

Application of dredging fu-organs in cerebral edema after stroke

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Abstract: Stroke is one of the most common diseases in neurology, and the brain edema after stroke is an important factor affecting the prognosis of patients. It is particularly important to reduce the volume of brain edema in clinic. By studying the mechanism of Tongfu agent, it is shown that it can effectively reduce the water content of brain tissue by inhibiting the expression of AQP-4, reducing the permeability of blood-brain barrier and reducing the damage of inflammatory molecules, and it has achieved good curative effect in clinic, which is one of the common treatment methods for brain edema.

Keywords: tongfu agent; rhubarb; stroke; brain edema

1. Introduction

Brain edema, a disease with increased water content in the brain parenchyma, is clinically manifested as headache, dizziness, or even disturbance of consciousness after increased intracranial pressure, with severe brain hernia, which can be life-threatening. This disease is common in clinic. With the younger onset of cerebrovascular disease and the larger base of elderly population, it is particularly important to treat it and improve its complications. No matter whether it is cerebral ischemia stroke or cerebral hemorrhage stroke, it can lead to tissue edema due to brain tissue ischemia and hypoxia. In modern medicine, mannitol, glycerol, fructose and other dehydrating agents and diuretics are often selected for treatment. However, due to many complications, which affect the curative effect, doctors in past dynasties have studied the effect of dredging fu-organs to achieve the effect of promoting diuresis and removing blood stasis to treat edema, and the effect is obvious, which is widely used in clinic. This paper reviews the research and treatment status of brain edema by dredging fu-organs.

2. The basis of application of the method of dredging fu-organs

The method of dredging fu-organs is a therapeutic principle that purges and moistens drugs to relieve constipation, expel pathogenic factors, remove heat, and expel water and drink to achieve clinical curative effect. Now it is extended to a therapeutic method of treating diseases by expelling pathogenic factors. The method of dredging fu-organs is not limited to gastrointestinal diseases, and has been widely used in multi-organ diseases [1-2]; The theory of dredging fu-organs originated from Neijing, and Zhang Yuansu was the first physician to apply the method of dredging fu-organs to stroke. Sanhua decoction (composed of rhubarb, magnolia bark, immature bitter orange and notopterygium root) created by Liu Wansu, a physician, is contained in Su Wen's Collection of Pathogenesis, Qi and Life-saving. "If you suddenly get dirty, your stool will be more secret and astringent, so it is advisable to use Sanhua decoction to relieve its stagnation." It has good curative effect in treating constipation caused by viscera in stroke, and it has become a representative prescription for treating stroke by dredging fu-organs, which is actually dredging fu-organs and damaging healthy qi, so this therapy is often used to treat acute stroke [3-5]. After Li Ying applied the method of dredging fu-organs to the treatment of apoplexy, he summarized that the method of dredging fu-organs can dredge the symptoms of Yangming's stomach and fu-organs. Second, with the help of catharsis, the upper disease can be treated below, and the upper "blood sugar" can be induced to descend, so that qi, blood, phlegm and heat can be dissipated; Third, purgative drugs can be used to remove blood stasis and phlegm, so that evil can be eliminated; The four urgently store yin, so that yin and body fluid can be stored and will not be exhausted [6]; The acute phase of stroke is an important period to determine the prognosis of the

disease, and the fu-organs should be dredged in time to help patients tide over the danger. According to Gao Zuming's statistical analysis, the most frequently used drugs for treating apoplexy with Tongfu prescription are rhubarb, immature bitter orange, mirabilite, magnolia officinalis, Trichosanthes kirilowii, peach kernel and Arisaema cum bile. 100% rhubarb was used in all prescriptions^[7], and the frequency of drug use in 120 prescriptions for treating acute cerebral hemorrhage was counted, as shown in Table 1. See Table 2, Table 3, Table 4, Table 5 and Table 6 for the descriptions of rhubarb, immature bitter orange, mirabilite, magnolia officinalis and Fructus Trichosanthis in herbal medicines of past dynasties. With the in-depth study of diseases by later doctors, the method of dredging fu-organs has become one of the important treatments for stroke emergency.

