

Mechanism of Pneumonia after Treatment of Phlegm Heat Fu Solid Type Stroke Using Xinglouchengqi Decoction

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Abstract: Stroke is a type of devastating cerebrovascular event that disrupts cerebral blood flow due to the blockage or burst of cerebral blood vessels, which easily causes physical disability and multiple functional impairments in patients. The mortality rate of stroke patients in China is the first in the world, and pulmonary infection is an important cause of impaired clinical outcomes in patients with acute stroke. The term stroke associated pneumonia (SAP) has been proposed so far, emphasizing the fact that the two are closely related in pathophysiology. TCM holds that phlegm heat Fu decoction is the most common syndromic form of stroke, and Hua Duan Fu method represents the prescription of Fang Xinghui Qi Decoction for treating stroke. Xinghui Qi Decoction is the most representative formula for treating stroke with phlegm heat Fu. The theory of traditional Chinese medicine (TCM) and the "bacteria intestine brain axis" proposed in modern medicine have a different variety. Many clinical trials have confirmed the exact clinical efficacy and neuroprotective effect of Xinghui Chengqi Decoction in treating SAP, however, the study of its effect mechanism is still insufficient. Therefore, the author intends to carry out a combined summary of histfang herbal chemical components, pharmacological effects and their mechanisms of action of xinglouchengqi Decoction to deeply explore the intestinal microecological mechanism of SAP and the effector mechanism of xinghuichengqi Decoction in treating post-stroke pneumonia of phlegm heat Fu solid type.

Keywords: xinglouchengqi decoction, stroke, stroke-related pneumonia, immunosuppression, pneumonodema

1. Introduction

Stroke associated pneumonia (stroke) is an inflammatory reaction of lung tissue that occurs after stroke, with aspiration being the main cause and symptoms such as fever, cough and dyspnea presenting as one of the most common complications of stroke, independently associated with nearly one-third of post-stroke deaths^[1-2]. Western medical treatment options include both general treatment and antibiotic therapy. But the long-term use of high-intensity antibiotics, although it can inhibit sensitive flora and control the further development of infection^[3], also leads to the variation of sensitive bacterial flora, the increase of bacterial resistance^[4], and reduce the clinical efficacy. Studies have shown that some TCMs have different degrees of bacteriostatic ability^[5]. Patients with pneumonia following stroke of the phlegm heat Fu Shi type exhibit wheezing Qi surge, body heat, depression of stools, and dry mouth with halitosis, while xingwuchengqi decoction is one of the representative formulas for invigorating the Tangfu method, which employs Dahuang and munnituangtong Fu organs, together with guaru and cholananxing to invigorate phlegm, and shows excellent therapeutic effects for post-stroke pneumonia due to phlegm heat Fu Shi. Therefore, the author intends to carry out a combined summary of histfang herbal chemical components, pharmacological effects and their mechanisms of action of xinglouchengqi Decoction to deeply explore the intestinal microecological mechanism of SAP and the effector mechanism of xinghuichengqi Decoction in treating post-stroke pneumonia of phlegm heat Fu solid type.

2. Mechanisms of pneumonia following stroke of the Fu Fu solid type of phlegm heat

2.1. Theory of traditional medicine

SAP does not have a disease name corresponding to it in the Chinese medicine, based on its pathogenetic characteristics and clinical symptoms, this disease can be classified into the category of

