
<th>ALP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>39</td>
<td>Before treatment</td>
<td>67.29±8.11</td>
<td>89.47±10.16</td>
<td>69.36±8.12</td>
<td>274.39±30.47</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>31.28±4.05 *</td>
<td>41.63±5.09 *</td>
<td>34.71±4.53 *</td>
<td>154.77±18.63 *</td>
</tr>
<tr>
<td>Observation</td>
<td>39</td>
<td>Before treatment</td>
<td>67.15±8.06</td>
<td>88.95±9.75</td>
<td>68.75±8.05</td>
<td>271.74±31.63</td>
</tr>
<tr>
<td>group</td>
<td></td>
<td>After treatment</td>
<td>17.32±2.71 *</td>
<td>20.74±3.11 *</td>
<td>17.66±2.18 *</td>
<td>71.63±9.05 *</td>
</tr>
</tbody>
</table>

Note: compared with same group before treatment, \*P<0.05; compared with control group after treatment, \#P<0.05.
HMGB1 belong to new inflammatory factors, excessive activation eventually causes MODS in patients with severe acute pancreatitis complicated by MODS are with higher mortality than patients with acute pancreatitis alone, and how to early restore homeostasis is the key to control the disease and protect the important viscera function. Continuous hemodialysis exchanges the substances in the blood through dispersion/convection and other ways, it help to clear away the metabolism waste and the excessively secreted inflammatory factors in the circulating blood, and it has been successfully applied in the treatment of organophosphorus poisoning and other acute events. The massive accumulation of metabolites is a core factor in occurrence and development of severe acute pancreatitis, and therefore, continuous hemodialysis was used in the treatment of patients with severe acute pancreatitis complicated by MODS in our hospital in the study in order to clarify its clinical application value. Systemic inflammatory response levels in patients with severe acute pancreatitis are positively correlated with the disease, IL-6 and IL-8 are the most common pro-inflammatory factors, and it has been confirmed in many studies that it massively exists in the circulating blood of patients with acute pancreatitis. MCP-1 and HMGB1 belong to new inflammatory factors, excessive activation of MCP-1 can cause inflammatory cell infiltration in the pancreas and local massive release of inflammatory mediators, and directly mediate pancreas damage process; HMGB1 is a late inflammatory mediator, which increases inflammation and leads to distant metastases of inflammation through several ways. In the study, the serum levels of above inflammatory cytokines were compared before and after the treatment, and it was found that serum IL-6, IL-8, MCP-1 and HMGB1 levels of both groups after treatment were lower than those before treatment, indicating that both therapies have obtained a certain effect. And serum IL-6, IL-8, MCP-1 and HMGB1 levels of observation group after treatment were lower than those of control group, showing that continuous blood purification can more effectively reduce the inflammatory factors in circulating blood and actively reduce the systemic inflammatory response in patients.

Inflammatory factors can cause microcirculation disorders via microvascular dilation, further cause damage to the mitochondrial membrane, and lead to systemic inflammatory response and MODS. Systemic inflammatory response is an important cause of MODS in patients with severe acute pancreatitis, it has been confirmed in the study that continuous blood purification can reduce the inflammatory factor levels in the circulating blood, but its changes to the liver, kidney and other target organ damage is still unknown. The liver is the first viscera involved by severe acute pancreatitis, the main manifestation is the increase in liver cell permeability and the decrease in synthesis ability, and the serological manifestation is the increase in ALT, AST and other liver enzyme levels, and the decomposition disorder and accumulation of TBIL, ALP and other metabolites in the body. In this study, serum ALT, AST, TBIL and ALP levels of observation group after treatment were significantly lower than those of control group, and it shows that continuous blood purification can effectively reduce liver function damage, which is speculated to be mainly related to the scavenging of inflammatory factors. The kidney is also the commonly involved organ by abdominal inflammation, the incidence of renal dysfunction in patients with severe acute pancreatitis is about more than 50%, and the main manifestations are the glomerular filtration dysfunction and the obstacles in discharging Scr, BUN and other metabolic materials. In the study, renal function was compared between the two groups of patients after treatment, and it was found that serum Scr and BUN levels of observation group after treatment were lower than those of control group, showing

