Mechanism of action of Shuxuening combination for acute cerebral infarction

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Abstract: Acute cerebral infarction has rapid onset, rapid development, complex disease, step aggravation, poor prognosis, and lack of safe and effective treatment countermeasures, which has become an urgent problem to be solved clinically. Early and timely administration of acute cerebral infarction and the combination of drugs are the key to treatment. Shuxuening is one of the commonly used Chinese medicine injections in the treatment of acute cerebral infarction. It can be combined with different western medicines to treat acute cerebral infarction to produce good effect, and alleviate the disadvantages of single drug treatment to a certain extent. This paper summarizes the mechanism of shuxuening combined with different western medicines in the treatment of acute cerebral infarction, and provides a new idea for the early combination of acute cerebral infarction and the treatment of integrated Chinese and western medicine.

Keywords: Acute cerebral infarction; Shuxuening; drug combination; traditional Chinese and western medicine; combine; treat; Research review

1. Preface

Cerebral infarction, also known as ischemic stroke, refers to a kind of clinical syndrome caused by various cerebrovascular diseases, resulting in local brain tissue ischemia, hypoxic necrosis, and the rapid occurrence of the corresponding neurological defects. Cerebral infarction is the most common type of stroke, accounting for approximately 70% – 80%[1]. Acute cerebral infarction (ACI), is a global concern because its incidence is the highest in Asia, especially in China and Eastern Europe[2]. In China, the incidence rate shows an increasing trend year by year, with more than 2 million new stroke cases reported every year. According to statistics, the current mortality rate of acute cerebral infarction has exceeded myocardial infarction, becoming the second largest cause of death among Chinese residents[3]. Risk factors for acute cerebral infarction include increased age, diabetes mellitus, hyperlipidemia, hypertension, obesity, etc., and they are vulnerable to various causes, such as vascular wall damage, altered blood composition, and hemodynamic changes[4]. The condition of acute cerebral infarction is aggravated by step, with the characteristics of high incidence rate, recurrence rate, disability rate and mortality rate[5]. It will bring a heavy burden to the family and the society. Therefore, very important for the early and effective integrated Chinese and western medicine treatment in ACI patients to improve the clinical efficacy and reduce the disability rate, mortality rate and recurrence rate. In recent years, Shuxuening is often used clinically together with different western medicines to treat acute cerebral infarction. Shuxueninging is a preparation of ginkgo biloba extract, which contains a variety of medicinal ingredients, and has the effect of activating blood circulation and removing blood stasis, connecting veins and relaxing collaterals, and invigorating qi and strengthening the brain. This paper summarizes the action mechanism of Shuxuening and different western medicines in the treatment of acute cerebral infarction, which provides a new idea for the early combination drug of acute cerebral infarction and the treatment of integrated Chinese and western medicine.

2. Shuxuening

A kind of Chinese medicine injection with the effect of blood activating blood and removing blood stasis. Traditional Chinese medicine injection is a sterile drug made into the injection of Chinese medicinal materials after extraction and purification. It has the advantages of low incidence of adverse
reactions, fast starting effect, multi-component, multi-target point and exact curative effect. According to the current analysis of the use of traditional Chinese medicine, Shuxuening injection ranks the first in medicine[6]. Shuxuening injection is an injection made of ginkgo biloba or ginkgo biloba extract. Pharmaceutical ingredients are ginkgo leaves as dry leaves of ginkgo trees, sweet, bitter, astringent, flat, heart, lung meridian, has the effect of collecting lung and relieving asthma, promoting blood circulation, removing blood stasis and relieving pain. Ginkgo biloba extract has protective effects on the cardiovascular system, brain and nervous system, liver, kidney and lung, and is commonly used clinically to treat ischemic cardiovascular and cerebrovascular diseases, coronary heart disease, angina pectoris, cerebral embolism, cerebral vasospasm and other diseases[7]. The ginkgo biloba extract contains diterpenoids, ginkgo flavonoid glycosides, ginkgo olactone and ginkolides[8]. The effect of Shuxuening injection in the treatment of acute cerebral infarction is to protect the brain tissue of the ischemic area, improve vascular endothelial injury, increase cerebral blood flow, expand cerebral blood vessels, improve microcirculation, antioxidant clearance and inhibit oxygen free radicals, antiplatelet formation, antiviral, antibacterial and anti-inflammatory, etc[9-12]. The specific mechanism of action is shown in Figure 1[13-15]. One of the key links of stroke treatment is the neuroprotection of ischemic brain injury. The latest understanding of this aspect is the early treatment of stroke and the treatment window[16].

