

Theory and Application of Mufangji Decoction in the Treatment of Heart Failure

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Abstract

Heart failure (HF) is one of the common cardiovascular diseases in clinic, and its mortality rate and readmission rate are high, which is the difficulty and focus of current research. In recent years, the treatment based on syndrome differentiation of traditional Chinese medicine and multi-target treatment of traditional Chinese medicine have attracted researchers' attention and become a new breakthrough in the treatment of heart failure. Mufangji Decoction is the classic prescription for treating compartment Zhiyin. Clinical research shows that Mufangji Decoction and its modified prescriptions can significantly improve the clinical symptoms of patients with heart failure. Increasing EF value and decreasing BNP level have a positive effect on the treatment of heart failure. This paper summarizes the theoretical, experimental and clinical research progress of Mufangji Decoction in the treatment of heart failure, with a view to providing unique exploration ideas for the treatment of heart failure and benefiting the clinic.

Keywords

Mufangji Decoction, Heart Failure, Theoretical Research, Experimental Research, Clinical Research

Heart failure is one of the common cardiovascular diseases in clinic. It is a group of complex clinical syndromes caused by abnormal changes in cardiac structure and/or function caused by a variety of reasons, resulting in dysfunction of ventricular systolic and/or diastolic function. It is the end stage of various organic heart diseases. It has many basic diseases and complex pathogenesis, which is the difficulty of clinical treatment. With the deepening understanding of modern medicine and the continuous development of new drugs and new technologies, breakthrough progress has been made in the treatment of heart failure. However, the mortality and rehospitalization rate of heart failure are still high due to various reasons such as drug side effects, adverse reactions and patient compliance. It has brought a heavy burden to patients and the whole society [1]. In recent years, the multi-target treatment of traditional Chinese medicine has gradually attracted the attention of researchers. Clinically, the traditional Chinese medicine prescription or traditional Chinese medicine compound based on traditional Chinese medicine prescription in the treatment of heart failure is more and more widely used and effective.

Mufangji Decoction is contained in *synopsis of the Golden Chamber*. Zhongjing uses it to treat compartment Zhiyin. In recent years, it has been applied to the clinical treatment of heart failure and achieved good curative effect. This paper makes a comprehensive analysis on the theoretical research of traditional Chinese medicine, clinical efficacy observation and experimental research of Mufangji Decoction in recent years, and deeply discusses the theory and application of Mufangji Decoction in the treatment of heart failure, in order to better enrich the theory of classic prescriptions in the treatment of heart failure, expand the application of classic prescriptions in the treatment

of heart failure, and benefit the clinic.

1. Theoretical research on the treatment of heart failure with Mufangji Decoction

According to the clinical manifestations of heart failure (such as dyspnea, fluid retention, etc.), Chinese medicine believes that it can be classified into edema, asthma, chest obstruction and other categories, and the pathogenesis is related to deficiency, blood stasis and water, and the main feature is the mixture of deficiency and excess. With the development of the disease, different TCM syndromes can appear for dialectical treatment [2-4]. Mufangji Decoction is mainly used to treat compartment Zhiyin with mixed cold and heat deficiency and excess, and its clinical effect is positive. The literature records on the application of Mufangji Decoction in the treatment of heart failure have existed since ancient times which provide a reference for the current understanding of Mufangji Decoction syndrome and its treatment of heart failure.

Synopsis of the Golden Chamber contains: "Diaphragmatic branch drink, the patient developed chest tightness, shortness of breath, discomfort under the heart, dark complexion and the pulse is tight sink. Ten days later, the doctor failed to cure by inducing vomiting and catharsis, so he applied Mufangji Decoction." The main symptom of this prescription is consistent with heart failure. According to the modern interpretation, the compartment is the diaphragm. From the theory of Zang Xiang, it is adjacent to the five Zang and six Fu organs. According to the meridian theory, except the bladder meridian, the other eleven meridians follow the diaphragm [5]. Zhongjing's definition of Zhiyin is: Cough, shortness of breath, inability to lie flat, edema. Therefore, compartment Zhiyin describes the etiology and symptoms of the disease treated by Mufangji Decoction, suggesting that the disease treated by Mufangji Decoction is a disease of cough, shortness of breath, edema and inability to lie flat caused by multiple visceral diseases. When the patient is full of asthma, it indicates that the patient has chest tightness, shortness of breath and ruffian under the heart. Combined with the treatise on febrile diseases, it is understood that the epigastric fullness and discomfort, and the face is swarthy, which is the conclusion of traditional Chinese medicine. The five colors of traditional Chinese medicine have different main diseases. The color black often indicates the patient's kidney deficiency, cold coagulation, blood stasis and water stagnation, which is highly consistent with the pathogenesis of blood stasis and water stagnation in heart failure. To sum up, the disease treated by Mufangji Decoction is the clinical syndrome of chest tightness, shortness of breath, edema, inability to lie flat and black face. This is highly consistent with the clinical manifestations of pulmonary circulation, digestive system and peripheral circulation congestion caused by force failure in modern medical center. Therefore, the clinical syndrome of Mufangji Decoction can be treated with Mufangji Decoction as long as we grasp the main symptom of Mufangji Decoction and the pathogenesis of blood stasis and water retention.

