

Research Progress on Clinical Application of Huanglian Wendan Decoction

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Abstract: Huanglian Wendan Decoction has achieved satisfactory results in the treatment of multiple systemic diseases in clinical application, including digestive system diseases, cardiovascular system diseases, mental and nervous system diseases, metabolic diseases, etc.[1]. This prescription has the effect of clearing heat and phlegm, removing annoyance and stimulating gallbladder, and reconciling spleen and stomach, so it is mostly used for phlegm, dampness, depression and heat in the above system diseases. In clinical application, we should take syndrome differentiation and treatment as the core, start from the pathogenesis, grasp the essence of the disease, add and subtract with the syndrome, and use flexibly to reflect the idea of "treating different diseases together" in traditional Chinese medicine[2]. In this paper, the relevant literature of Huanglian Wendan Decoction was analyzed and summarized in combination with our own clinical experience, so as to provide beneficial reference for the subsequent development of clinical application of this decoction.

Huanglian Wendan Decoction was first recorded in Lu Tingzhen's "Six Reasons and Strips" in the Qing Dynasty. The ingredients of Huanglian Wendan decoction were Coptis Chinensis, Pinellia ternate, Poria cocos, Citri Reticulatae, Pericarpium Aurantii, Fructus, Bambusae Caulis in Taenias, radix glycyrrhizae preparata and Rhizoma Zingiberis Recens. It is derived from the decoction of Wen Dan contained in the Treatise on "Sanyin Ji Yi Bingzheng Fang Lun" by Chen Wuze in Song Dynasty[3](see Table 1). Wendan Decoction opens Yang and adds the pain of Coptis coptitis to reduce the reverse, which strengthens the efficacy of the original recipe in clearing heat, resolving phlegm, and regulating qi[4], and has an obvious effect on qi stagnation and phlegm generation, and the diseases caused by bile stagnation and phlegm disturbance[2]. In the square, coptis is the king, heat and fire, dryness and phlegm; Minister of pinellia, dryness, phlegm, and stomach ; two

medicines in combination, bitter drop. With tangerine peel for regulating qi stagnation, drying dampness and removing phlegm, and aurantium for reducing qi and guiding stagnation, eliminating phlegm and removing ruffian; two drugs combined effects, warm and cool together, enhance phlegm and qi. Remove heat and phlegm, in addition to annoyance and stop vomiting of bamboo shavings. The poria cocos with strengthening spleen and improving water, and the ginger with softening and softening stomach are the source of eliminating phlegm [5]. Take licorice as a medicine to reconcile the whole prescription. Comprehensive the whole prescription, Xinkai bitter drop, warm and cool, not cold and not dry, regulating qi and phlegm, spittoon treatment, and stomach and gallbladder, all kinds of diseases are removed (see Figure 1).

Table 1. The ingredients of Huanglian Wendan decoction

Ingredients	Sanyin Ji Yi Bingzheng Fang Lun	Six Reasons and Strips
Coptis Chinensis	×	√
Pinellia ternate	√	√
Poria cocos	√	√
Citri Reticulatae Pericarpium	√	√
Aurantii Fructus	√	√
Bambusae Caulis In Taenias	√	√
radix glycyrrhizae preparata	√	√
Rhizoma Zingiberis Recens	√	√
Ziziphus jujuba Mill.	√	×

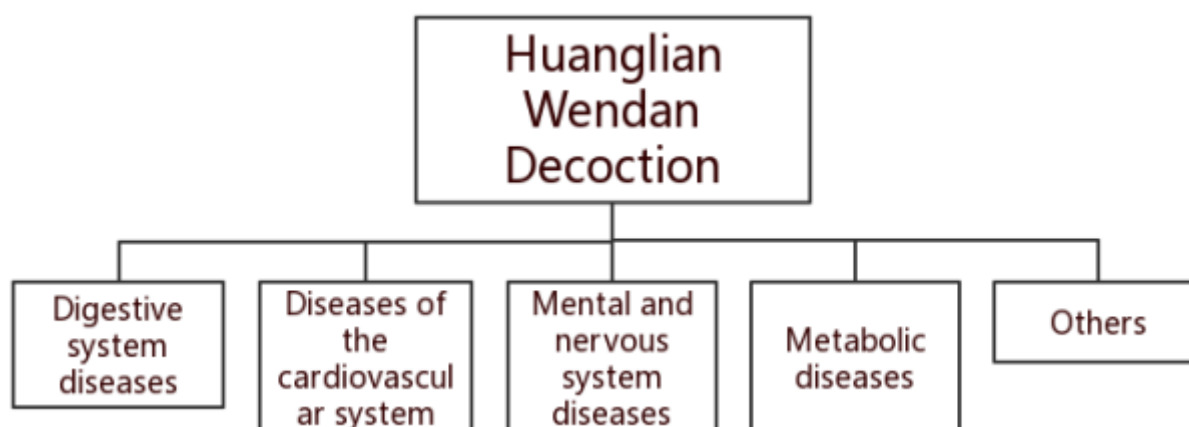


Figure 1. Multiple systemic diseases

1. Treatment of Digestive System Diseases

Huanglian Wendan Decoction is effective in the treatment of dampness and heat of spleen and stomach, bile stagnation, and phlegm-disturbed digestive system diseases. Diseases of the digestive system are mainly due to the spleen and stomach. The spleen and stomach in the middle of the coke, the main qi machine, rise and fall. If the spleen is out of circulation, the qi machine rises and falls,

