Effect of Maixuekang enteric coated tablets on absorption of hematoma and treatment of acute cerebral hemorrhage patients with cerebral edema

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ABSTRACT

Objective: To study the clinical efficacy of Maixuekang in treating acute cerebral hemorrhage hematomas and promoting brain hemorrhage. Methods: A total of 192 patients with acute intracerebral hemorrhage treated within 3 hours in our hospital during April 2013 to February 2015 were selected. After admission immediately apply brain CT, blood, coagulation function tests were carried out. They were randomly divided into 2 groups. Both groups had anti-infective, mannitol and other conventional treatment. Observation group were treated with enteric-coated tablets Maixuekang on this basis. Clinical efficacy, various stages of treatment of cerebral hematoma volume, brain edema volume, NIHSS score were compared. Results: Before treatment, difference in edema volume and NIHSS scores were not statistically significant ($P>0.05$). After 14 d and 28 d treatment, edema volume of observation group were significantly smaller than those of control group ($P<0.01$); NIHSS score of observation group were significantly lower than those of control group ($P<0.01$); 28 d after treatment total effective rate of observation group was significantly higher than that of the control group ($P<0.01$). Conclusions: Maixuekang enteric-coated tablets as a thrombin inhibitor, can effectively reduce a series of pathological changes after acute cerebral hemorrhage caused by partial thrombin content, promote absorption of hematoma and neurological recovery. The side effects is small, safe and worthy of promotion.

1. Introduction

Cerebral hemorrhage refers to a non-traumatic bleeding within the brain parenchyma due to rupture of blood vessels, accounting for about 30% of all stroke, with acute mortality as high as 30% to 40%[1]. Acute cerebral hemorrhage is of high mortality, high morbidity characteristics, resulting in a chain reaction after cerebral hemorrhage, hematoma produce metabolites, apoptosis, vascular spasm, releasing neurotoxic substances, and further lead to brain damage. Epidemiological studies have shown that the incidence of cerebrovascular disease is high, namely diabetes, high cholesterol, hypertension, vascular aging, smoking and other unhealthy living habits. Cerebral hemorrhage is often due to emotional, hard, strenuous exercise, disease, while more have varying degrees of cognitive impairment, movement disorders, language disorders, treatment, and seriously affect the quality of life of patients. The study aims to explore the effect of Maixuekang enteric-coated tablets on patients with acute cerebral hemorrhage.

2. Materials and methods

2.1. General Information

During April 2013 to February 2015 in our hospital, 192 cases with acute cerebral hemorrhage were selected, who were in line with the Fourth National Stroke Conference cerebral hemorrhage diagnostic criteria and were diagnosed by brain CT. Selected standard were as follows: (1) patients were on the first onset; (2) regional onset of basal ganglia, onset time was not more than 3 times; (3) the amount of bleeding < 30 mL; (4) the families of all the patients signed the informed consent, and were willing to work with the study.
Exclusion criteria were as follows: (1) associated with arteriovenous malformation, brain hemorrhage, intracranial aneurysms patients; (2) with severe hypertension, diabetes patients; (3) mental retardation, disturbance of consciousness, not well with the treatment and patient examination; (3) associated with an important organ disease and bone and joint patients. All patients were admitted to hospital immediately after brain CT, the hematoma volume measurement using the cross-sectional area of Tada formula interception largest section. Each 15 min blood coagulation function and blood plasma TAT in 3H were measured. All patients were randomly divided into two groups. Control group (96 cases) were treated by routine treatment, the observation group by combined with vein blood Kang enteric coated tablets. Age, gender, history of hypertension, history of diabetes and other general conditions showed no statistically significant difference (P>0.01), and were comparable.

2.2. Method

Two groups were treated with conventional treatment, including blood pressure control, anti infection and dehydration treatment, intravenous infusion of 20% mannitol to alleviate brain edema, intracranial pressure, cerebral protection dose of edaravone and vitamins to promote brain cell metabolism, energy adding, regulation of balance of water and electrolyte. Patients with infection were treated with antibiotics, and the patients with hypertension were treated with antihypertensive drugs. Observation group in the conventional treatment received Maixuekang enteric coated tablets (Guizhou Xinbang Pharmaceutical Co., Ltd. production). After 24 h patients with bleeding <10 mL started to have treatment, 3 times/d, 4 g/times; after 48 h patients with hemorrhage >10 mL started to have treatment, 3 times/d, 4 g/times. The course was 28 d. Other drugs could not be used during the medication, such as anti coagulation, blood circulation and so on.

