Effects of Xuefu Zhuyu Decoction combined with conventional therapy on inflammatory response, oxidative stress, endothelium and related factors in patients with acute cerebral infarction

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ABSTRACT

Objective: To explore the effects of Xuefu Zhuyu Decoction combined with conventional therapy on inflammatory response, oxidative stress, endothelium and related factors in patients with acute cerebral infarction. Methods: A total of 162 patients with acute cerebral infarction admitted to our hospital from November 2016 to January 1818 were selected as subjects. According to the random sampling method, the subjects were divided into 81 cases in the control group and 81 cases in the observation group. The control group was treated with conventional intracranial pressure, anticoagulation, anti-oxidation and lipid-lowering treatment. The observation group was treated with Xuefu Zhuyu Decoction on the basis of the control group. The changes of inflammatory response, oxidative stress, endothelium and related factors were compared and analyzed. Results: Before treatment, the levels of TNF-a, CRP, SOD, MDA, AOPPS, NO, ET-1, MMP-9, PAF and IGF-1 in the two groups were not significantly different, and there was no statistical significance. After treatment, the levels of TNF-a and CRP in the two groups were significantly lower than those before treatment, and the levels of TNF-a and CRP in the observation group were significantly lower than control group; the levels of MDA and AOPPS in the two groups were significantly lower than those before treatment, while the level of SOD was significantly higher than before treatment, and the levels of MDA and AOPPS in the observation group were significantly lower than control group; the level of ET-1 in the two groups was significantly lower than that before treatment, while the level of NO was significantly higher than that before the treatment, and in the observation group the level of ET-1 was significantly lower than the control group, while the level of NO was significantly higher. In the control group; the levels of MMP-9 and PAF in the two groups were significantly lower than those before treatment, while the level of IGF-1 was significantly higher than before treatment, and the levels of MMP-9 and PAF in the observation group were significantly lower than control group, while the level of IGF-1 was significantly higher than control group. Conclusions: Xuefu Zhuyu Decoction combined with conventional treatment of acute cerebral infarction can effectively reduce inflammation and oxidative stress, improve vascular endothelial function and nerve function, and significantly reduce the degree of brain injury, which has clinical significance.

1. Introduction

Acute cerebral infarction is a type of stroke with clinical features of high morbidity, disability and mortality[1-3]. At present, western medicine for treating cerebral infarction mainly adopts conventional treatments such as respiratory support, cardiac monitoring, blood pressure and lipid regulation, antithrombotic, anticoagulation, vasodilation and neuroprotection. Among them, aspirin has anti-platelet aggregation and reduces the mortality of patients during follow-up; Edaravone as an antioxidant, atorvastatin is a lipid-lowering drug, both of which have neuroprotective effects[4]. At present, the study found that Chinese and Western medicine has a significant effect on acute cerebral infarction[5,6]. Xuefu Zhuyu Decoction is a traditional Chinese medicine prescription, which has the effect of promoting blood circulation, relieving pain and...
improving blood microcirculation and anticoagulation[7]. This study analyzed the effects of Xuefu Zhuyu Decoction combined with conventional therapy on biochemical indicators in patients with acute cerebral infarction.

2. Materials and methods

2.1 General information

A total of 162 patients with acute cerebral infarction admitted to the Shiyan City People’s Hospital from November 2016 to January 2018 were selected as the study subjects. They were divided into the control group and the observation group according to the lottery method, 81 cases in each group. There were 43 males and 38 females, aged 49-78 years old; NIHSS scores 17-25 points; onset to visit time 3-15 h; In the observation group: 41 males and 40 females, aged 51-79 years old; NIHSS score 18-23 points, onset to visit time 4-13 h; There were no significant differences in background data between gender and age, NIHSS score and disease duration (P>0.05). The patient and their family agreed to sign the informed consent form, and the study was approved by the ethics committee of our hospital.

2.2 Inclusion criteria

Inclusion criteria: All patients met the relevant diagnostic criteria for acute cerebral infarction and were diagnosed by magnetic resonance imaging (MRI) and cranial CT examination[4]; the time from onset to visit was within 48 h; age >18 years. Exclusion criteria: hemorrhagic stroke; pregnant or lactating women; used similar drugs in this study within 1 month before treatment; combined with brain tumors, autoimmune diseases, diabetes, coronary heart disease, systemic infections and vital organs dysfunction; who had contraindication to this study drug.

