Effect of butylphthalide injection on inflammatory factors, neurological factors and hemorheology in patients with acute cerebral infarction

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ABSTRACT

Objective: To investigate the effects of butylphthalide injection on inflammatory factors, neurological factors and hemorheology in patients with acute cerebral infarction. Methods: The patients in the observation group were treated with intravenous infusion of butylphthalide on the basis of the control group, 120 cases of acute cerebral infarction patients are randomly divided into control group (n=60) and observation group (n=60), patients in the control group were given conventional therapy, on the basis of the therapy of the control group, the observation group were treated with intravenous infusion of butylphthalide. Both groups were given sufficient treatment for 14 d, the levels of inflammatory factors, neurological factors and hemorheology were compared before and after the treatment. Results: The levels of serum hs-CRP, TNF-α, NSE, MBP, S100B, whole blood viscosity, plasma specific viscosity, hematocrit and platelet aggregation rate in the two groups before treatment were no significant difference. After treatment, the levels of hs-CRP, TNF-α in the observation group and observation group were (4.96±1.14) mg/L, (5.54±1.20) mg/L and (7.54±0.93) mg/L, (8.32±1.31) mg/L, which were significantly lower than those in the same group before treatment, and the level of hs-CRP, TNF-α in the observation group were significantly lower than those in the control group; the levels of NSE, MBP, S100B in the observation group and observation group were (6.38±2.39) μg/L, (10.19±5.28) μg/L, (0.98±0.09) ng/L and (11.73±2.43) μg/L, (17.43±4.51) μg/L, (1.85±0.12) ng/L, which were significantly lower than those in the same group before treatment, and the observation group levels were significantly lower than those in the control group; the levels of whole blood viscosity, plasma specific viscosity, hematocrit and platelet aggregation rate in the observation group and observation group were (15.17±0.89) mPas, (13.32±0.22) mPas, (0.35±0.13)% and (0.32±0.08)% and (5.68±0.91) mPas, (1.63±0.24) mPas, (0.41±0.14)% and (0.40±0.11)% which were significantly lower than those in the same group before treatment, and the observation group levels were significantly lower than those in the control group. Conclusion: On the basis of conventional treatment, the addition of butylphthalide can effectively reduce the level of serum inflammatory factors, promote the repair of nerve function, improve the level of hemorheology, which has important clinical value.

1. Introduction

Acute cerebral infarction refers to brain tissue necrosis caused by sudden interruption of blood supply in the brain. It is a common disease in neurology department[1]. In recent years, related studies have shown that inflammation, nerve function and hemorheology are closely related to the occurrence and development of ACI.

Controlling the changes of the above indicators in patients can help reduce the morbidity and mortality of patients, and promote the rehabilitation of patients as soon as possible[2-4]. Butylphthalide injection is a new type of neuroprotective drug, which has significant effect on improving cerebral perfusion and neurological deficit in ischemic area[5,6]. The aim of this study was to investigate the effects of butylphthalide injection on inflammatory factors, nerve factors and hemorheology in patients with ACI. The results are reported as follows:
2. Research objects and methods

2.1. Research subjects

Select 120 patients with acute cerebral infarction admitted to our hospital from November 2016 to April 2017 as the research object. All subjects were in line with the screening criteria for this study; inclusion criteria: (1) in line with China's guidelines for diagnosis and treatment of acute ischemic stroke guidelines (2010 edition); (2) infarction by MRI or head CT confirmed; (3) onset less than 72 h; (4) age onset less than 75 years old; (5) all subjects and their families informed consent, signed informed consent and voluntarily joined the treatment. Exclusion criteria: (1) suffering from severe cardiovascular disease, liver and kidney dysfunction, cancer; (2) suffering from immune and infectious diseases; (3) associated with other intracranial lesions; (4) multiple organ failure patients; (5) failed to complete the treatment according to the course of treatment, half-way off cases, and clinical data at admission incomplete. All patients were divided into control group (n = 60) and observation group (n = 60) according to randomized data table. There were 33 males and 27 females in the control group, ranging in age from 30 to 68 years. The observation group consisted of 35 males and 25 females, aged 32 to 69 years old. There was no significant difference in the general clinical data between the two groups (P>0.05). All subjects and their families informed consent, signed informed consent and voluntarily joined the treatment.

2.2. Treatment

The control group were given routine treatment, the specific methods are as follows: 100 mg oral aspirin, atorvastatin 20 mg, 1 times a day; intravenous infusion of deproteinated calf serum injection 20 mL, shuxueying Injection 20 mL, 1 times a day, and maintain water and electrolyte balance in patients, for 14 consecutive days. On the basis of the observation group, intravenous injection of butyraldehyde injection 100 mL, 2 times a day, 100 mL/times, continuous treatment for 14 d.

2.3. Hemorheological index test

Hemorheological index test: 5 mL elbow venous blood was drawn in both groups before and after treatment. The whole blood specific viscosity, plasma specific viscosity, hematocrit and platelet aggregation rate were measured by cone-plate measurement.