2.3. Evaluation Method

2.3.1. Cerebral edema and cerebral hematoma volume

Plus CT system was used to calculate the volume of brain edema, the volume of brain edema volume was measured by Image-Pro. Hematoma volume was measured by using the Tada formula to calculate[2] the maximum interception of cross section. The brain edema and hematoma volume were calculated and recorded before treatment, 7 d, 14 d and 28 d.

2.3.2. Neural function score (NIHSS)

Before treatment, 7 d, 14 d, 28 d neurological function was evaluated. The scale was on the level of consciousness, gaze and vision, facial paralysis, upper and lower limbs movement, feeling, language and other aspects of the evaluation. The total score was 45 points, the lower score on behalf of the nerve function defect was more light.

2.3.3. Clinical efficacy

Markedly: clear consciousness, or substantially completely functional language, limb function, vision and other barrier-free, self-care, fully or hematoma>70% absorption; Effective: patients could not completely take care of themselves, hematoma absorb was 50% to 70%; Invalid: no mitigating or aggravating symptoms.

2.4. Statistical method

SPSS18.0 software was used, the measurement data were expressed as mean±sd and analyzed by t test; count data were expressed as percentage expression and were analyzed by chi square test. P<0.05 was regarded as significant difference.

3. Results

3.1. Comparison of edema volume

There was no significant difference in volume of brain edema between two groups after 7 d of treatment. There were significant differences in volume of brain edema after 28 days treatment (P<0.05). Before treatment, 7 days, 14 d, 28 d after treatment, difference in edema volume between two groups were statistical significance (P>0.01) (Table 1).

### Table 1
Comparison of edema volume between two groups before and after treatment (cm³).

<table>
<thead>
<tr>
<th>Groups</th>
<th>Before treatment</th>
<th>7 days</th>
<th>14 days</th>
<th>28 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observer group</td>
<td>25.87±5.38</td>
<td>21.52±5.14</td>
<td>18.73±4.65</td>
<td>14.25±4.30</td>
</tr>
<tr>
<td>Control group</td>
<td>26.12±6.22</td>
<td>23.76±5.68</td>
<td>22.01±4.42</td>
<td>20.33±3.97</td>
</tr>
<tr>
<td>t</td>
<td>0.00</td>
<td>2.684</td>
<td>6.76</td>
<td>11.28</td>
</tr>
<tr>
<td>P</td>
<td>1</td>
<td>0.03</td>
<td>0.00</td>
<td>0.00</td>
</tr>
</tbody>
</table>

3.2. NIHSS

NIHSS scores of two groups were significantly decreased (P<0.01) after 28 d treatment. Before treatment, there was no significant difference between the two groups (P>0.01), 14 d and 28 d after treatment, the observation group was significantly better than the control group (P<0.01) (Table 2).

### Table 2
NIHSS score (points).

<table>
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</table>

3.3. Comparison of clinical efficacy

In treatment group 51 cases were markedly effective (53.12%), 15 cases were effective (15.63%), 30 cases were invalid (31.25%). The total effective rate was 68.75%. In the control group, markedly effective in 42 cases (43.75%), effective in 9 cases (9.38%), invalid in 45 cases (46.88%), the total efficiency was 53.12%; the total effective rate of observation group was significantly higher than that of the control group (P<0.01).
According to Matsushita et al., characteristics of coagulation and anticoagulation main effect protease in the blood coagulation cascade, showing the Thrombin is a multifunctional serine protease, which is also the and endothelial cell adhesion molecule expression, inflammatory process. The mechanism is firstly due to local brain tissue injury induced by thrombin; secondly thrombin or within the plasma prothrombin with blood-brain barrier into the brain tissue after damage. Under the combined action, the thrombin concentration of the brain tissue around the hematoma is too high. Brain cell death rate, brain tissue water content and the concentration and content of thrombin were positively related.