2.3 Treatment method

Patients in the control group received routine symptomatic supportive therapy such as respiratory support, intracranial pressure reduction, antiplatelet aggregation, and neuroprotection: aspirin (Bayer Health Care Co., Ltd., Approval number: J20130078) orally after meals, 100 mg/time, once/d; Edaravone (Guo Rui Pharmaceutical Co., Ltd., Guoyao Pharmaceutical Co., Ltd., Approval number: H20000056), taking 30 mg dissolved in 100 mL normal saline, intravenous drip, 2 times/d; oral aspirin, (11.56±2.33) mg/L, which was obviously lower than the control group [(38.59±5.32) mg/L], which was obviously lower than the control group [(38.59±5.32) mg/L, (11.56±2.33) mg/L] (<0.05); and the levels of TNF-α and CRP in the two groups were significantly lower than those before treatment (P<0.05); and the levels of TNF-α and CRP in the observation group were [(23.51±3.78) ng/L, (7.68±2.27) mg/L], which was obviously lower than the control group [(38.59±5.32) ng/L, (11.56±2.33) mg/L] (P<0.05). (Table 1)

2.4 Observation indicators

The venous blood of the patients before and after treatment was collected and used for the detection of relevant biochemical indicators. Tumor necrosis factor-α (TNF-α), C-reactive protein (CRP), superoxide dismutase (SOD), malondialdehyde (MDA), advanced protein oxidation products (AOPPS), endothelin-1 (ET-1) Nitric oxide (NO), matrix metalloproteinase (MMP-9), platelet activating factor (PAF), and insulin-like growth factor-1 (IGF-1) were all detected by enzyme-linked immunosorbent assay (kits purchased from Shanghai Bangyi Biotech Co., Ltd.).

2.5 Statistical methods

The data were processed by SPSS 20.0 software. The chi-square test and t-test were used to compare the count data and the measurement data. The inflammation index, oxidative stress, endothelium and related factors were expressed by (x±s), P<0.05 was significant difference.

3. Results

3.1 Inflammatory factors

Before treatment, the levels of TNF-α and CRP in the two groups were not significantly different (P>0.05). After treatment, the levels of TNF-α and CRP in the two groups were significantly lower than those before treatment (P<0.05); and the levels of TNF-α and CRP in the observation group were [(23.51±3.78) ng/L, (7.68±2.27) mg/L], which was obviously lower than the control group [(38.59±5.32) ng/L, (11.56±2.33) mg/L] (P<0.05). (Table 1)

3.2 Oxidative stress factor

Before treatment, the difference of SOD, MDA and AOPPS levels between the two groups was not significant (P>0.05). After treatment, MDA and AOPPS were significantly lower in the two
groups than before treatment ($P<0.05$), while SOD was significantly higher than before treatment ($P<0.05$); and in observed group MDA, AOPPS ($[5.77±0.52] \mu$mol/L, $[29.86±3.30] \mu$mol/L), which was significantly lower than the control group ($[9.06±0.78] \mu$mol/L, $[48.73±5.82] \mu$mol/L) ($P<0.05$), while SOD($[131.59±9.65] \mu$g/mL) was significantly higher than the control group ($[108.50±8.30] \mu$g/mL) ($P<0.05$). (Table 2)

### 3.3 Endothelium index

Before treatment, the difference of NO and ET-1 levels between the two groups was not significant ($P>0.05$). After treatment, ET-1 in the two groups was significantly lower than before treatment ($P<0.05$), while NO was significantly higher than before treatment ($P<0.05$); and the observed group ET-1 ($[37.50±5.29] \mu$g/L) was significantly lower than the control group ($[53.40±7.04] \mu$g/L) ($P<0.05$), and NO ($[81.75±10.91] \mu$mol/L) was significantly higher than the control group ($[65.41±7.27] \mu$mol/L) ($P<0.05$). (Table 3)