Table 1: Statistics on the Frequency of Drugs Used for Clearing Fu-organs

ordinal	medicine	frequency
one	Chinese rhubarb	81
2	dried immature fruit of citron or trifoliate orange	18
three	Glauber's salt	11
four	Trichosanthes kirilowii	11

Table 2: Sexual and Taste Efficacy of Rhubarb

source	Sexual taste	efficacy
Shennong Jing Baicao	Bitter and cold	Regulating blood stasis, closing down, cold and heat, breaking abdominal mass, staying for food, cleaning the stomach, promoting innovation, promoting diuresis and Gu Dao, regulating Chinese food, and calming the five internal organs.
Famous doctors don't record	Major Cold	Calm stomach and lower qi, remove phlegm, heat between intestines, abdominal distension, female cold blood stagnation, small abdominal pain, and retention of old blood.
Theory of medicinal properties	Bitter and sweet	Digestion, cleansing five zang-organs, dredging women's menstrual cycle, benefiting edema, breaking phlegm, gathering cold and hot food, and benefiting the large intestine to stick heat and toxic swelling.
Kaibao materia medica	Bitter and severe cold	Calm stomach and lower qi, remove phlegm, heat between intestines, abdominal distension, female cold blood stagnation, small abdominal pain, and retention of old blood.

Table 3: Sexual and Taste Efficacy of Fructus Aurantii Immaturus

source	Sexual taste	efficacy
Shennong Herbal Classic	Bitter and cold	Indications: strong wind in the skin, such as bitter and itchy beans, eliminating cold and heat, heat stagnation and stopping dysentery.
Famous doctors don't record	Sour and slightly cold	The main purpose is to eliminate the weakness of chest and ribs, stop water supply, break the fruit, eliminate fullness, anxiety under the heart, sudden pain, adverse qi, rib wind pain, calm stomach qi, stop diarrhea and improve eyesight.
Theory of medicinal properties	Bitter and bitter	Relieve typhoid fever and knot chest, and use it in the soup of sinking chest. Asthma and cough in the main body, cold injury in the kidney. Yin flaccidity and qi, add and use it.
Rihuazi materia medica		Spleen strengthening, appetizing, regulating five zang-organs, lowering qi, stopping vomiting, eliminating phlegm, treating nausea, cholera, diarrhea, resolving food stagnation, eliminating phlegm, expelling wind, improving eyesight, edema of lung qi, benefiting large intestine and itchy skin.
Kaibao materia medica	Bitter, sour and slightly cold	Eliminate phlegm addiction in chest and hypochondrium, stop water supply, break firm, relieve fullness, anxiety, sudden pain, aversion to qi, hypochondriac wind pain, calm stomach qi, stop diarrhea and improve eyesight.

Table 4: Sexual and Taste Efficacy of Glauber's Salt

source	Sexual taste	efficacy
Shennong Herbal Classic	Bitter and cold	The main five zang-organs accumulate heat, the stomach is open and closed, the accumulated diet is washed away, the old is introduced to bring forth the new, and the evil spirits are removed.
Famous doctors don't record	Bitter, bitter, bitter.	Indications: accumulation of five internal organs, prolonged fever, gastric obstruction, elimination of pathogenic factors, blood stasis, weak abdominal contraction, dredging meridians, facilitating urination and defecation, relieving stranguria, and promoting innovation.
Theory of medicinal properties	salty	Can pass women's month closure, abdominal mass, scrofula and jaundice. The main abortion, suffering from lacquer sore juice. Treating diseases at times and stifling heat can disperse evil blood.
Herbal medicine is elegant and half-elegant.	bitter cold	Governing all diseases, except cold and heat pathogens, accumulating six fu organs, and consolidating addiction; Can change 72 kinds of stones.
Kaibao materia medica	Bitter and bitter, severe cold	Control accumulation of five internal organs, chronic fever, stomach obstruction, elimination of pathogenic factors, retention of blood, stagnation of phlegm in abdomen, dredging meridians, facilitating urination and defecation, breaking five stranguria, and promoting innovation.

Table 5: Sexual and Taste Efficacy of Magnolia Officinalis

source	Sexual taste	efficacy
Shennong Herbal Classic	Bitter and warm	Indications: apoplexy, typhoid fever, headache, cold and heat, palpitation, qi and blood stagnation, and muscle death.
Famous doctors don't record	Great temperature	Regulating middle warmer, invigorating qi, eliminating phlegm, lowering qi, treating cholera and abdominal pain, fullness, cold in the stomach, vomiting in the chest, diarrhea, stranguria, relieving convulsion, removing heat, relieving boredom and thickening the stomach.
Kaibao materia medica	Bitterness and high temperature	Warming the middle energizer, invigorating qi, eliminating phlegm and lowering qi, treating cholera and abdominal pain, fullness, cold in the stomach, vomiting in the chest, diarrhea, stranguria, relieving convulsion, retaining heat, relieving boredom and thickening the stomach.
Rihuazi materia medica		Spleen strengthening, appetizing, regulating five zang-organs, lowering qi, stopping vomiting, eliminating phlegm, treating nausea, cholera, diarrhea, resolving food stagnation, eliminating phlegm, expelling wind, improving eyesight, edema of lung qi, benefiting large intestine and itchy skin.
Medicinal nature fu	Bitter, pungent and warm,	It can rise and fall, and the yin is in the yang. It has two functions: bitter energy can lower qi, removing excess and relieving abdominal distension; warming energy can replenish qi, removing dampness and dispersing stagnation and regulating middle energizer.