Mufangji Decoction consists of fangji, Gypsum, cinnamon twig and ginseng. Fangji was first seen in Zhang Zhongjing's treatise on Febrile Diseases and *synopsis of the golden chamber*. Zhongjing often uses it to treat various edema, which is scattered in chapters such as phlegm drink, water Qi and stroke calendar Festival. For example, Fangji Huangqi Decoction is mainly used for treating feng shui with exterior deficiency and unconsolidation, Fangji Fuling Decoction is mainly used for treating pi shui with spleen deficiency, Jijiaoli Huang Pill mainly treats phlegm retention in gastrointestinal tract [6]. Fangji generally refers to the dry roots of Fangji family or Aristolochiaceae plants. Due to the renal damage of Aristolochiaceae Fangji, Fangji family Fangji is now used clinically, that is, Fangji wood and Fangji powder, which are the roots of Fangji family plants Fangji wood and Fangji powder respectively; its nature is bitter and cold. It can dispel wind, relieve pain, diuresis and detumescence. It can benefit water and detumescence in the prescription. cinnamon twig is the representative drug of Wenyang Huayin. It is pungent and warm. It can enter to the heart, lung and bladder meridians. It has the effects of sweating and relieving muscles, warming and dredging meridians, dispersing cold and relieving pain, helping yang to turn Qi, and calming and reducing Qi. It is compatible with self-defense and can use water to drink and disperse Qi to treat the ruffian under the heart. Ginseng is sweet and slightly cold. It has the effects of greatly tonifying vitality, restoring pulse and strengthening blood, generating fluid and nourishing blood, tonifying spleen and lungs, calming nerves and benefiting intelligence. *Shennong's herbal classic* says that taking it for a long time can lighten the body and prolong the year. It can greatly tonify the heart and lung vitality in this prescription, which can not only combine cinnamon twigs to replenish qi and warm yang, but also enhance the diuretic effect of self-defense; Gypsum tastes pungent and slightly cold. According to *Shennong's classic of Materia Medica Zhongpin* [7]: "the wind is cold and hot in the main body, and the heart is against Qi and asthma". It has the effects of clearing heat and water, eliminating annoyance and thirst. Its sexual sedimentation can calm the evil above and make the heat of cinnamon twigs.

To sum up, in Mufangjitang, fangji attacks chases the water to drink, ginseng greatly replenishes the vitality to

strengthen the health, Guizhi is pungent, dredges the heart Yang, melts Qi and water to control the upward rush of water and gas, gypsum relieves thirst and main asthma, and all drugs are used together to play the function of Tongyang dispersing drink, clearing heat and benefiting water.

2. Clinical study of Mufangji Decoction in the treatment of heart failure

In recent years, many doctors have made an in-depth exploration on the clinical efficacy of Mufangji Decoction and its modified compound in the treatment of heart failure. From the aspects of improving the efficacy, alleviating symptoms and improving a variety of relevant indicators, they have conducted a multi-directional study on the effectiveness and safety of Mufangji Decoction in the treatment of heart failure. The results show that Mufangji Decoction can effectively improve the clinical symptoms of palpitation, asthma, edema and oliguria in patients with heart failure. At the same time, Mufangji Decoction can also improve the common laboratory indexes of heart failure such as brain natriuretic peptide (BNP) and left ventricular ejection fraction (LVEF). In addition, compared with the control group treated with western medicine alone, the treatment group combined with Mufangji Decoction can shorten the length of hospital stay, reduce the incidence of adverse reactions and improve the quality of life of patients with heart failure.

