Effect of breviscapine in combined with octreotide on the inflammatory reaction and vasoactive substances in patients with severe acute pancreatitis

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ABSTRACT

Objective: To explore the effect of breviscapine in combined with octreotide on the inflammatory reaction and vasoactive substances in patients with severe acute pancreatitis (SAP). Methods: A total of 72 patients with SAP who were admitted in our hospital from January, 2014 to November, 2016 were included in the study and randomized into the observation group and the control group. The patients in the two groups were given gastrointestinal decompression, water deprivation, fasting, infection prevention, and acid-base imbalance and electrolyte disturbance correcting. The patients in the control group were given micropump intravenous injection of octreotide (0.6 mg) and normal saline (48 mL), 1 time/12 h. On this basis, the patients in the observation group were given intravenous injection of breviscapine (20 mg) and 5% glucose (250 mL), 1 time/d. After 10 d-treatment, the efficacy was evaluated. The morning fasting peripheral venous blood before and after treatment in the two groups was collected. ELISA was used to detect CRP, TNF-α, IL-8, IL-15, NO, and vWF. RIA was used to detect the plasma TXB₂, 6-keto-PGF₁α, and ET concentration. The full automatic blood rheometer was used to detect HCT, EAI, whole blood low shear viscosity, whose blood high shear viscosity, and plasma viscosity. Results: HCT, EAI, whole blood low shear viscosity, whose blood high shear viscosity, and plasma viscosity after treatment in the observation group were significantly lower than those in the control group (P<0.05). The serum CRP, IL-8, IL-15, and TNF-α levels after treatment in the observation group were significantly lower than those in the control group (P<0.05). The plasma ET, TXB₂, and vWF levels after treatment in the observation group were significantly lower than those in the control group (P<0.05), while 6-keto-PGF₁α and NO levels were significantly higher than those in the control group (P<0.05). Conclusions: Breviscapine in combined with octreotide can effectively inhibit the inflammatory reaction in patients with SAP, improve the vascular endothelial function, hemodynamics, and microcirculation disturbance, and promote the recovery.

1. Introduction

Severe acute pancreatitis (SAP) is a common severe acute abdomen in the clinic, and an acute inflammatory reaction caused by digestion, edema, hemorrhage, and necrosis of pancreatic tissues due to the activation of trypsin. The pancreatic local inflammatory reaction is the main characteristic of SAP; moreover, microcirculation is involved in the occurrence and development of SAP. Breviscapine is a drug which can promote the blood circulation and remove the blood stasis, and has effects of anti-apoptosis, expanding the microvessels, and improving the microcirculation. Octreotide is a kind of somatostatin analogue, can effectively inhibit the secretion of pancreas, and is a common
drug in the treatment of SAP\textsuperscript{[4]}. The study is aimed to explore the effect of breviscapine in combined with octreotide on the inflammatory reaction and vasoactive substances in patients with SAP.

2. Materials and methods

2.1. General materials

A total of 72 patients with SAP who were admitted in our hospital from January, 2014 to November, 2016 were included in the study and randomized into the observation group and the control group with 36 cases in each group. In the observation group, 22 were male, and 14 were female; aged from 26 to 65 years old, with an average age of $(49.3\pm4.3)$ years old; course from 2 to 55 h, with an average course of $(8.7\pm1.5)$ h. In the control group, 21 were male, and 15 were female; aged from 25 to 65 years old, with an average age of $(48.7\pm4.2)$ years old; course from 2 to 56 h, with an average course of $(8.8\pm1.4)$ h. The comparison of gender, age, and course between the two groups was not statistically significant ($P>0.05$).

2.2. Inclusion and exclusion criteria

Inclusion criteria: (1) those who were in accordance with the diagnostic criteria of SAP\textsuperscript{[5]}; (2) those whose onset time was less than 72 h; (3) those whose APACH\textsuperscript{II} was greater than 8 scores; (4) those who had signed the informed consents. Exclusion criteria: (1) those who had heart, liver, and renal dysfunction; (2) those who had severe hematological system and nervous system diseases, and malignant tumor; (3) those who had surgical indications; (4) those who were pregnant or at the lactation period; (5) those who were allergic to related drugs.

2.3. Methods

The patients in the two groups were given gastrointestinal decompression, water deprivation, fasting, infection prevention, and acid-base imbalance and electrolyte disturbance correcting. The patients in the control group were given micropump intravenous injection of octreotide (produced by Beijing Baiao Pharmaceutical Co. Ltd, Approval No. H20061309, 0.6 mg) and normal saline (48 mL), 1 time/12 h. On this basis, the patients in the observation group were given intravenous injection of breviscapine (produced by Hebei Shineway Pharmaceutical Co. Ltd, Approval No.Z13020778, 20 mg) and 5% glucose (250 mL), 1 time/d. After 10 d-treatment, the efficacy was evaluated.