### 3.4 Related factors

Before treatment, there was no significant difference in the levels of MMP-9, PAF and IGF-1 between the two groups ($P>0.05$). After treatment, MMP-9 and PAF in the two groups were significantly lower than before treatment ($P<0.05$), while IGF-1 was significantly higher than before treatment ($P<0.05$); and in the observed group MMP-9, PAF($[74.16±6.29] \mu$g/mL, $[79.75±8.64] \mu$g/mL) was significantly lower than the control group ($[103.41±9.76] \mu$g/mL, $[130.52±14.71] \mu$g/mL) ($P<0.05$), while IGF-1 ($[65.81±8.92] \mu$g/mL) was significantly higher than the control group ($[51.16±7.49] \mu$g/mL) ($P<0.05$). (Table 4)

### 4. Discussion

Stroke is a relatively common cardio-cerebral vascular disease, and it is the third leading cause of death in the world. The vast majority of strokes are acute cerebral infarction. The disease is rapid onset and the mortality rate is extremely high. If not treated promptly, the patient’s neurological function will be seriously damaged[8-10]. The occurrence and development of acute cerebral infarction is closely related to blood circulation disorder in the brain. Aspirin, edaravone and atorvastatin are recommended conventional drugs for the treatment of acute cerebral infarction, which have effect of anti-platelet aggregation and inhibit thrombus formation, improving brain blood microcirculation; anti-oxidation, scavenging free radicals; blood lipid regulation and neuroprotective effects[4]. Traditional Chinese medicine believes that this disease belongs to the category of “stroke disease”. The Chinese Medicine Encephalopathy Department emphasizes that the main treatment principle is promoting blood circulation to remove meridian obstruction regardless of the acute or remission stroke[11]. Xuefu Zhusyu Decoction is a traditional Chinese medicine that promotes blood circulation, anticoagulation and immune enhancement[12-14]. In order to further improve the patient’s therapeutic effect and improve the condition of the patient, this study used Xuefu Zhusyu Decoction combined with conventional treatment for acute cerebral infarction to explore the effects of this regimen on inflammatory response, oxidative stress, endothelium and related factors. Details are as follows.

Atherosclerosis is an important pathophysiological basis of acute cerebral infarction, and inflammatory response is closely related to the formation of atherosclerosis. Therefore, inflammatory factors such as TNF-α and CRP play important roles in the development of acute cerebral infarction[15]. The study found that the levels of TNF-α and CRP in the two groups were significantly lower than those before treatment, and the observation group was significantly lower than the control group. It is suggested that the combination of Xuefu Zhusyu Decoction can significantly reduce the level of inflammatory factors and inhibit the inflammatory response in patients with conventional treatment. The reason may be mainly related to the heat-clearing and detoxifying Chinese medicine ingredients such as the habitat, red peony and licorice in Xuefu Zhusyu Decoction. The study found that oxidative stress is closely related to the onset of acute cerebral infarction. When the cerebral vessels are blocked and the peripheral nerve cells are damaged by ischemia and hypoxia, the body will directly damage the cell membrane by releasing a large number of oxygen free radicals, resulting in serious neurological function damage[16,17]. Long-term ischemia and hypoxia can promote the occurrence of lipid peroxidation, and then synthesize a large number of oxidative metabolites such as MDA, AOPPS and other cytokines, and quickly consume antioxidant substances such as SOD in the body. The study found that after treatment, MDA and AOPPS in the two groups were significantly lower than before treatment, and SOD was significantly higher than before treatment; and MDA and AOPPS in the observation group were dramatically lower than those in the control group, and SOD was significantly higher than the control.

### Table 3.

Comparative analysis of endothelial markers in both groups ($n=81$).

<table>
<thead>
<tr>
<th>Group</th>
<th>Time</th>
<th>NO ($\mu$mol/L)</th>
<th>ET-1 (ng/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>Before treatment</td>
<td>50.39±6.23</td>
<td>87.69±9.68</td>
</tr>
<tr>
<td></td>
<td>After treatment</td>
<td>65.41±7.27</td>
<td>53.40±7.04</td>
</tr>
<tr>
<td>Observation group</td>
<td>Before treatment</td>
<td>49.87±5.80</td>
<td>86.92±10.25</td>
</tr>
<tr>
<td></td>
<td>After treatment</td>
<td>81.75±10.91*</td>
<td>37.50±5.29*</td>
</tr>
</tbody>
</table>

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

### Table 4.

Comparative analysis of related factors in both groups ($n=81$).

