

Research progress of modified Wendan Decoction in the treatment of insomnia

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Abstract: We call insomnia when the quality and quantity of sleep can not meet the needs of daily life. At present, western medicine is mostly used in the clinical treatment of insomnia, but western medicine is dependent, and withdrawal reaction is more likely to occur after withdrawal. Traditional Chinese medicine has a long history in treating insomnia. Traditional Chinese medicine has significant advantages in treating insomnia and its complications, less side effects and systemic conditioning, so as to prevent disease. Huanglian Wendan Decoction is a classic prescription for the treatment of insomnia. This paper discusses its research progress from the aspects of principles, methods, prescriptions, clinical research and treatment experience of Huanglian Wendan Decoction in the treatment of insomnia, so as to pave the way for the clinical treatment of insomnia.

1. Introduction

Insomnia means that when sleep conditions are available, most patients can not meet their physical and mental needs due to subjective anxiety, thoughtfulness, irritability and other emotions, and may lead to impairment of body function. A conference study in 2019 showed that the prevalence of insomnia symptoms or insomnia disorders in the world fluctuated between 4-50% [1]. Insomnia is a risk factor for cardiovascular and cerebrovascular diseases [2] [3]. Studies have shown that insomnia increases the risk of stroke and myocardial infarction. In severe cases, it makes people depressed, anxious and even suicidal; At the same time, the non-standard use of sleeping pills in chronic patients aggravates the sleep disorder [4].

The etiology and pathogenesis of sleep arousal are still under study. At present, the more recognized theory at home and abroad is neurobiological mechanism [5], and the future research direction will focus on the therapeutic targets for the treatment of sleep and awakening neurons as much as possible. The main means of treating insomnia include medication, physical therapy and psychotherapy. Western medicine treatment [6] can immediately alleviate the problem of insufficient sleep depth, aggravate insomnia and increase the risk of anxiety and depression after long-term use. Therefore, for insomnia patients with short course of disease and acute onset, the effect of sedative and sleeping pills is clear, while for patients with sleep disorders with longer course of disease, the effect of medication is not satisfactory, resulting in non-standard medication and frequent sleep disorders. Psychotherapy is one of the non drug treatment methods. Clinical research shows that [7] psychotherapy combined with traditional Chinese medicine decoction can improve the sleep

treatment of patients with anxiety and depression.

2. Theoretical study on the treatment of insomnia with Wendan Decoction

Insomnia is called insomnia in traditional Chinese medicine. Its core pathogenesis is visceral dysfunction, Yang does not enter Yin, and Yin and Yang lose communication. This paper mainly expounds phlegm heat internal disturbance insomnia. Feeling external evil or internal injury seven emotions leads to dysfunction of heart, liver and gallbladder, disturbance of mind and spirit, and Yang Qi floats outside. Emotional disorder or improper diet cause phlegm heat to disturb the clear orifices, the loss of the gods, the disturbance of courage, easy to wake up, easy to panic and so on. The gallbladder is based on the rise and development. The gallbladder belongs to Shaoyang, which is the hub for the rise and fall of the Qi machine. Therefore, the gallbladder can assist the operation of the Qi machine and generate Qi and blood. Under the control of the cardinal of danshaoyang, the Qi is protected by Lida table during the day to maintain the awakening state and daily activities of the human body. At night, the Qi can sleep only when it enters Yin from Yang. If the gallbladder axis is unfavorable and the Yin and yang are unbalanced, the Defensive Qi lurks inside during the day and floats outside at night, resulting in fatigue, irritability and abnormal sleep during the day. In addition, if you are brave enough to make a decision, you will have different thoughts and worries. From the physiological characteristics, bile Yin and bile Yang are used for each other 《The function of carrying bile in Waijing Weiyan is to store and excrete bile. Bile Qi is mainly excreted. The bile belongs to the six Fu organs. It transmits chemicals but does not store them. It is solid and dissatisfied. Therefore, only when Yang Qi rises sufficiently can it promote the settlement of Yin fluid, then the bile master decides that the physiological function is normal. From the pathological point of view, the gallbladder uses Yang Qi, likes to warm and dislikes cold, so the deficiency of gallbladder Yang is unable to relieve gallbladder Yin, and the bile fluid is formed by the accumulation of gallbladder Yin. It is cold and cold in nature, stored too much, and accumulated cold phlegm, which further consumes gallbladder Yang, stagnates Qi, floats Yang Qi, turns depression into fire, and disturbs the mind. Therefore, cholepathy can not regulate sleep, anxiety, impatience and other emotions 《Lingshu · obscenity and evil dreams says that the performance of timidity and dreaminess is to quarrel and fight with others, think more and worry more. Zhu Liangchun [8], a master of traditional Chinese medicine, proposed that insomnia is mostly seen in the syndrome of cold and phlegm heat in clinic. The treatment takes clearing heat, resolving phlegm and calming nerves as the method and Wendan Decoction as the cutting method, which has achieved many results.