Table 6: Sexual and Taste Efficacy of Trichosanthes kirilowii

source	Sexual taste	efficacy
Shennong Herbal Classic	Bitter and cold	Indications: thirst quenching, body heat, vexation, fever, tonic, calming the middle energizer, and persistent injury.
Famous doctors don't record		It is mainly used to treat stomach and intestines heat, eight jaundice, yellow face, dry lips and mouth, shortness of breath, and diuresis.
Rihuazi materia medica	Bitter and cold	Tonify asthenia and fatigue, dry mouth, moisten heart and lungs, treat hand and face wrinkles, hematemesis, diarrhea due to intestinal wind, and red and white dysentery.
Medicinal nature fu	Bitter and cold	Shen also, Yin also. It has two functions: quenching thirst, relieving vexation and fever, tonifying deficiency and dredging menstruation.

3. Pathogenesis of brain edema

Brain edema is a kind of clinical syndrome often caused by stroke, and it is an important factor affecting the prognosis and progress of the disease. Both types of strokes can cause brain edema. The pathogenesis of hemorrhagic stroke is summarized as hyperactivity of liver yang, disturbance of wind and fire, disorder of qi, blood and yin, blood escaping from the pulse, blood stasis in brain collaterals and body fluid overflow. Ischemic stroke is mostly caused by the patient's old age and physical weakness, with phlegm and turbidity, qi deficiency and inability to promote blood circulation, phlegm and blood stasis are intertwined, and stagnant in the pulse will produce water^[8], that is, the theory of blood syndrome says: "Blood stasis will turn into phlegm and water for a long time"^[9]. Phlegm, blood stasis and water are not only pathological products caused by stroke, but also the cause of complications^[10]. Through clinical observation, Yang Aixue summarized the pathogenesis of cerebral hemorrhage in acute stroke as diarrhea, phlegm and blood stasis accumulated in intestines and fu organs, which disturbed the spirit. The self-made prescription of Xingnao Huatan Tongfu Yin can improve brain circulation, reduce gastrointestinal pressure, reduce blood viscosity and other aspects to eliminate brain edema and relieve patients' symptoms^[11]. Modern medical research shows that the pathological mechanism of ischemic brain edema is caused by many factors, such as the up-regulation of aquaporin after brain tissue injury, the transient increase of TNF- α and the increase of MMP, which lead to the destruction of blood-brain barrier and the increase of capillary permeability, resulting in water and blood components in brain tissue entering the brain parenchyma, forming edema, brain tissue ischemia and hypoxia, and Na⁺-K⁺-ATPase damaging the osmotic pressure inside and outside the cell, causing the water outside the cell to flow into the cell; Inflammatory reactions produced by various cytokines and the action of a large number of oxygen free radicals after ischemia-reperfusion injury are the main causes of ischemic edema^[12-13]; The mechanism of hemorrhagic edema is ischemia, hypoxia and clot retraction caused by local hematoma, the dissolution of red blood cells and hemoglobin, the opening of blood-brain barrier, a series of cascade reactions after thrombin activation, inflammatory reaction and complement system activation^[14]. It is generally believed that the pathogenesis of stroke belongs to the deficiency of the essence and the excess of the essence, so it is of great significance to intervene at this time to determine the outcome of the disease. In acute stage, apoplexy is mainly treated by phlegm-heat and excess of fu-organs, and qi-flow disorder. In the treatment of cerebral edema caused by apoplexy, the methods of clearing occupying space and improving edema, dredging the fu-organs, promoting blood circulation, resolving phlegm and promoting diuresis are adopted.