'wind and warm diseases', 'lung heat diseases', 'cough' and other pulmonary diseases. It was stated in Danxi Xinfu Fu Yu stroke: "" fire loaded phlegm, so tongue strong non-verbal, mouth eye drinking oblique, phlegm sialorrhoea also "", and cloud "" hemiplegia, a large rate of phlegm "", indicating that phlegm is an important cause of stroke. According to the medical Zong Jin book: "" an obese person with multiple strokes, with his Qi enriched in the exterior, but apologize also in the interior, the lungs are the channels of the air entry and exit. In human obesity, he has shortness of breath, acute lung evil Sheng, lung jinkemi, and bile are liver Zhi Fu "", and thus phlegm sialorrhoea is accumulated "", indicating that "" phlegm "" is also an important pathological factor that causes "" shortness of breath and lung evil Sheng "" after stroke. SAP onset, unsurprising vs. internal injury. From the aspect of internal injury, the lung is toward the Baimai Dynasty and is physiologically interconnected with the Wuzhuang six Fu organs through EPI, meridians, and semiqi Xuezhiliquid, as the internal meridian cloud states that "" the Wuzang six Fu organs are capable of doing all things cough, not only the lungs alone "", and the Jingyue book states that "" the cough of internal injury, which first injures the spleen, must be done by the spleen as well as the lungs, for which the lung is marked "", The specimen relationship of his heart disease to lung disease was elucidated from a holistic view. After stroke, the fasciae become congested, and the camp is blocked, the condition is spongy and prolongs without healing, and the disease tends to progress outward, involving the lung, then causing an abnormal airway lift and fall. For the external sense, the lungs are Huacai, belong to Jiao Qi, integrate globally, communicate with the outside world, and 6_rbatiorculties if they invade the human body are the first responsibility for the lung, as "" warm evil is accepted, firstly make the lung and reverse transmit the pericardium "", "" fan wind is mostly introduced from the dorsal five viscera Yu, such as the heart is affected, the lung disease is the most urgent, the Qi of the lung is resting, and you risk so on "". All of the above indicate that patients' Yin and Wei deficiency or choroid emptiness, then wind evil invades the human body, with moderate body deviation, dysfunction of the flow of Qi and blood, and meridian block is stroke, at which time the body has weak ability of guarding outside, and the lung by six masturbation evil develops sap. In conclusion, the onset of sap is caused by internal injury to Zang Fu organs after stroke or combined with external sense of the evil of hexamasturbation, and the pathological nature is an inclusion in this false standard, an inclusion due to the false effect.

2.2. Modern medical research

Altered local colonization with microbiota after stroke, such as immune decline, dysphagia, and invasive manipulation, are highly susceptible to triggering sap. And SAP causes poor outcome in stroke patients, which increases the mortality rate by nearly two-fold after 3 years^[6]. Studies have shown that in the acute phase of stroke, the main pathogenic species include gram negative bacteria, gram positive bacteria, fungi and anaerobes. Westendorp et AL7 found that the pathogenic bacterial type of sap is highly similar to early-onset nosocomial pneumonia or aspiration syndrome, which may be attributed to the significantly increased aspiration rate after stroke. Zhang Xingfeng et al^[8] found that the overall infection rate of multi drug resistant bacteria in patients with sap was 49.32%, and the pathogenic bacteria were relatively resistant to several common antimicrobials in clinic. SAP pathogenesis is mainly:

(1) Aspiration: stroke patients have impaired swallowing function, have more oral secretions and food debris, and are prone to aspiration to form aspiration pneumonia. The swallowing and protective cough reflexes are diminished in the setting of impaired consciousness after stroke, leaving the patient mostly in sleep with covert aspiration. In addition, patients with impaired consciousness, unfavorable mobility, prolonged bed rest, and stasis and congestion of lung tissue under the force of gravity, also develop bacterial infection. Niimi et al^[9] found an association between reduced frequency of spontaneous swallowing and low levels of neuropeptide substance P in saliva in patients with acute stroke. Substance P is a neuropeptide secreted by dopaminergic neurons upon stimulation, which is secreted into the pharynx and trachea and is involved in motor regulation, and the neurotransmitter dopamine is suppressed during cerebrovascular disease, where its production is reduced, causing a diminished swallowing and cough reflex^[10], thus leading to pulmonary infections.

(2) Immunosuppressive status after stroke: a series of cascades after ischemic hypoxic insult and reperfusion injury in the acute phase of stroke cause local immune changes in the brain, which produce various proinflammatory factors, chemokines, reactive oxygen species (ROS) clusters and nitrogen radicals and other harmful substances, creating a high-density inflammatory environment in the brain. Although this inflammatory response can absorb necrotic cell debris and repair damaged blood vessels, it also disrupts the integrity of the blood-brain barrier^[11] and activates the peripheral immune system^[12], causing further inflammatory damage, which was also confirmed through clinical studies that the brain tissue of patients with middle cerebral artery malignant infarction is replete with a large number of