Qi stagnation and Jin stop, depression and heat, and then produce sputum, damp heat and other pathological products. Dampness and heat trapped in the spleen and stomach, phlegm and heat cross the liver and gallbladder, resulting in liver loss, bile stagnation, liver and stomach discord, resulting in abdominal distension, diarrhea, constipation, jaundice, bitter and unpleasant mouth, even vomiting and a series of digestive symptoms[6](see Fig. 1). Professor Li Xian[7] believes that "phlegm dampness and depressurization of heat" is the root of digestive system diseases. According to Chai Lin[8], the fundamental method to treat internal injury of spleen and stomach is the method of Xinkai and bitter descent. Chen Guiguan[9] used Huanglian Wendan Decoction in the treatment of dampness-heat stomach ruffian disease of spleen and stomach, which can improve the serum MTL and GAS levels of patients, improve the gastrointestinal environment of patients, reduce the clinical symptoms of patients, and do not increase adverse reactions, with significant curative effect. Liu Wenyao[10] used Huanglian Wendan Decoction combined with Liujunzi decoction combined with western medicine to treat chronic atrophic gastritis with spleen deficiency and dampness heat, and found that this formula could well protect the gastric mucosa and promote the reversal and repair of gastric mucosa with atrophic intestinal degeneration. Zhang Zhipeng et al.[11] used Huanglian Wendan Decoction to treat liver cancer with phlegm and heat accumulation. They believed that the early liver cancer syndrome was mainly characterized by phlegm and heat accumulation. Therefore, the basic treatment principle was to relieve liver and qi, remove phlegm and heat, and eliminate phlegm and heat to balance and warm the bile. Professor Li Xian[7] has widely applied Huanglian Wendan Decoction to treat various digestive system diseases with phlegm dampness, and stagnation heat as the main pathogenesis, such as bile reflux gastritis, recurrent oral ulcer, fatty liver, etc., and achieved satisfactory therapeutic effects (see Figure 2).



Figure 2. A series of digestive symptoms

2. Diseases of the Cardiovascular System

The main pathological basis of cardiovascular disease is atherosclerosis[12](see Box 1), and its pathogenesis is mainly manifested by the syndrome of deficiency of heart and spleen, as well as kidney deficiency of different degrees, while the standard is blood stasis and phlegm turbidity. Coronary heart disease is a common cardiovascular disease in clinical practice[13]. He Junming[14] et al. found that Huanglian Wendan decoction in the treatment of stable angina pectoris syndrome of coronary heart disease belongs to phlegm and heart interaction, which can significantly improve the clinical efficacy, and play a certain role in the improvement of angina pectoris symptoms and blood lipids. The combination with conventional drugs can also further improve the clinical efficacy. Zheng Hong[15] used Huanglian Wendan Decoction to treat heart failure. He believed that heart failure was a syndrome of deficiency and deficiency, and the underlying pathogenesis was heart and pulse strength failure. However, solid pathogens such as phlegm, water, and blood stasis would appear in different stages of the development of the disease, so long as the basic pathogenesis of heart disturbance caused by phlegm and heat could be effective. Shen Zhengyan[16] found that the

addition and reduction of Huanglian Wendan decoction could effectively improve the clinical symptoms of patients with hypertension. Liu Li[17] et al. believed that intestinal microbiota could affect the occurrence and development of essential hypertension by inhibiting the release of inflammatory factors, repairing insulin signaling pathways, improving vascular endothelial function, inhibiting oxidative stress and vasculitis, inhibiting matrix metalloproteinases, and regulating the brain-gut-microecological axis. And Huanglian Wendan decoction can regulate blood pressure by improving intestinal flora. Zeng Ziling[18] believed that premature ventricular contractions belong to the category of "palpitations" in traditional Chinese medicine, and its pathogenesis can be divided into two aspects: deficiency and deficiency of qi, blood and Yin and Yang in the zang Fu organs; deficiency and deficiency of Yin and Yang in the reality are mainly caused by the evil spirits of water dampness and phlegm, blood stasis and fiery. Phlegm, heat, and stasis is one of the important pathogenesis of palpitation, which is common in clinical practice. The application of Huanglian Wendan decoction combined with Taohong Siwu decoction in the treatment of premature ventricular contractions of phlegm-heat stasis type can significantly improve the symptoms of palpitations, chest tightness, shortness of breath, chest pain, upset insomnia, timidity and easy panic, fatigue, abdominal distension, dry mouth and bitter mouth, and improve the clinical efficacy (see Figure 3).