4. Pathological mechanism of treating edema with drugs for clearing fu organs

Sanhua decoction is a representative prescription for dredging fu-organs and promoting diuresis. Zhang Changguo and others used thread embolism method to prepare cerebral ischemia model, and studied the mechanism of improving brain edema after cerebral ischemia with Tongfu decoction. The experiment showed that the brain water content in Sanhua decoction treatment group was lower than that in model group at all times, by inhibiting the expression of AQP-4 and its level and the permeability of blood-brain barrier^[15]; Fan Kaifang and others confirmed through experiments that Sanhua decoction can improve brain edema after cerebral ischemia-reperfusion to a certain extent; Based on data mining, rhubarb is the most frequently used drug to treat brain edema after cerebral hemorrhage. Rhubarb has the effects of purging, removing blood stasis, dredging channels, clearing heat, cooling blood and detoxifying, and its nature is bitter and cold, dredging intestines and stomach, reducing intracranial pressure and relieving brain edema^[16-17]. Tang Yuping's experimental study shows that rhubarb, an important drug in Tongfu agent, has the characteristics of improving brain edema, and its mechanism is mainly to intervene AQP-4, reduce endothelial cell damage and improve the degree of blood-brain barrier damage to promote the recovery of brain edema^[18]. Peng Shaopeng et al. conducted an experimental study on the application of emodin in brain edema after cerebral hemorrhage. Emodin can effectively reduce the water content and AQP-4 level of brain tissue and reduce the release of inflammatory factors^[19]; It provides a scientific basis for the clinical use of purgative drugs in the treatment of this kind of diseases.

5. Clinical and experimental study on drugs for relieving fu-organs

Chen Fengting and other experiments observed that Tongfu mixture (such as rhubarb, radix aucklandiae, peach kernel, radix aucklandiae, radish seed, etc.) was administered rectally to treat acute brain edema secondary to cerebral infarction, and the overall effective rate reached 87.5%. The

compatibility of drugs can improve inflammation, inhibit platelet coagulation, scavenge oxygen free radicals, and reduce capillary permeability, which not only can reduce the adverse reactions of dehydrating agents, but also has a significant therapeutic effect on increased intracranial pressure [20]. Zhang Yong divided 60 patients with cerebral edema clinically diagnosed as cerebral hemorrhage into two groups. The treatment group was treated with clinical basic treatment and Tongfu Xiezhuo recipe (rhubarb, mirabilite, leech, *Alisma orientalis* and *Dianmai*), while the control group was treated with dehydration. The treatment group had obvious curative effect through CT brain edema zone absorption area, Glasgow coma score coefficient and symptom improvement, which was better than western medicine alone and had high safety [21]. Cong Dawei et al. treated 60 cases of senile severe cerebral hemorrhage with Tongfu Xiezhuo recipe (*Dianmai*, rhubarb, mirabilite, *Alisma orientalis*, etc.) and compared the curative effect with that of 60 cases of control group. The results showed that the growth rate of brain water volume in Tongfu Xiezhuo recipe treatment group was significantly lower than that in control group, and the improvement of neurological function, the reduction rate of patients' living ability and complications were better than those in conventional treatment group [22]. Sun Shaogang divided 133 patients with acute cerebral hemorrhage and brain edema into rhubarb group (45 cases), senna group (45 cases) and control group (43 cases). The experimental results showed that after treatment, the recovery of neurological deficit, the reduction of hematoma volume and edema area of brain tissue were better than those of the control group. Both rhubarb and senna were cathartic drugs, which could restore the body by reducing gastrointestinal pressure [23]. The experimental study shows that it is scientific and safe to apply the method of purging diarrhea and dredging fu-organs to clinical acute brain edema. Li Junhong divided 70 patients with cerebral edema into Dachengqi Decoction as the treatment group and the routine treatment control group for experimental study. The total effective rate of the treatment group reached 94.29%, and the curative effect was obvious because the control group reduced intracranial pressure with turbid qi by rushing down and dredging fu organs, and the symptoms improved [24]. Zhang Qiqi and others selected 64 patients with acute cerebral hemorrhage and divided them into raw rhubarb granule treatment group and western medicine comprehensive treatment control group. By comparing the scores of NIHSS, mRankin and BI with the absorption of cerebral hemorrhage, the results showed that the curative effect of the treatment group was better than that of the control group, which confirmed that rhubarb could alleviate the brain edema that would cause secondary nerve injury by improving the damage of blood-brain barrier [25].

6. Summary

Brain edema is one of the most common complications after stroke. It is characterized by high disability rate and high mortality rate, so the treatment of brain edema is particularly important and has important influence on the prognosis of patients' diseases. In recent years, the research on traditional Chinese medicine for treating stroke has become more and more mature. Through a large number of clinical and experimental studies, it has been shown that purgative agents, such as rhubarb and mirabilite, have obvious improvement effects on brain edema. Purgative agents have the functions of promoting diuresis, purging heat, attacking accumulation, and making pathogens have a way out. Turbid gas comes out with stool. Its mechanism mainly includes reducing the volume of brain edema, inhibiting the release of inflammatory factors, blood-brain barrier permeability and cell apoptosis, which is beneficial to.

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