peripheral immune cells ^[13]. From this, the body begins to initiate neuroprotective mechanisms manifested by a shift from stroke induced local brain damage to systemic immunosuppression, as evident from the dramatic changes in the immune organs spleen and its surrounding natural killer cells ^[14]. Chamorro et al ^[15] suggested that IL - 6, TNF - α released after ischemic stroke Immunomodulatory mediators such as IL-6 and IL-10 act on the thalamus pituitary adrenal gland (HPA) axis, sympathetic nervous system, parasympathetic nervous system and other neuroendocrine pathways, while the secreted catecholamines, adrenocortical hormone, acetylcholine, act on the spleen, lymph nodes, thymus and other lymphoid organs, further lymphocytes, neutrophils, monocytes, macrophages and natural killer cells and other functions, activity decreases ^[16], eventually Cause systemic immunosuppression. Although down-regulation of immune responses may guarantee that inflammatory substances are damaging to brain neurons at a low level, excessive immunosuppression increases the susceptibility to post-stroke and significantly worsens the clinical outcome of stroke patients "".

(3) Neurogenic pulmonary edema: some scholars found that the formation of neurogenic pulmonary edema is associated with the impairment of pulmonary vascular permeability ^[17]. Critically ill stroke patients experience a dramatic increase in intracranial pressure, abnormal excitatory discharge of sympathetic nerves, and secretion of a large number of serum catecholamines, which cause the systemic circulation and pulmonary veins to strongly contract, the resistance of the pulmonary circulation to rise, markedly elevated hydrostatic pressure, and then develop pressure pulmonary edema ^[17]. At the same time, the acutely elevated pressure on capillaries will trigger impact injury, damage the structure of vascular endothelium, make pulmonary vascular permeability change, and a large amount of protein extravasation will also form pulmonary edema ^[17]. The middle-aged and old patients themselves have poor cardiopulmonary function, while the neurogenic pulmonary edema caused by stroke will further trigger acute respiratory insufficiency, hypoxemia, and even respiratory failure, which makes the lung environment disordered and immune function decreased, and then lung infection occurs.

3. Mechanism of action of xinglouchengqi decoction

3.1. Group squares, solutions

Clinical practice of xinglouchengqi decoction is based on whole guarou 30 g, cholenanxing 6 g, Dahuang 10g (back and bottom), and Mangxiao 10g (subduction) were applied in a ratio, which can effectively clear away hot phlegm and turbid toxins. 1,2 this party obeyed the TCM theory of "" rush is treating its standard "" and the Chinese medicine idea of "" lung and large intestine coincides with dryness, which can be treated with xingwuchengqi Decoction (xingwuchengqi Decoction) due to hyperactivity of phlegm and subsequently confusion, slurring of speech, and hemiplegia. 3 ^[18]. Fang Zhong Da Huang as the Jun drug, which is characterized by cold taste and bitter properties in the spleen, stomach, large intestine, liver, and pericardium, and has the efficacy of clearing heat and passing the intestine, detoxifying herbal blood, removing blood stasis, and eliminating dampness and eliminating yellow, exerting the laxative effect of dissipating the intestine and stomach, and is suitable for hot junction constipation. "" Zhihua Yi Yun: "" Rheum odors turbid, falls straight down, goes without keeping eyes, has chop to capture the force of gate, so general No It is known that Rheum dahliae has an outstandingly high force of descending. Mountain nitrous taste is salty and bitter, sexual cold, returns to stomach and large intestine, has the efficacy of clearing heat and fire, drying laxatives, soft firmness and eliminating swelling, and is mostly used for stool constipation, hot and constipation, etc. Munnit is required for the use of Chen medicines and rhubarb, which can be both under bitter and cold conditions and can be soft and firm, so that the power of hot push and push of water is quite high ^[19]. Guar taste Gan, slightly bitter, sexual cold, resolve phlegm and pass for adjuvant. According to the Shen Nong Ben Cao Jing Yun: "" heat urbates inside, Ping to Xianhan and Zuo to bitter Gan "" ^[20], therefore, this party uses Dahuang of bitter cold with mountain nitrates of salty and cold, Zuo to ganhan with Guare of Tongfu for Zizhi heat. Bilinan Xing taste bitter, micro Xin, sex cooling, return lung, liver and spleen meridians, has the efficacy of clearing away heat and removing phlegm, resting wind and startling, used for phlegm and hot cough, stroke sputum vagus and so on. The four drug compatibility ensemble Tong Fu Fu is responsible for removing heat and clearing heat and eliminating phlegm ^[21].