2.4. Statistical analysis

SPSS 22.0 software was used for statistical analysis of data. In the study, the levels of inflammatory cytokines, neurokines and hemorheology in the patients were all in accordance with the normal distribution, expressed as Mean ± SD, the t-test . The statistical results with P<0.05 said there is a significant difference.

3. Results

3.1. Comparison of two groups serum inflammatory cytokines levels

The levels of inflammatory cytokines in both groups before and after treatment are shown in Table 1. The levels of hs-CRP and TNF-α before treatment in both groups were similar, with no significant difference (P>0.05). The levels of hs-CRP and TNF-α in the observation group and the control group after treatment were (4.98 ± 1.14) mg/L, (5.54 ± 1.29) mg/L, and (7.54 ± 0.93) mg/L, (8.32 ± 1.31) ng/L, compared with before treatment in this group, hs-CRP, TNF-α level decreased significantly, and the observation group was significantly lower than the control group (all P<0.05).

### Table 1.
Comparison of serum levels of inflammatory cytokines.

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Treatment time</th>
<th>hs-CRP (mg/L)</th>
<th>TNF-α (ng/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>60</td>
<td>Before treatment</td>
<td>13.67±1.31</td>
<td>11.82±2.89</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>7.54±0.93</td>
<td>8.32±1.31</td>
</tr>
<tr>
<td>Observation group</td>
<td>60</td>
<td>Before treatment</td>
<td>13.82±1.29</td>
<td>11.77±1.56</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>4.98±1.14</td>
<td>5.54±1.29</td>
</tr>
</tbody>
</table>

Note: compared to pretreatment levels in the group, *P<0.05; compared to the control group after treatment, "P<0.05.

### Table 2
Two groups sera levels of neurokines.

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Treatment time</th>
<th>NSE (ng/L)</th>
<th>MBP (ng/L)</th>
<th>S100B (ng/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>60</td>
<td>Before treatment</td>
<td>22.48±6.95</td>
<td>32.83±6.02</td>
<td>3.38±0.19</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>11.73±2.43</td>
<td>17.32±4.51</td>
<td>1.65±0.12</td>
</tr>
<tr>
<td>Observation group</td>
<td>60</td>
<td>Before treatment</td>
<td>22.45±6.04</td>
<td>32.78±5.99</td>
<td>3.35±0.20</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>6.38±2.39</td>
<td>10.19±2.88</td>
<td>0.96±0.09</td>
</tr>
</tbody>
</table>

Note: compared to pretreatment levels in the group, *P<0.05; compared to the control group after treatment, "P<0.05.
Table 3.
Hemorheological changes in the two groups.

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Treatment time</th>
<th>Whole blood specific viscosity (mPa·s)</th>
<th>Plasma specific viscosity (mPa·s)</th>
<th>Hematocrit</th>
<th>Platelet aggregation rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>60</td>
<td>Before treatment</td>
<td>6.29±1.17</td>
<td>1.98±0.23</td>
<td>0.48±0.15</td>
<td>0.46±0.16</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>5.88±0.91</td>
<td>1.68±0.24</td>
<td>0.41±0.14</td>
<td>0.40±0.11</td>
</tr>
<tr>
<td>Observation group</td>
<td>60</td>
<td>Before treatment</td>
<td>6.35±1.18</td>
<td>1.97±0.21</td>
<td>0.49±0.17</td>
<td>0.48±0.12</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>5.72±0.89</td>
<td>1.32±0.22</td>
<td>0.35±0.13</td>
<td>0.32±0.08</td>
</tr>
</tbody>
</table>

Note: compared to pretreatment levels in the group, *p<0.05; compared to the control group after treatment, **p<0.05.

3.2 Comparison of two groups neurokines levels

Serum levels of neurokines in both groups before and after treatment are shown in Table 2. The levels of NSE, MBP and S100B before treatment in both groups were similar, with no significant difference (P>0.05). The levels of NSE, MBP and S100B in the observation group after treatment were (6.38±2.39) μg/L, (10.19±3.28) μg/L and (0.96±0.09) ng/L respectively and the levels of NSE, MBP and S100B in the control group after treatment were (11.73±2.43) μg/L, (17.43±4.51) μg/L and (1.65±0.12) ng/L respectively. Compared with those in the group before treatment, the levels of three significantly decreased, and the observation group was significantly lower than the control group (p<0.05).

3.3 Comparison of two groups of patients with changes in blood rheology

Hemorheological changes in both groups before and after treatment are shown in Table 3. Before treatment, whole blood viscosity, plasma specific viscosity, hematocrit and platelet aggregation rate were close, no significant difference (P>0.05). The whole blood specific viscosity, plasma specific viscosity, hematocrit and platelet aggregation rate in the observation group after treatment were (5.17±0.59) mPa·s, (1.32±0.22) mPa·s, (0.35±0.13)% and (0.32±0.08)% respectively. The whole blood specific viscosity, plasma specific viscosity, hematocrit and platelet aggregation rate in the control group were (5.68±0.91) mPa·s, (1.63±0.24) mPa·s, (0.41±0.14)% and (0.40±0.11)% respectively. Compared with the group before treatment, the four levels were significantly decreased, and the observation group was significantly lower than the control group (p<0.05).