Diseases of the cardiovascular system

- Coronary heart disease
 - Stable angina pectoris syndrome of coronary heart disease belongs to phlegm and heat interaction type
- Heart failure
 - Heart failure was a syndrome of deficiency and deficiency, and the underlying pathogenesis was heart and pulse strength failure
- Hypertension
 - Regulate blood pressure by improving intestinal flora.
- Premature ventricular contractions
 - Its pathogenesis can be divided into two aspects: deficiency and deficiency of qi, blood and Yin and Yang in the zang Fu organs; deficiency and deficiency of Yin and Yang in the reality are mainly caused by the evil spirits of water dampness and phlegm, blood stasis and fiery.

Figure 3. Diseases of the cardiovascular system's pathogenesis

3. Mental and Nervous System Diseases

Huanglian Wendan Decoction has a good curative effect on anxiety, depression, insomnia, dementia, stroke, and other mental and nervous system diseases(see Fig. 2). In recent years, the prevalence of depression has been increasing[19]. Liu Jianshe[20] believed that the disease was caused by the junction of phlegm, fire and stagnation in the heart, spleen, liver, and gallbladder, which affected Qi and caused diseases of the heart, spleen, liver and gallbladder. Its flexible use of Huanglian Wendan decoction to treat depression caused by various reasons, combined with psychological counseling, the effect is remarkable. According to Li Fengyun[21], depression syndrome can be divided into two types according to the condition, but patients often have the combination of deficiency and reality. The use of Huanglian Wendan decoction combined with acorus gladiolus can ease the liver, regulate qi and relieve depression, clear the heart, remove phlegm and annoyance, nourish the mind, calm the mind and open the mind, restore the functions of the zang-fu organs, regulate the Yin and Yang qi and blood of the zang-fu organs, and thus improve the clinical symptoms of patients. Zhang Dandan[22] started to treat anxiety neurosis in the elderly

from the "middle and positive gallbladder loss", believing that the disease was caused by abnormal function of the viscera, that is, disharmony between the gallbladder and stomach, internal disturbance of phlegm and heat, evil of shaoyang, stagnation of heat in liver and gallbladder, and disturbance of mind. The treatment was to clear the gallbladder and stomach, regulate qi, and reduce phlegm, and Huanglian Wendan Decoction was selected to increase and reduce the effect, which was satisfactory. Li Ling [23] believed that poststroke depression mainly belongs to the type of internal disturbance of phlegm and heat, and the traditional Chinese medicine treatment is mainly to clear heat and remove phlegm. The decoction of Huanglian Wendan can effectively improve patients' negative emotions and improve their sleep quality, spiritual quality, and quality of life. Cai Yanfei[24] et al. believe that for stroke patients in the recovery period, how to effectively improve their sleep quality and cognitive function is particularly important, and the application of Huanglian Wendan decoction combined with acupuncture in the recovery period of stroke patients with phlegm heat and fu-solid type is conducive to improving their sleep quality and promoting the recovery of cognitive function. Insomnia refers to a sleep disorder syndrome in which the quality of sleep cannot meet the physiological needs of individuals and thus affects the daily activities of patients[25]. Li Linlin[26] et al. believed that in the treatment of insomnia with internal disturbance of phlegm and heat, the method of clearing heat and removing phlegm and mediating calm mind should be taken, and the decoction of Huanglian Wendan should be added and reduced. The treatment effect is satisfactory, and the adverse reactions are less and the recurrence rate is low. Zhang Yonghua [27] thought in the treatment of insomnia should be "Yin and Yang, heavy modern, gu taste", on the medicine, pay attention to the interaction of qi, phlegm, lowering, therapeutic principles with phlegm heat is given priority to, complementary with tonifying qi and blood, yangxin nerves, party choose flavored huanglian wendan tang, can have anti-anxiety and calm, and coordination of brain, inhibition, Achieve sedative, hypnotic and neuroendocrine regulation. Zheng Wanli et al.[28] chose Huanglian Wendan decoction combined with acupuncture to treat vascular dementia, believing that this method could improve patients' psychological and intellectual status and cognitive impairment. Dou Jinjin et al.[29] found that adding or removing Huanglian Wendan decoction could improve learning and memory impairment in rats with vascular dementia. It has also been reported that Huanglian Wendan Decoction has been used in the treatment of autism, Tourette's disease, epilepsy[30], schizophrenia cardiac neurosis[31] and other psychiatric and nervous system diseases, with satisfactory results (see Figure 4).