According to Matsushita et al., it is reported that after 24 h, there are a large number of astrocytes and neurons apoptosis in cerebral hemorrhage, focusing on the focus around the lesion. Qu et al. found that mean hematoma in the sample around the necrosis and apoptosis ratio were 25.87% and 35.15%[6]. Apoptosis phenomena appears in a 1-5 days. In addition, in the rat cerebral hemorrhage test, after the autologous blood injection of 4 h, the apoptosis of the phenomenon, 48 to 72 h apoptosis reached its peak, and continued for more than 4 weeks. The above research shows that the main manifestations of cell death after intracerebral hemorrhage are apoptosis, which has the characteristics of large extent of damage and long duration. Due to the accumulation of red blood cell dissolved toxic products, bleeding after massive thrombin release, the complement system activation and other reasons, the common cause of apoptosis after intracerebral hemorrhage, the complex pathological process. The specific mechanism may be shown as follows: (1) activation of cysteine aspartate specific protease, resulting in apoptosis[7]. This protease is the downstream product of many cytokines in the inflammatory response, and plays an important role in the inflammatory response. In addition, intracellular calcium content of ultra high may be an important cause of cell apoptosis; (2) the activation of nuclear factor-KB, affect inflammatory cytokine expression; by complement pathway mediated cerebral hemorrhage cerebral hematoma surrounding brain tissue inflammatory reaction, a large number of activation white blood cells release of proteolytic enzymes, free radicals and other active substances directly cause cell death.

The mechanism of effect of thrombin on the water content of brain tissues are as follows: (1) raised the blood cerebrospinal fluid barrier on glial end feet membrane water channel protein 4 expression down-regulation[8] in the cerebrovascular endothelial cell associated protein claudin-5 expression, cause a contraction of vascular endothelial cells, and cell space is increased, intercellular connection compactness lower; upregulation of vascular cell adhesion molecule and endothelial cell adhesion molecule expression, inflammatory mediators release a lot, further enhance the capillary permeability. Caused vascular edema, leukocyte adhesion, infiltration, substance induced thromboxane release, narrowing of blood vessels in the cross section, blood flow to the brain reduce, and cause hematoma shrink blood vessels and due to the loss of endothelial release of endothelin can lead to vasoconstriction, causing cytotoxic edema caused by cerebral ischemia.

Maixuekang belongs to pure natural single preparation, drawing fresh leeches and Maixuekang capsule is made under low temperature and low pressure, and fully guarantee the active ingredients. Its main effective component is hirudin, hirudin thrombin has strong inhibition, is currently the strongest known specific inhibitors of thrombin. The anti coagulation factor, promote fibrin degradation has an important role in, and thrombin in a 1:1 ratio by non covalent bond with formation of inactive complexes to block the biological effect[9], in prolonged prothrombin time, thrombin time has a remarkable effect, reduce the blood thick, effectively inhibit thrombosis formation; can enhance the phagocytic cells, improve microcirculation, to rupture repair blood vessels, absorption of hematoma and brain neurons can promote the recovery. The results of this study showed that the effect of pulse blood Kang in promoting hematoma absorption and improving neurological function is significant, can effectively improve the quality of life of patients.

4. Discussion

Cerebral hemorrhage is a serious cerebrovascular disease, with a high disability rate. The survivors have poor prognosis, which is a multi factor and multi link involved in the complex pathological process[3].

Thrombin is a multifunctional serine protease, which is also the main effect protease in the blood coagulation cascade, showing the characteristics of coagulation and anti-coagulation[4]. It plays an important role in the final step in blood clotting, and can promote the fast form stable lesions on the surface of the blood coagulation blood clots. At the same time, it has the effect on cell biology, high concentration of cell toxicity, low concentration. It plays a protective role, and is a kind of extracellular signal molecules. Patients with cerebral hemorrhage will have hematoma, releasing a large amount of thrombin. The mechanism is firstly due to local brain tissue injury induced by thrombin; secondly thrombin or within the plasma prothrombin with blood-brain barrier into the brain tissue after damage. Under the combined action, the thrombin concentration of the brain tissue around the hematoma is too high. Brain cell death rate, brain tissue water content and the concentration and content of thrombin were positively related[8].

References