4. Discussion

The pathogenesis of ACI is complex, and its recognized risk factors include hypertension, coronary heart disease, diabetes mellitus, hyperlipidemia, smoking, drinking, obesity and other[5]. In patients with onset, or may appear ill-defined and progressive decline in muscle strength, severe cases can lead to patient disturbance of consciousness and even endanger the lives of patients[9]. Therefore, taking active and effective drug treatment is very important for patients. Butylphthalide, a synthetic racemic α-butylinphthalide, is a new drug developed in recent years for the treatment of ACI disease[10]. Clinical studies have shown that butylphthalide can improve central nervous system injury in patients with ACI, and thus help patients recover after neurological injury[11]. It has been confirmed by modern pharmacology that butylphthalide can block multiple pathological stages of brain injury caused by cerebral infarction and has a strong anti-cerebral ischemia effect. At the same time, it can obviously reduce the infarction area caused by focal cerebral ischemia. Reduce cerebral edema, improve blood circulation and brain energy metabolism in ischemic brain areas, inhibit neuronal apoptosis, inhibit platelet aggregation and prevent cerebral thrombosis[12,13].

ACI is often found to be closely related to local or systemic inflammation, and the inflammatory response runs through the whole process of ACI. Currently, cytokines such as hs-CRP and TNF-α are commonly used as inflammatory markers of ACI[14,15]. Among them, hs-CRP is an acute phase protein synthesized by hepatocytes and can induce the formation of thrombus and embolism by inducing the secretion of inflammatory cytokines, increasing the instability of atherosclerotic plaque and thus detecting the intervention of ACI. And prognosis, TNF-α is an inflammatory factor secreted mainly by monocytes-macrophages, which can aggravate cerebral ischemia and nerve injury by inducing network cascade reaction, inducing apoptosis and destroying the blood-brain barrier[16]. In addition, studies have also found that large areas of brain infarction, the patient's CRP, TNF-α levels will be significantly increased[7]. The results of this study showed: compared with before treatment, the levels of hs-CRP and TNF-α in the observation group after treatment with butanide were significantly lower than those in the control group after treatment. Butylphthalide can reduce serum levels of inflammatory cytokines in patients with butylphthalide may be due to inhibition of intracellular calcium overload, reduce intracellular arachidonic acid content, inhibit the expression of inflammatory cytokines and reduce cerebral edema related.

NSE is an acid protease found in neurons and neuroendocrine cells that is involved in the glycolysis process and has the highest activity in brain tissue cells. When ischemia occurs in the brain, the membrane structure of neurons is disrupted and NSE is released into the cerebrospinal fluid and into the blood circulation through the blood-brain barrier. Changes in NSE levels can therefore be used to predict changes in patient status and prognosis in patients with acute cerebral infarction[18]. MBP is a single chain flexible polypeptide, approximately 18.5 kDa, located in the dense myelin and nucleus. When acute cerebral infarction occurs, the brain tissue is in the state of hypoxia and hypoxia, and the damaged brain tissue affects the myelin sheath. In addition, the permeability of the blood-brain barrier increases after brain injury, resulting in considerable increase of MBP level in peripheral blood. Therefore, MBP can be used to measure the severity of the disease[19]. As a member of S100 protein family, S100B protein is a kind of calcium-binding protein with many biological activities, mainly distributed in Schwann cells and glial cells[20]. Studies have shown that S100B protein can be used as a biochemical marker to reflect the extent of brain injury when S100B protein can cross the blood-brain barrier and enter the peripheral blood from the central nervous system when pathological changes occur in the brain tissue[21]. The results of this study showed that the levels of NSE, MBP and S100B in the observation group after treatment with butanide were significantly lower than those before treatment and significantly lower than those in the control...
group after treatment. These results indicate that diphenyleptoleptide can protect neurons, myelin and glial cells and repair brain injury in patients with cerebral infarction. The specific mechanism of action may be: Butyralphaldehyde can inhibit the neuronal apoptosis and protect the nervous system by inhibiting the expression of caspase-3 in the ischemic penumbra zone near the infarct site after cerebral ischemia-reperfusion injury. Studies have shown that changes in hemorhoeology and ACI occurrence and development are closely related. In patients with ACI after the increase in blood viscosity, increased hemocrit, slowed blood flow, microcirculation decreased perfusion, resulting in ischemic changes in the brain, and further increase the symptoms of cerebral infarction[22]. The results of this study showed that compared with before treatment, the whole blood specific viscosity, plasma specific viscosity, hemocrit and platelet aggregation rate in the observation group after treatment with butan dine were significantly lower than those in the control group after treatment. Butyralphaldehyde can effectively improve the blood rheology of patients with ACI, which may improve microcirculation, promote blood flow, and help to restore the supply of cerebral blood flow in the infarction site, which is consistent with Wu Juan and other reports[23].

In summary: the conventional treatment based on the use of butyralphaldehyde can reduce the level of serum inflammatory cytokines, promote the repair of neurological function, improve the level of hemorhoeology, have a good effect in the treatment of acute cerebral infarction, worth clinical promotion.

References