Qian Jing [8] et al. studied the modified Mufangji Decoction in the treatment of patients with chronic congestive heart failure with Yang deficiency, blood stasis and water stagnation syndrome, and found that the modified Mufangji Decoction has good curative effect and safety, which can improve the EF value of patients, reduce the BNP level of patients, and improve the systolic and diastolic function of patients to a certain extent. Lu Weiya [7] observed that juanyingxin Decoction (mufangji decoction combined with Tingli Dazao xiefei Decoction) was used to treat patients with chronic left heart failure. It was found that the levels of serum NT-proBNP, GDF-15 and Ivper in the treatment group were decreased, and LVEF and Ivper were increased. It was considered that on the basis of routine treatment of chronic heart failure with western medicine, juanyingxin decoction combined with juanyingxin decoction was better than simple western medicine. Wu Jinfei [9] applied Mufangji Decoction combined with Zhenwu Decoction to treat chronic heart failure with deficiency of heart and kidney yang. He found that Mufangji Decoction combined with Zhenwu Decoction can not only improve its clinical efficacy, but also improve its EF value and BNP and shorten its hospitalization time. Lei linli [10] and others observed the efficacy of modified Mufangji Decoction in the treatment of acute attack of chronic heart failure and found that modified Mufangji Decoction can improve the systolic and diastolic function of patients and reduce the levels of NT proBNP, CysC and CA125. It has significant clinical therapeutic effect and high safety.

3. Experimental study on the treatment of heart failure with Mufangji Decoction

With the continuous development of modern science and technology, more progress has been made in the experimental research on the treatment of heart failure with Mufangji Decoction, mainly focusing on the pharmacological analysis of the components of Mufangji Decoction and its overall action mechanism [11].

Modern pharmacological studies show that ginsenoside and ginseng polysaccharide is the main chemical components of ginseng. Studies have shown that it can inhibit the activity of Na-K-ATPase through competitive binding with adrenergic receptor, slow down heart rate, enhance myocardial contractility and increase cardiac output [12]. Animal experiments also found that ginseng liquid can reduce the affinity of hemoglobin for oxygen, release more oxygen to tissues and increase the amount of oxygen free radicals, so as to protect myocardium [13]. Cinnamaldehyde and cinnamic acid are the effective components of Cinnamon Twig, which have the effects of diuresis, hypotension and vasodilation [14]. Tetrandrine is the alkaloid with the strongest activity of tetrandrine. Kong Xiaoxu et al found that it has the effects of inhibiting the proliferation and vasodilation of vascular smooth muscle cells, anti myocardial ischemia-reperfusion injury and anti arrhythmia, and plays an important role in cardiovascular diseases [15].

Xu Lin and others have proved through experiments that Mufangji Decoction can improve rat cardiac function, significantly increase cardiac SERCA2a content, increase EF value, reduce LVS value and reduce TNF- α . The concentrations of ET-1, ang II and IL-6 can reduce the end systolic diameter of left ventricle and improve systolic function. It is proposed that the mechanism of Mufangji Decoction in the treatment of heart failure may be related to improving the secretion of neurohumoral factors and inflammatory factors and inhibiting ventricular remodeling in rats with heart failure [16].

By studying the effect of Mufangji Decoction on right heart failure caused by pulmonary hypertension, Jiang Cen and others found that P and P/V decreased in varying degrees, while pa-at and pa-at/ET increased in varying

degrees in each dose group of Mufangji Decoction. The right heart function was improved, the levels of AngII, plasma BNP, re Nin and were significantly reduced, the degree of myocardial fiber injury and fibrosis were reduced, the number of cardiomyocyte apoptosis was reduced, and LXR was up-regulated α And down regulate NF KB and TNF- α Protein expression, indicating that Mufangji Decoction may pass through the nuclear receptor LXR α The regulated NF KB signaling pathway improves the cardiac function, reduces the level of neuroendocrine factors and reduces cardiomyocyte apoptosis in rats with right heart failure induced by monocrotaline induced pulmonary hypertension [17].

4. Thinking and Prospect

Mufangji Decoction is widely used in clinic, especially in the treatment of heart failure caused by a variety of heart diseases. Summarizing the theoretical interpretation of ancient and modern literature, it can be seen that clinically, as long as we grasp the main symptoms and pathogenesis characteristics, we can be as effective as drum. Clinical investigation and research found that the application of Mufangji Decoction or its modified compound based on this formula has a stable and satisfactory curative effect in the treatment of heart failure, which guides the direction for researchers and scholars of heart failure. The main mechanism of heart failure is related to the over activation of neuroendocrine system, myocardial injury, apoptosis and myocardial hypertrophy caused by a variety of cytokines including inflammatory factors and multiple signal pathways related to myocardial hypertrophy [18-20]. However, at present, the modern research mechanism and relevant targets of Mufangji Decoction in the treatment of heart failure still need to be supplemented. Therefore, taking the syndrome of Mufangji Decoction as the starting point, comprehensively using multi omics technologies such as network pharmacology and metabolomics, and comprehensively grasping, dynamically adjusting and accurately treating heart failure is our future research direction. It can also become a new direction of new drug research and development and clinical application of traditional Chinese medicine.

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