<table>
<thead>
<tr>
<th>Group</th>
<th>Time</th>
<th>MMP-9 (ng/mL)</th>
<th>PAF (pg/mL)</th>
<th>IGF-1 (ng/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>Before treatment</td>
<td>156.75±13.78</td>
<td>226.73±25.26</td>
<td>28.99±5.11</td>
</tr>
<tr>
<td></td>
<td>After treatment</td>
<td>103.41±9.76*</td>
<td>130.52±14.71</td>
<td>51.16±7.49*</td>
</tr>
<tr>
<td>Observation group</td>
<td>Before treatment</td>
<td>159.20±11.57</td>
<td>229.60±27.54</td>
<td>29.30±4.87</td>
</tr>
<tr>
<td></td>
<td>After treatment</td>
<td>74.16±6.29*</td>
<td>79.57±8.64*</td>
<td>65.81±8.92*</td>
</tr>
</tbody>
</table>

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

group. It is suggested that Xuefu Zhuyu Decoction combined with conventional treatment can effectively inhibit the oxidative stress response of patients and reduce the degree of neurological damage. The reasons may be: 1) In conventional treatment, edaravone exerts a significant free radical scavenging effect, improves the body’s antioxidant response, and thus protects nerve cells from free radicals; 2) In Xuefu Zhuyu Decoction, peach kernel, Red peony root, angelica, safflower, and Chuanxiong can invigorate the circulation of blood and remove stasis; Angelica, habitat can nourish blood; Bupleurum and scorpion can relieve liver and qi; Achyranthes can break through sputum, lead blood stasis to descend; Qi, Platycodon grandiflorum can acticate lung Qi and let drugs upgoing, liquorice can reconcile the above drugs, blood circulation and qi regulation; and then effectively improve the brain blood microcirculation, increase coronary blood flow, improve the state of ischemia and hypoxia, inhibit oxygen free, the formation of the base achieves the purpose of reducing the oxidative stress response of the body.

NO and ET-1 can respectively reflect the vasodilatation and contraction state of the vascular endothelium, and the normal state, the ratio of the two is balanced. If the patient has acute cerebral infarction, the supply of cerebral blood flow is insufficient, the neurovascular is in a contracted state, and the neurovascular endothelium is damaged. The balance maintained by both will be broken[18]. This study found that after treatment, ET-1 in the two groups was significantly lower than before treatment, and NO was significantly higher than before treatment; and the ET-1 in the observation group was significantly lower than that in the control group, and NO was significantly higher than the control group. It is suggested that Xuefu Zhuyu Decoction combined with conventional treatment can effectively improve the vascular endothelial function of patients. The reason may be related to the significant reduction of oxidative inflammatory response in combination therapy, and the specific reasons need further study. In addition, MMP-9 can promote the damage of atherosclerotic plaque by degrading elasticity and collagen and aggravate the patient’s condition[19]; PAF is a phospholipid compound, which can aggravate the brain damage by promoting inflammation, promoting oxidation and promoting thrombosis[20]; IGF-1 is a neurotrophic trophic factor[21]. This study found that after treatment, MMP-9 and PAF were significantly lower in the two groups than before treatment, while IGF-1 was significantly higher than before treatment; and MMP-9 and PAF in the observation group were significantly lower than those in the control group, while IGF-1 was significantly higher than the control group. It is further confirmed that Xuefu Zhuyu Decoction combined with conventional treatment can effectively improve the patient’s condition, reduce the degree of brain damage and have the function of protecting nerve.

In summary, Xuefu Zhuyu Decoction combined with conventional treatment of acute cerebral infarction can effectively reduce inflammation and oxidative stress, improve vascular endothelial function and nerve function, and significantly reduce the degree of brain injury, which has clinical significance.

References