2.4. Observation indicators

The morning fasting peripheral venous blood before and after treatment in the two groups was collected. ELISA was used to detect CRP, TNF-\alpha, IL-8, IL-15, NO, and vWF. RIA was used to detect the plasma TXB\textsubscript{2}, 6-keto-PGF\textsubscript{1\alpha}, and ET concentration. The full automatic blood rheometer was used to detect HCT, EAI, whole blood low shear viscosity, whose blood high shear viscosity, and plasma viscosity.

2.5. Statistical analysis

SPSS 19.0 software was used for the statistical analysis. The measurement data were expressed as mean$\pm$SD, and $t$ test was used. Chi-square test was used for the enumeration data. $P<0.05$ was regarded as statistically significant.

3. Results

3.1. Comparison of the levels of the serum inflammatory cytokines before and after treatment between the two groups

The serum CRP, IL-8, IL-15, and TNF-\alpha levels after treatment in the two groups were significantly reduced when compared with before treatment ($P<0.05$). The serum CRP, IL-8, IL-15, and TNF-\alpha levels after treatment in the observation group were significantly lower than those in the control group ($P<0.05$) (Table 1).

3.2. Comparison of the vascular endothelial function indicators before and after treatment between the two groups

The plasma ET, TXB\textsubscript{2}, and vWF levels after treatment in the two groups were significantly reduced when compared with before treatment ($P<0.05$), while 6-keto-PGF\textsubscript{1\alpha} and NO levels were significantly elevated ($P<0.05$). The plasma ET, TXB\textsubscript{2}, and vWF levels after treatment in the observation group were significantly lower than those in the control group ($P<0.05$) (Table 2).

3.3. Comparison of the hemorheology before and after treatment between the two groups

HCT, EAI, whole blood low shear viscosity, whose blood high shear viscosity, and plasma viscosity after treatment in the two groups were significantly reduced when compared with before treatment ($P<0.05$). HCT, EAI, whole blood low shear viscosity,
Table 1
Comparison of the levels of the serum inflammatory cytokines before and after treatment between the two groups (n=36, mean±SD).

<table>
<thead>
<tr>
<th>Groups</th>
<th>Time</th>
<th>CRP</th>
<th>IL-8</th>
<th>IL-15</th>
<th>TNF-α</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>Before treatment</td>
<td>152.46±58.71</td>
<td>57.31±25.47</td>
<td>93.35±12.53</td>
<td>37.63±6.69</td>
</tr>
<tr>
<td>Control</td>
<td>Before treatment</td>
<td>151.62±61.24</td>
<td>57.23±24.26</td>
<td>92.42±11.67</td>
<td>37.82±6.13</td>
</tr>
<tr>
<td></td>
<td>After treatment</td>
<td>18.24±3.26</td>
<td>42.75±18.28</td>
<td>26.35±9.69</td>
<td>18.32±5.42</td>
</tr>
</tbody>
</table>

P<0.05, when compared with before treatment; *P<0.05, when compared with the control group.

Table 2
Comparison of the vascular endothelial function indicators before and after treatment between the two groups (n=36, mean±SD).

<table>
<thead>
<tr>
<th>Groups</th>
<th>Time</th>
<th>ET</th>
<th>TXB2</th>
<th>6-keto-PGF</th>
<th>NO</th>
<th>vWF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>Before treatment</td>
<td>135.71±7.36</td>
<td>315.48±16.54</td>
<td>89.78±5.32</td>
<td>4.11±0.47</td>
<td>256.45±36.29</td>
</tr>
<tr>
<td></td>
<td>After treatment</td>
<td>105.49±7.27</td>
<td>262.74±27.82</td>
<td>102.13±4.27</td>
<td>9.35±0.74</td>
<td>108.74±12.77</td>
</tr>
<tr>
<td>Control</td>
<td>Before treatment</td>
<td>135.82±6.75</td>
<td>315.75±18.39</td>
<td>89.75±5.41</td>
<td>4.12±0.45</td>
<td>257.32±37.45</td>
</tr>
<tr>
<td></td>
<td>After treatment</td>
<td>121.31±6.45</td>
<td>296.57±23.32</td>
<td>94.32±4.57</td>
<td>5.21±0.48</td>
<td>197.75±19.42</td>
</tr>
</tbody>
</table>

P<0.05, when compared with before treatment; *P<0.05, when compared with the control group.

whose blood high shear viscosity, and plasma viscosity after treatment in the observation group were significantly lower than those in the control group (P<0.05) (Table 3).