![Figure 1: The mechanism of action of Shuxuening](image)

At present, for the treatment of acute cerebral infarction, clinical Shuxuening combined with western medicine including edaravone, rosuvastatin, naloxone, etc. This paper aims to review the action mechanism and adverse effects of Shuxuening combination, and to provide ideas and basis for the clinical treatment of acute cerebral infarction.

3. Shuxuening was used in combination

3.1. Shuxuening combined with idaravone

As a new brain protective agent, Edaravone is an antioxidant and free radical scavenger. Brain-protective agents can prolong the treatment time window of acute cerebral infarction. Edaravone has small molecular weight, it has lipophilic groups, and the permeability of blood and brain barrier is up to 60%. Intravenous administration can remove highly cytotoxic hydroxyl groups in the brain, reduce cascade damage caused by free radicals, inhibit delayed neuronal death; inhibit lipid peroxidation, inhibit peroxidation of brain cells, including vascular endothelial cells and nerve cells, effectively reduce the area of ischemic penumbra, reduce ischemia and its tissue damage, cerebral edema, and improve nerve function[17-18]. However, this product can cause the reduction of white blood cells, platelets, red pigment, nausea and vomiting, abnormal liver and kidney function, and other symptoms, and we should pay attention to the side effects when taking medication[19].

Shuxuening combined with edaravone for the treatment of acute cerebral infarction, Guo Pengpeng et al[20] considered to improve the treatment effect, reduce the serum levels of IL-6 and TNF-a in patients, and improve the degree of neurological deficiency; Cheng Zejun et al[21] believed that it can effectively improve the function of vascular endothelial cells, inhibit the expression of inflammatory factors, and have a protective effect on the brain tissue, thus improving the therapeutic efficacy and...
improving the prognosis and quality of survival of patients; Huang Fang et al.[22] The study believes to effectively control related inflammatory indicators, and high safety, conducive to the recovery of patients; Yang Li et al.[21] believed that the combination of the two can reduce the blood viscosity, reduce the red blood cell aggregation, effectively improve the blood rheology of patients, promote the recovery of nerve function, and effectively improve the nerve function deficiency of cerebral infarction. In conclusion, Shuxuening and edaravone can play a significant synergistic effect, strengthen the protection of ischemic cerebral injury, improve clinical neurological function, and effectively reduce the mortality and disability rate of acute cerebral infarction, relieve patients' pain, improve their living ability and quality of life. And the combination of both patients does not increase the adverse effects and has a high safety, has a high clinical application value[24],

3.2. Shuxuening combined with rosuvastatin

Acute cerebral infarction is mostly atherothrombotic cerebral infarction, and patients are often complicated with hyperlipidemia. Elevated blood lipid level is closely related to atherosclerotic thrombosis, which can directly affect the condition and condition of atherosclerotic thrombosis. Therefore, lipid lowering is an important link in the treatment of acute cerebral infarction, and the blood lipid level of patients in time is effectively regulated clinically[25]. Studies have reported[26-27], Rosuvastatin, simvastatin, atorvastatin and other drugs are commonly used in clinical lipid-lowering drugs, all have good blood lipid reduction effect, but rosuvastatin is more advantageous in improving the neurological function and short-term prognosis in patients with acute cerebral infarction. The Rosuvastatin, As a hydroxymethyl glutarate monoacyl-coenzyme A (hydroxymethylglutaric acid monoacyl coenzyme A, HMG-GoA) reductase inhibitors, Can competitively bind to the active site of the HMG-GoA reductase to inhibit its effects, And inhibits cholesterol synthesis, Simulstimulation of cell surface LDL receptors to increase their synthesis and decrease blood LDL levels, Effectively reduce blood lipid levels, Thus reducing the blood viscosity, Improving blood rheological levels, To improve the atherosclerotic thrombosis, So as to achieve the therapeutic effect of treating cerebral infarction[28]. In addition, rosuvastatin can also promote the formation of collateral circulation, improve the ability of brain tissue to withstand hypoxia, balance the supply and demand relationship between brain tissue and oxygen, and improve the state of cerebral ischemia and hypoxia. In addition, rosuvastatin can also dilate blood vessels, reduce vascular resistance, increase blood perfusion, improve brain tissue, and reduce the body inflammatory response, improve vascular endothelial function, so as to stabilize atherosclerotic plaque, and prevent the formation of thrombosis[29]. In short, acute cerebral infarction is treated by regulating fat, promoting the formation of collateral circulation, and inhibiting the inflammatory reaction.

Wang Yudong et al.[30] The study showed that the clinical effect of rosuvastatin injection in patients with acute cerebral infarction is clear, its positive effect in reducing the inflammatory response in patients, regulating the plaque stability and improving the nerve function of patients is more significant than a single rosuvastatin treatment, and will not increase the occurrence of adverse drug reactions. The combination of high doses of rosuvastatin is better for patients.