3.2. Modern pharmacological actions

Rhubarb has a large variety of chemical components, including anthraquinones, anthrones, stilbenes, phenylbutanones, pyranones, naphthalene glycosides, tannins, acyl glycosides, and so on ^[22]. The main components of Rhubarb Anthraquinones are emodin, aloe emodin, rhein, emodin methyl ether, and rhein,

which have laxative, antitumor, antiviral, and anti-inflammatory effects; The main components of anthraquinones are sennosides a ~ D, rhubarb xanthones a ~ C, et al [23]. Studies have shown that the pharmacodynamic basis of rhubarb's descending effect is generally an anthraquinone glycoside and a double anthracene sennoside component [24]. Sennoside a [25], an anthranoid component of rhubarb, is the main component of rhubarb that exerts a laxative effect. Aloe emodin glycoside, a glucoside that also contains an anthrone backbone, is also metabolized by the gut flora to produce aloe Rhein anthrone, which has laxative effects [26]. The chemical constituents of guar are mainly amino acids, organic acids, terpenoids, plant sterols, flavonoids, alkaloids and nucleosides, lignans [27]. Studies have shown that guar is commonly used in the treatment of lung hot cough, phlegm turbid yellow and thick, and chest Bi heart pain and other syndromes [28]. The main components of amino acids in guar are glutamic acid, arginine, lysine, etc., and the amino acids are the main active substances in guar to exert phlegm effect. Aspartate can promote cellular immunity, thereby reducing secretions; Cysteine can make sputum viscosity lower and easy to expectorate [29]; Methionine can be converted into cysteine and cystine in vivo to achieve synergistic effects [30]. The components of organic acids are mainly butyric acid, succinic acid, hexanoic acid, etc., and their pharmacological effects mainly include anti-inflammatory, anti platelet aggregation, anti-oxidation and some other pharmacological effects; Terpenes have anti-inflammatory, anti-tumor effects [31]. The main components of plant sterols are α - Spinachsterol, stigmasterol, and β - Sitosterol, etc., phyosterols act by inhibiting the absorption of cholesterol, thereby reducing the concentration of cholesterol in the blood, which in turn plays a role in the treatment of diseases such as coronary heart disease, atherosclerosis, etc. [32]. The flavonoid components are mainly apigenin, luteolin, etc., whose pharmacological effects, in addition to anti-inflammatory, antiviral, antipyretic, have antioxidant, antitumor, anti-aging, improved microcirculation, hypoglycemic, etc. [33]. Alkaloids are effective constituents of many Chinese herbs, have strong physiological activity, are commonly used in the treatment of cardiovascular and cerebrovascular diseases, and also play an important role in anti-inflammatory, antiviral, antibacterial, anticancer, etc. [34]; Nucleoside composition is important for biological cells to maintain life, in which the main effects of adenosine are anticoagulant, analgesic, anti-inflammatory and dilated coronary arteries, and other effects [35]. Chemical composition studies of cholangiocarcinoma Cholanthopanax is produced by the combination of the fine powder of Cassia with cow, sheep, or pig bile that has been gunned and processed into a square or cylinder shape of brownish yellow, gray brown, or brown black [36], and the shelled cholanthopanax is less toxic than that of Tiannan [37], which is generally used to treat hot sputum cough [38]. Their chemical composition is relatively complex, most of the chemical components are derived from aspartic star with bile, and less new chemical components have been generated by gunning [39], and the components of biliary star mainly include amino acids, flavonoids, organic acids, alkaloids and nucleosides, phytosterols, bile acids, volatiles and newly generated glycosaminogenic components and their dehydrated products, sulfoglycoside components Lactic acid and its glycosides, butanedioic acid and its glycosides, free cholic acid and its glycosides, sulfonated cholic acid components, etc. [40]. Bile acid composition is mainly cholic acid, glycochenodeoxycholic acid, Hyodeoxycholic Acid, etc., bile acid composition is the main component of bile, and its pharmacological effects are mainly reflected in the strong inhibition of gram positive bacteria [41], in addition, in anti-inflammatory, antipyretic, analgesic and antitussive antiasthmatic effects [42]; Volatile substances mainly include limonene, octadecanal, n-octanol, styrene and so on, and their effects mainly include antioxidant, antitumor, anti-inflammatory, antibacterial and so on [43]. The main components of munnits are aqueous sodium sulfate with a small amount of inorganic salts, which can synergize the efficacy of Radix Dahuang Datong Fu under the attack. When oral administration of Mangxiao, because of the poor absorption of sulfate ions by the human intestinal wall, it leads to a poor concentration in the intestine and external production, hinders the absorption of water and so on in the intestine, causes mechanical irritation in the intestine, promotes intestinal peristalsis, and is conducive to defecation [44]. When used medically, Mangxiao should not be co fried with Fangzhong rhubarb, which would otherwise lead to decreased dissolution of anthraquinones components from rhubarb [45].