4. Discussion

The clinical research[6] shows that the pancreatic tissue damage in patients can produce a large amount of inflammatory mediators and vasoactive substances, resulting in an increased blood viscosity and microvascular spasm, microvascular thrombus, local circulation disturbance, reduced blood flow volume, ischemia and necrosis. The modern pharmacological study[7] shows that can effectively reduce the blood viscosity, inhibit the platelet aggregation, improve the oxidative stress, expand the local vessels, improve the microcirculation, increase the local blood flow volume, protect the tissues and organs from multiple target points and multiple ways, and reduce the serum inflammatory cytokine level in order to alleviate the pancreatic injury. Octreotide can inhibit the secretion of pancreatic and pancreatic juice, promote the pancreatic tissue cells, alleviate the parenchymal cell damage, inhibit the platelet aggregation, and improve the hemorheology[8]. It is reported that brevescapine in combined with octreotide in the treatment of SAP can effectively reduce the blood viscosity, correct ischemic state, improve the tissue hypoxia tolerance, improve the pancreatic tissue microcirculation, and effectively protect the pancreatic tissue[9]. The results in the study showed that HCT, EAI, whole blood low shear viscosity, whose blood high shear viscosity, and plasma viscosity after treatment in the observation group were significantly lower than those in the control group (P<0.05), indicating that brevescapine in combined with octreotide in the treatment of SAP can effectively improve the hemorheology, and effectively protect the pancreatic tissues.

CRP is an acute phase protein, can activate the complement and strengthen the physiological activity of phagocytes, and can be significantly elevated in the early stage of inflammatory reaction, whose level can directly decide the inflammatory reaction degree in patients with SAP[10]. TNF-α is an initial factor to mediate the release of inflammatory cytokines, induce the chemotaxis and adhesion of leukocytes, expand the inflammatory reaction, and is an important factor to induce the local tissue necrosis[11]. IL-8 can attract and activate the neutrophil activity, promote the neutrophils to directionally migrate to the reaction site, release the active substance, and induce the histocyte damage[12]. IL-15 is an initial factor for inflammatory reaction, can stimulate the inflammation of T lymphocytes and NK cell, and induce various inflammatory reaction[13]. The results in the study showed that the serum CRP, IL-8, IL-15, and TNF-α levels after treatment in the observation group were significantly lower than those in the control group (P<0.05), indicating that brevescapine in combined with

Table 3
Comparison of the hemorheology before and after treatment between the two groups (n=36, mean±SD).

<table>
<thead>
<tr>
<th>Groups</th>
<th>Time</th>
<th>HCT</th>
<th>EAI</th>
<th>Plasma viscosity</th>
<th>Whole blood low shear viscosity</th>
<th>Whole blood high shear viscosity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>Before treatment</td>
<td>0.63±0.08</td>
<td>5.12±0.51</td>
<td>5.51±0.54</td>
<td>11.09±1.37</td>
<td>5.36±0.47</td>
</tr>
<tr>
<td></td>
<td>After treatment</td>
<td>0.38±0.05</td>
<td>3.97±0.35</td>
<td>3.79±0.38</td>
<td>6.89±0.84</td>
<td>3.45±0.38</td>
</tr>
<tr>
<td>Control</td>
<td>Before treatment</td>
<td>0.63±0.09</td>
<td>5.12±0.50</td>
<td>5.52±0.53</td>
<td>11.07±1.31</td>
<td>5.35±0.49</td>
</tr>
<tr>
<td></td>
<td>After treatment</td>
<td>0.50±0.06</td>
<td>4.65±0.46</td>
<td>5.02±0.48</td>
<td>8.95±1.13</td>
<td>4.82±0.46</td>
</tr>
</tbody>
</table>

P<0.05, when compared with before treatment; *P<0.05, when compared with the control group.
octreotide in the treatment of SAP can effectively inhibit the levels of inflammatory cytokines in order to improve the inflammatory cytokines, and promote the recovery.

The abnormal hemorheology in patients with SAP can damage the vascular endothelium, increase the microcirculation resistance, promote the thrombosis, and cause the ischemia and necrosis of pancreas, while the vasoactive substances play an important role in the microcirculation disturbance in patients with SAP[14]. ET is an active substance secreted by the endothelial cells, can cause the local microvascular spasm and ischemia of pancreas, resulting in microcirculation disturbance[15]. TXB\textsubscript{2} and 6-keto-PGF\textsubscript{1α} are the metabolites of TXA\textsubscript{2} and PGI\textsubscript{2}. TXA\textsubscript{2} is a platelet aggregation accelerant and microvascular substance with strong contraction, can induce local or systemic coagulation disorder, and aggravate the local microcirculation disturbance in patients with SAP, while PGI\textsubscript{2} can antagonize TXA\textsubscript{2}, inhibit the platelet aggregation and leukocyte activation, and prevent the release of lysosome into the tissues[16]. vWF is an important marker for vascular endothelial damage. NO release obstacle is an important factor for developing vascular endothelial dysfunction, platelet aggregation, and thrombosis[17].

The results in the study showed that the plasma ET, TXB\textsubscript{2}, and vWF levels after treatment in the observation group were significantly lower than those in the control group (\(P<0.05\)), while 6-keto-PGF\textsubscript{1α} and NO levels were significantly higher than those in the control group (\(P<0.05\)), indicating that breviscapine in combined with octreotide in the treatment of SAP can effectively improve the vascular endothelial function and the microcirculation disturbance.

In conclusion, breviscapine in combined with octreotide can effectively inhibit the inflammatory reaction in patients with SAP, improve the vascular endothelial function, hemodynamics, and microcirculation disturbance, and promote the recovery.

References