3.3. Shuxuening combination with naloxone

During acute cerebral infarction, ischemia and hypoxia occur in the brain, and the body is in a state of stress. The hypothalamus will release factors, prompting the release of large amounts of beta-endorphin in the anterior pituitary gland, reducing blood flow and inhibiting neuronal electrical activity, and causing persistent brain injury and ischemic cerebral edema. In addition, the increase of endorphin can inhibit respiratory and circulation function, resulting in abnormal emotional behavior, increase oxygen consumption of brain cells, inhibit nerve excitability and somomotor function. Meanwhile, beta-endophpins significantly promoted Ca2+ Release causes Ca2+ The concentration was abnormally elevated and activated membrane phospholipid A2 and phospholipase C, which degrade membrane phospholipids, causing thromboxane A2Increasing release, resulting to platelet aggregation, increased the extent of thrombus, and forming brain edema[31].

Naloxone is an opioid receptor antagonist that easily crosses the blood-CSF barrier and suppresses the release of beta-endorphin from the anterior pituitary and inactivates beta-endorphin, thus blocking the brain damage process caused by beta-endorphin itself[32]. Naloxone can stimulate the generation of overloaded oxidase in the body, and protect the organs by removing free radicals; improve the disorder of magnesium ions in nerve cells, inhibit the activity of microglia under brain injury, effectively reduce inflammation, improve calcitonin gene, and protect neurons. And reduced the cardiovascular nervous
central function, inhibited the peripheral blood vessels, better regulate blood pressure, and inhibited the central nervous damage\cite{33}. Although the effect of naloxone in acute cerebral infarction is fast and reliable, because the longer the patient, the more serious the neuronal damage, so the clinical need for early administration, so that the neurons are not to beta-endorphin secondary damage, to obtain better treatment effect. A number of clinical studies\cite{34-35} reported that the early treatment of acute cerebral infarction combined with naloxone can accelerate the blood flow and antiplatelet formation in the ischemic area, effectively improve the following environment, protect the brain cells, and block the process of secondary brain injury. The combined use of the two has an obvious synergistic effect, which can promote the recovery of neurological defect, shorten the course of disease, reduce the consciousness disorder, shorten the duration of the consciousness disorder, reduce the mortality rate and disability rate, which has the advantages of fast effect, safety and efficiency, and has no serious adverse reactions, and has good clinical application value.

4. Summary

The combination of treatment in acute cerebral infarction has a significant synergistic effect, increasing the clinical efficacy, protecting the brain, and improving the neurological function. The effects of different combination treatments is different, which is summarized in Table 1.

<table>
<thead>
<tr>
<th>Therapy method</th>
<th>Mechanism of action</th>
<th>Advantage</th>
<th>Untoward effect</th>
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<tbody>
<tr>
<td>Shuxuening combination with idaravone</td>
<td>Cleange free radicals and suppress inflammation</td>
<td>Multipathway protection against ischemia-reperfusion brain injury, prolonging the acute phase treatment time window</td>
<td>Does not increase adverse reactions, and has a high safety, has a high application value</td>
</tr>
<tr>
<td>Shuxuening combination with rosuvastatin</td>
<td>To reduce the inflammatory response and regulate the stability of plaques in patients</td>
<td>Assist Shuxuening to improve the neurological function of patients, and play a better treatment effect of cerebral infarction</td>
<td>Without increasing adverse effects, the combination of high doses is better</td>
</tr>
<tr>
<td>Shuxuening combination with naloxone</td>
<td>Early administration of naloxone protected neurons from secondary beta-endorphin damage</td>
<td>Assist shuxuening to accelerate blood flow, anti-platelet formation, effectively improve the environment, protect brain cells, and block the process of secondary brain injury</td>
<td>No serious adverse reactions, which have good clinical application value</td>
</tr>
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</table>

Acute cerebral infarction is a series of cascade reactions will occur after ischemia. There are potential interventional ways for each process of ischemic cascade. Combined combination can interfere with the multi-factorial and multi-link pathological process of IS, and greatly optimize the selection of targets. In this paper, we review the action mechanism and adverse reaction of Shuxuening and three different western medicines in the treatment of acute cerebral infarction, the early use of edaravone and other neuroprotective agents and the selection of Shuxuening combined with symptomatic western medicine treatment according to the patients' symptoms are very important. Therefore, the key to treatment lies in timely early treatment and precise combination medication, and advocating early treatment of integrated Chinese and western medicine.
References