4. Mechanism of treatment of post-stroke pneumonia by xingshuchengqi Decoction in phlegm heat Fu solid type

4.1. Theory of traditional medicine

The physiological relationship between the lung and the large intestine is manifested in two aspects: air machine lifting and lifting, and the metabolism of dzu liquid: the lung master catharsizes the Suu drop in terms of air machine lifting, and its air moves down and travels to the large intestine, assisting the large intestine to conduct dross; Aspect of body fluid metabolism the lung acts as a source above the

water to carry the whole body of the body of the body, which exempts the large intestine from being subjected to water dampness, ensuring stool conduction and compliance. On the pathological relationship, if the lung is attacked by disease evil, which affects the function of naqing and drainage of the lung, Xuan Su disorders, lifting and lifting disadvantages, and lung qi cannot be reached, then Fu Qi will not work, drowsiness, and difficulty in stool expulsion; The large intestine uncleaved Fu Qi can obstruct the lung up and reverse, interfering with the physiological function of the lung, so that the patients experience symptoms such as cough, phlegm, asthma, and tightness. On conduction, the normal conduction of polyglutamine hinges on the lung and large intestine to play an important role, if the lung disease is not accompanied by an announcement, dysfunctional water channels are regulated, water and fluid metabolism is disordered, and excessive water dampness leads to cloacal flow. And loss of large intestine conduction, with turbid air smoked back on the lung, which in turn can cause or aggravate lung disease.

4.2. Modern medical research

It is believed that the close relationship between lung and intestine is due to the following morphological and structural basis: most of the parenchyma of organs of the respiratory and digestive systems are derived from the primitive digestive canal, while the epithelial tissues are derived and developed from the endoderm of the gastrula^[46], and the lung and intestine share the same origin in morphology and structure. Mucosal immune system: digestive tract and respiratory tract through the lymphatic system together constitute an important part of the common mucosal immune system in the human body, and different regional metastasis of immune response is achieved through mucosal immunity^[47]. Signaling pathways: at present, basic experimental studies have shown that there are numerous signaling pathways that are bidirectionally regulated between the lung and the large intestine. Zheng XURUI et al^[48] started with the extracellular signal regulated kinase (ERK) signaling pathway to explore the theory of "" lung and large intestine superficially "", and found that the increased level of ERK mRNA in the colon tissue was observed in the lung disease state, meanwhile, enteropathy could also promote the abnormal expression of ERK mRNA in the lung tissue.

5. Conclusion

In conclusion, stroke associated pneumonia is different from other common respiratory diseases, which are closely related to neurological impairment, with its own unique and complex physiopathological alterations. First line antimicrobial agents in western medicine, although effective in killing pathogenic bacteria, the use of drugs can also lead to increased pulmonary symptoms, increase recurrence rates, and affect prognosis. In recent years, the clinical experiments of traditional Chinese medicine for the treatment of this disease have made tremendous progress, and the use of integrated traditional Chinese and Western medicine treatment, multi-target, multi-directional and multi choice interventions, which can play a role of enhancing and attenuating, and play a mainstay in the process of clinical prevention and treatment of SAP. Currently, there are still some problems to be solved in SAP related research: 1. Most of the clinical studies are of low quality, have poor internal trueness, and lack multicenter, large sample clinical randomized controlled trials and basic research. 2. The diagnostic criteria of traditional Chinese medicine (TCM), syndrome differentiation and classification have not been fully unified, and there is a lack of further characteristic understanding. Therefore, in the future research of TCM, it is still necessary to further accumulate reliable clinical evidence, to strengthen the internal understanding of TCM on sap, to deepen the efficacy evaluation of Research Indicators on tested drugs, to fully exploit the potential of integrated traditional Chinese and Western medicine to treat sap, and thus to seek more general well-being for a wide range of patients.

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