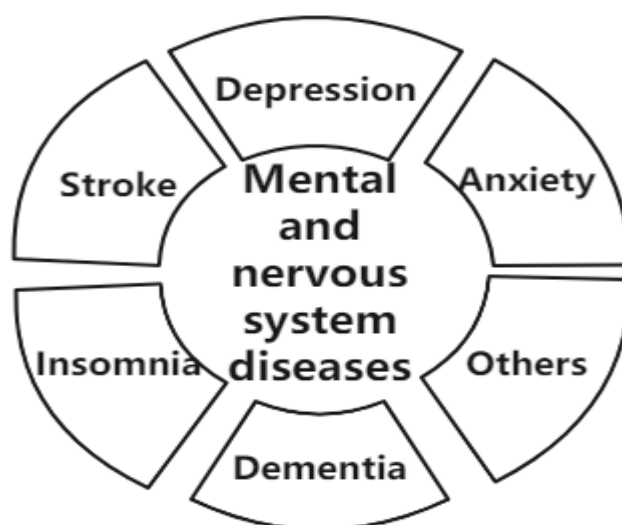


Figure 4. Mental and nervous system diseases

4. Metabolic Diseases

Li Yuting[1] et al. believed that the etiology and pathogenesis of metabolic diseases were Qi stagnation and phlegm coagulation, and blood stasis. Wang Tiefeng[32] et al. believe that metabolic syndrome can be understood as a state of fat, people with more phlegm, phlegm dampness, spleen dysfunction, and Wendan decoction and its modified recipe, as prescriptions for regulating qi and huatan, are widely used in the clinical treatment of metabolic syndrome. Ma Xiao[33] et al. used a modified Huanglian Wendan decoction to treat metabolic syndrome with phlegm dampness syndrome and found that it could improve the glucose and lipid metabolism function of patients and reduce the level of inflammatory factors. Liu Zijun[34] et al. found that serum containing Huanglian Wendan decoction could improve adipocyte insulin resistance of rat adipocytes through the phosphatidylinositol 3 kinase (PI3K) -glucose transporter 4(GLUT4) signaling pathway. Huang Xiuzhen[35] used Huanglian Wendan Decoction and Danzhi Xiaoyao powder to effectively treat type 2 diabetes mellitus complicated with generalized anxiety by soothing the liver and invigorating the spleen, removing heat and eliminating phlegm to achieve both symptoms and root causes.

5. Others

Professor Cao Zhengliu[36] thinks weak sperm with the basic pathogenesis is deficiency or kidney Yang, deficiency of kidney essence, and modern rhythms and ways of eating, living, working, easy to cause liver depression while fire, phlegm and hot, long yun of damp heat evil bet on renal damage of kidney Yin, phlegmy wet the evil viscous easily block/reduce sperm vitality, Therefore, phlegm, dampness, heat and depression are important pathogenic factors excluding deficiency of kidney essence qi and imbalance of Yin and Yang. For dampness-heat Qi stagnation of asthenospermia, the treatment should be to clear the dampness heat, soothing the liver and relieving the bile as the method, the recipe of Huanglian Wendan decoction, can clear the lower coke damp heat, but also can soothe the liver and relieving the bile, but also help the spleen and stomach transport water dampness, to achieve the purpose of the treatment of asthenospermia caused by dampness-heat Qi stagnation. In addition, Li Yanzhu et al.[37] used Huanglian Wendan Decoction to treat Meihe Qi, Tan Meidan et al. [31] used this recipe to treat biyuan and chronic cough, and Huang Hai used this recipe to treat ear canal occlusion, all of which achieved good curative effects.

Traditional Chinese medicine believes that "all diseases are caused by phlegm" and "strange diseases are treated with phlegm". Therefore, Huanglian Wendan decoction, which has the functions of clearing heat, promoting bile, regulating qi, and removing phlegm, has achieved satisfactory results in the treatment of multiple systemic diseases in the human body, and can effectively reduce the adverse reactions brought by western medicine and reduce the recurrence rate of diseases. However, THE clinical application should be based on the different physical constitution of the patient, the different symptoms, and the different pathogenesis of the disease, which fully reflects the idea of "different treatment of the same disease" and "different treatment of different diseases" in traditional Chinese medicine. Further research on Huanglian Wendan decoction is helpful to expand its clinical application scope and improve clinical efficacy. However, at present, there is still a lack of pharmacological research on this formula. It is necessary to further study the material basis, mechanism of action, metabolic law, target of action, dose-effect relationship, and other aspects of this formula, to provide a more objective scientific basis for clinical application. Thus will broaden the horizon of traditional Chinese medicine treatment, better play the clinical value of traditional Chinese medicine.

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Data Availability

No new data is used or generated.

Conflict of Interest

There is no conflict of interest between all authors.

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