3. Overview of prescription and syndrome research

The recipe of Wendan Decoction [9] is named Wendan. The liver and gallbladder are physiologically internal and external to each other, and the liver is the master of strategy, and the gallbladder is determined to reach the Qi machine together. Therefore, Wendan is mostly the meaning of dredging and benefiting the Qi machine. If Shaoyang has no rising Qi, stagnation of fire and internal knot, connecting with the liver, the soul will have no peace, and if it involves the stomach, it will be "restless". Wendan Decoction, a prescription, was first recorded in the important prescription for emergency. The prescription includes *Pinellia ternata*, *Fructus aurantii*, ginger, bamboo Ru, orange peel and licorice. It is recorded that "gall cold" is the main cause of asthenia and insomnia. *Pinellia ternata* and ginger are the highlights of the prescription. The theory of blood syndrome says that *Pinellia ternata* is "the most Xin reducing Qi", and the amount of ginger is the heaviest. Lantai criterion contains "blindly ginger and foot dispelling cold". The Xin temperature is divergent, raising the Yang Qi, combining the rise and fall of *Pinellia ternata* and bamboo Ru, smoothing the Qi

mechanism and harmonizing the Yin and Yang. Ginger and roasted licorice combine to make the Qi of Shaoyang rise; Poria cocos benefits water and dampness; Zhuru and Fructus aurantii reduce Qi, have no intention of cooling and restraining, reduce cold phlegm of gallbladder, lead deficiency Yang and float fire down; Pinellia ternata and orange peel can invigorate the spleen and stomach, dissolve phlegm and stomach to stop vomiting. Rhizoma Coptidis can clear the heart and stomach fire and stop vomiting. Zhuru and Fructus aurantii can reduce the adverse effect, but there is no disadvantage of cooling. It can not only reduce the cold phlegm of gallbladder, but also reduce the negative deficiency Yang floating fire. Huanglian Wendan Decoction is clinically applicable to young and middle-aged people to reconcile liver and stomach, smooth Qi and clear phlegm heat. The key pathogenesis is phlegm, heat and dampness. It mainly treats insomnia, upset, stomach ruff, dry mouth, bitter mouth, dizziness, anxiety and other diseases.

There is evidence to follow in the treatment of insomnia from the digestive system. Studies have shown that neurotransmitters are one of the important mechanisms for the treatment of arousal system. In addition, sleep related neuropeptides such as 5-HT, VIP and cholecystokinin are found not only in the brain, but also in the gastrointestinal tract. Some studies [10] believe that short chain fatty acids regulate the synthesis of 5-HT and improve gastrointestinal flora, so as to treat insomnia. Huanglian Wendan Decoction [11] can inhibit the expression of excitatory neurotransmitters, up regulate inhibitory neurotransmitters, prolong total sleep time and improve sleep efficiency. Pharmacological studies have found that the mechanism of Huanglian Wendan Decoction [12] in the treatment of sleep disorders is sedative, anti anxiety, inhibiting central muscle and reducing brain excitability; Pinellia ternata [13] reduces SOD activity in blood cells and no activity in vivo, inhibits lipid peroxidation to reduce the excitability of central nervous system and achieve sedative and hypnotic effect. The main active components of Coptis [14] are berberine, berberine and jatrorrhizine, which regulate the level of monoamine neurotransmitters in the brain. Poria cocos [15] improves difficulty in falling asleep and increases sleep duration. The effective component of Zhuru [16] is triterpenoids, which can improve sleep quality and memory.