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Time</th>
<th>Scr</th>
<th>BUN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>39</td>
<td>Before treatment</td>
<td>251.28±30.79</td>
<td>29.37±3.62</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>171.49±19.53</td>
<td>19.11±2.43</td>
</tr>
<tr>
<td>Observation</td>
<td>39</td>
<td>Before treatment</td>
<td>251.64±31.62</td>
<td>29.45±3.59</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>115.38±15.49</td>
<td>12.05±1.74</td>
</tr>
</tbody>
</table>

Comparison of serum renal function index levels between two groups before and after treatment.

Analysis of serum renal function indexes Scr (μmol/L) and BUN (mmol/L) between two groups of patients was as follows: before treatment, serum Scr and BUN levels were not significantly different between two groups of patients (P>0.05); after treatment, serum Scr and BUN levels of both groups were significantly lower than those before treatment (P<0.05), and serum Scr and BUN levels of observation group were significantly lower than those of control group (P<0.05), shown in Table 3.

3.3 Renal function

Note: compared with same group before treatment, *P*<0.05; compared with control group after treatment, **P**<0.05.

4. Discussion

Patients with severe acute pancreatitis are first characterized by severe systemic inflammatory response, and trypsin autodigestion causes pancreatic tissue to massively release pro-inflammatory factors, further induces the generation of more inflammatory mediators and forms "waterfall effect", which increases systemic inflammatory response while attacks surrounding tissue organs and eventually causes MODS. Patients with severe acute pancreatitis complicated by MODS are with higher mortality than patients with acute pancreatitis alone, and how to early restore homeostasis is the key to control the disease and protect the important viscera function. Continuous hemodialysis exchanges the substances in the blood through dispersion/convection and other ways, it help to clear away the metabolism waste and the excessively secreted inflammatory factors in the circulating blood, and it has been successfully applied in the treatment of organophosphorus poisoning and other acute events. The massive accumulation of metabolites is a core factor in occurrence and development of severe acute pancreatitis, and therefore, continuous hemodialysis was used in the treatment of patients with severe acute pancreatitis complicated by MODS in our hospital in the study in order to clarify its clinical application value. Systemic inflammatory response levels in patients with severe acute pancreatitis are positively correlated with the disease, IL-6 and IL-8 are the most common pro-inflammatory factors, and it has been confirmed in many studies that it massively exists in the circulating blood of patients with acute pancreatitis. MCP-1 and HMGB1 belong to new inflammatory factors, excessive activation of MCP-1 can cause inflammatory cell infiltration in the pancreas and local massive release of inflammatory mediators, and directly mediate pancreas damage process; HMGB1 is a late inflammatory mediator, which increases inflammation and leads to distant metastases of inflammation through several ways. In the study, the serum levels of above inflammatory cytokines were compared before and after the treatment, and it was found that serum IL-6, IL-8, MCP-1 and HMGB1 levels of both groups after treatment were lower than those before treatment, indicating that both therapies have obtained a certain effect. And serum IL-6, IL-8, MCP-1 and HMGB1 levels of observation group after treatment were lower than those of control group, showing that continuous blood purification can more effectively reduce the inflammatory factors in circulating blood and actively reduce the systemic inflammatory response in patients.

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that continuous hemodialysis can also effectively optimize the renal function, and reduce inflammatory medium damage to the kidney. It is thus clear that continuous blood purification based on routine treatment can effectively reduce the systemic inflammatory response, and actively protect the liver and kidney function of patients with severe acute pancreatitis complicated by MODS, it is an effective and reasonable adjuvant therapy, and it can be applied in clinical practice in the future.

References