4. Research status

4.1 Basic test research

Ma Boyan [17] and others randomly divided 28 mice into 4 groups: normal group, model group, Wendan Decoction group and diazepam group. After corresponding intervention measures were given respectively, the results showed that Wendan Decoction had an important regulatory effect on cholecystokinin 8 in subcortical and hypothalamus of insomnia rats, which showed the feasibility of treating insomnia from the digestive system. Zhang Hui [18] et al. Randomly divided 90 healthy mice into five groups: normal group, blank group, western medicine group and large, medium and small dose groups of traditional Chinese medicine. They were given corresponding intervention measures to measure the contents of c-fos and cjun in hippocampus of rats in each group. The research showed that the brain function was protected by inhibiting the expression of immediate early genes in brain tissue.

4.2 Clinical trial research

Cai Zhiguo [11] and others randomly divided 60 patients into control group and observation group, with 30 cases in each group. The observation group was treated with Huanglian Wendan Decoction, and the control group was treated with estazolam tablets to observe polysomnography. The therapeutic effect was 11.4 ± 3.2 in the treatment group and 7.2 ± 2.6 in the control group. Huanglian Wendan Decoction can improve the sleep time and sleep efficiency of EEG. Ding Hongyu [19]

randomly divided 90 patients with insomnia into observation group and control group with 45 cases in each group. The observation group was treated with Danzhi Xiaoyao decoction combined with Huanglian Wendan Decoction, and the control group was treated with zolpidem tablets 2mg / time for 4 weeks. The incidence of adverse reactions in the observation group was 8.9%, significantly lower than that in the control group 24.5%. Therefore, Huanglian Wendan Decoction Combined with Danzhi Xiaoyao Powder can improve the sleep quality of patients, the side effects of drugs are small. Jia Hui [20] and others randomly divided 62 patients with insomnia into control group and experimental group. The control group was given estazolam tablets. The experimental group was treated with Huanglian Wendan Decoction on the basis of conventional drugs. Pittsburgh sleep quality index was observed. After 4 weeks of treatment, Pittsburgh sleep quality index in the treatment group was 17.86 ± 2.56 and Pittsburgh sleep quality index in the control group was 14.53 ± 2.58 , the effect of the observation group on insomnia was better than that of the control group. Gong Xuequan [21] divided 80 patients with insomnia into two groups, with 40 cases in each group. The treatment group used Huanglian Wendan Decoction and the control group used zolpidem tablets. The total effective rate of the treatment group was 87.5%, which was greater than 60% of the control group. The curative effect of Huanglian

Wendan Decoction was significantly better than zolpidem tablets.

5. Clinical experience

Jing Yue Quan Shu expounds that external or internal injuries weaken the spleen and stomach, gather moisture and generate phlegm, block Qi and Qi, disturb the orifices, have many dreams, sleep is easy to wake up, and modern doctors often have the theory of treating insomnia from the spleen and stomach, with reliable results. Examples of practical cases:

Zhang, female, 43 years old, employee, first diagnosed on June 15, 2021. Chief complaint: insomnia for 5 years, aggravated for 1 month. The patient had poor sleep quality in the past 5 years. He took estazolam tablets orally for many times. He could sleep for 2-3H after taking 2 tablets every night, and his sleep improved slightly. After that, he took traditional Chinese medicine decoction for many times in the local clinic, and the symptoms were alleviated. Since then, the above symptoms have occurred many times, and insomnia is light and heavy. The patient is fat, easy to panic and fear, has a lot of thoughts, is upset and impatient, has a hard and dry mouth, has a sticky mouth, is dizzy, has a heavy head, has a bloated stomach, has poor appetite, is tired, has a dry stool and is difficult to solve. He will go on a four or five-day trip and adjust his urine. The tongue is red, the fur in the tongue is yellow, thick and greasy, and the number of pulse strings. It was diagnosed as insomnia (gallbladder deficiency and phlegm disturbance syndrome), which was treated by clearing heat and resolving phlegm, promoting Qi, nourishing blood and calming nerves, and modified by Huanglian Wendan Decoction and Suanzaoren Decoction. The specific decoction is as follows: Coptis chinensis, tangerine peel, Zhuru, Fructus aurantii, Pinellia ternata and Codonopsis pilosula 12g each, roasted licorice and Polygala tenuifolia 6G each, Poria cocos, sour jujube kernel and calcined keel 20g each, and North sorghum 30g. 7 doses, decoction, 1 dose per day, warm every morning and evening. Follow up visit on June 22. After taking the above medicine, the patient's sleep improved. Considering that the side effects of sleeping pills are large, the patient was reduced to 1 tablet and could sleep for 4 hours. The mood is still irritable, there is still stomach distention, dizziness is reduced, food intake is general, I wake up occasionally at night, there is yellow phlegm in the pharynx, it is easy to cough up, the stool is sticky and not smooth, urination is adjustable, the tongue is red, the moss is thin and yellow, and the pulse is fine and slippery. Considering that the patient is upset and impatient, strengthen the function of calming the mind and removing Qi and distension, add 14 doses of cauliflower 30g, radish 20g and Gansong 6G, and take the same method as above. Insomnia

symptoms improved after 3 weeks of medication.

According to: the characteristic of insomnia with gall disease is insomnia with anxiety and tension. The patient is always worried and easily frightened. The Qi of Shaoyang cannot rise. The gallbladder Yin is cool, the phlegm is turbid by itself, and the heat is gathered to clear the orifices. Combined with the tongue and pulse, the syndrome of phlegm heat internal disturbance is dialectical. The formula is based on Wendan Decoction to smooth the Qi machine, Huanglian to clear the heart and stomach fire, Suanzaoren and Chuanxiong to raise the gallbladder Yang, so as to make Polygala tenuifolia and reduce the phlegm of gall cold. Pinellia ternata and Zhuru rise and drop the ventilator, the keel is an important town of Fuyang, North sorghum rice and stomach calming nerves, as well as the patient's stomach distention and dry stool. Considering the adverse Qi mechanism, insufficient blood, nocturnal vine nourishing blood and calming nerves, semen Raphani and Glycyrrhiza can regulate the Qi mechanism of spleen and stomach, and improve the performance of loss of appetite.

6. Discussion

By searching the literature, it is found that the pharmacological research and theoretical basis of Huanglian Wendan Decoction in the treatment of insomnia are sufficient, and the basic test and clinical test research show that Huanglian Wendan Decoction has achieved good curative effect whether it is treated with traditional Chinese medicine alone or combined with other drugs. However, there are still some limitations: the basic experimental research literature of Huanglian Wendan Decoction in the treatment of insomnia is few, and there is a lack of research on the sedative and hypnotic components of specific drugs in Huanglian Wendan Decoction; There are few clinical trials, especially randomized controlled trials with sedatives and sleeping pills. There is insufficient clinical evidence on the clinical efficacy and adverse reaction rate of Huanglian Wendan Decoction in the treatment of insomnia; There is no latest research result on the mechanism of Huanglian Wendan Decoction in the treatment of insomnia. Taking "stomach disharmony leads to restlessness" as the theoretical basis of insomnia, clearing heat, resolving phlegm and calming nerves as the main treatment method, Huanglian Wendan Decoction as the main formula, and adding and subtracting drugs according to tongue and pulse, symptoms and patients' physique, so as to achieve three cause treatment with satisfactory effect, so as to provide reference for clinical treatment of sleep disorders.

7. Outlook

In conclusion, Huanglian Wendan Decoction has great development space in the study of clinical or biological mechanism in the treatment of sleep disorders. Therefore, we should conduct high-quality clinical and basic experimental research on the treatment of insomnia with Huanglian Wendan Decoction, and conduct comprehensive and systematic research on its effectiveness, safety, effective components and action mechanism, so as to timely update the medical records and clinical experience of Wendan Decoction in the treatment of insomnia, so as to provide treatment ideas for clinical treatment.

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