Clinical Research Progress of Chinese Medicine in the Treatment of Insomnia of Heart-Kidney Disorder

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Keywords: Insomnia, Heart and Kidney Disorder, Chinese Medicine Therapy, Review, Research Progress

Abstract: With the rapid development of modern society and the high pressure of people's work and life, the incidence of insomnia has increased significantly, which seriously affects people's physiological and psychological health. Studies have shown that modern medicine is effective in improving patients' insomnia symptoms in the short term, but there are adverse effects such as drug side effects and drug dependence, and patients do not benefit well in the long term. Chinese medicine has developed a rich theoretical system in its long-term struggle with insomnia, emphasizing the typical clinical manifestations of insomnia of the heart-kidney type, and has developed a unique treatment method with Chinese medicine characteristics based on the combination of disease identification and evidence identification, and many clinical trials have proved its efficacy and safety.

Insomnia is a disease characterized by long-term inability to obtain normal sleep or difficulty in falling asleep or maintaining sleep, or difficulty in sleeping deeply, and in severe cases, difficulty in sleeping through the night. Chinese medicine classifies insomnia as "sleeplessness", "eyes not closing", "restlessness", etc. It is classified by the four diagnoses of looking, smelling, inquiring and cutting, and is classified by clinical evidence of Chinese medicine. Insomnia Chinese Medicine Clinical Practice Guidelines¹ It is divided into nine types of symptoms, including liver stagnation and fire, phlegm-heat internal disturbance, yin deficiency and fire, loss of harmony of stomach qi, blood stasis and internal obstruction, heart fire, heart and spleen deficiency, heart and gallbladder qi deficiency, and heart and kidney non-interaction. Geng Hongjiao et al.² used a cross-sectional survey and retrospective analysis to conclude that the heart-kidney disjunction syndrome is the main type of insomnia, with a frequency of 49.3%. Studies in the literature³⁴ The literature and clinical observation also suggest that the heart-kidney disorder is more common in insomnia and has typical symptoms. Modern medicine mainly uses benzodiazepine receptor agonists or melatonin receptor agonists, antidepressants with sedative effect, etc.⁵ However, there are many adverse reactions such as drug side effects and drug dependence, and patients do not benefit well in the long term. The author summarized the effective clinical reports of Chinese medicine for the treatment of insomnia of the heart-kidney disorder in the past five years, aiming to provide a clinical basis for the identification and treatment of insomnia of the heart-kidney disorder in Chinese medicine.
1. Chinese Medicine Understanding of Insomnia of the Heart-Kidney Disorder

Zhang Zhongjing of the Han Dynasty pioneered the treatment of insomnia of the type of non-interaction between the heart and kidneys, and his treatise on Shao-Yin in the Treatise on Miscellaneous Diseases of Typhoid Fever explicitly stated that "Shao-Yin disease, the heart is troubled and cannot lie down, Huang Lian Agaricus Tang is the mainstay. It is based on Shaoyin (Hand Shaoyin Heart, Foot Shaoyin Kidney), nourishing Yin and lowering fire, which is a model for the treatment of insomnia of the heart-kidney type in later times. In the Song Dynasty, Yan Youhe first proposed the basic pathogenesis of insomnia in which the heart and kidneys do not intermingle, and discussed in Yan's Jisheng Fang that "thinking and thinking are sad, fatigue hurts the kidneys, the heart and kidneys do not intermingle, and the essence is not fixed... Dreaming and restlessness." In the Ming Dynasty, Xu Chunfu further elucidated the basic pathogenesis of insomnia in which the heart and kidneys are not intermingled - the kidney water is insufficient to help the heart fire, and the heart fire is hyperactive, and his book "The Complete Book of Ancient and Modern Medicine" states that "there are cases in which the heart yang is hyperactive because the kidney water is insufficient and the true yin does not rise... If the heart fire does not go down to the kidneys, and the heart and kidneys are out of sympathy, then the heart fire alone will disturb the mind and cause sleeplessness at night. This laid the foundation for the treatment of insomnia of the heart-kidney disorder in later generations. In the Qing Dynasty, Chen Shiduo once again enriched the understanding of the pathogenesis of insomnia of the heart-kidney disjunction type, and put forward the theoretical understanding that the kidney water is too cold and the heart fire is too hot, so that the heart and kidney do not intersect. The reason why the heart and kidneys do not intersect is that the heart is too hot and the kidneys are too cold... too cold, the water sinks to the bottom and does not intersect with the heart. In the Qing dynasty, "Medical recipe to identify difficult" discusses that "fear and fear hurt the kidney, the kidney energy is taken away by fear and the heart cannot be alone - the evidence of sleeplessness is like this" based on the view of the mutual use of the heart and kidney physiological state, the first time to put forward the understanding of emotional and mental factors leading to insomnia of the heart and kidney non-crossing type. In the Qing Dynasty, Zheng Shouquan expanded the understanding of insomnia of the type of non-intercourse between the heart and kidney, and believed that the deficiency of kidney yang could also lead to non-intercourse between the heart and kidney. Zhang Xichen, a famous doctor in recent times, proposed that the orderly rise and fall of the spleen and stomach qi is the key to the intersection of the heart and kidney, and the "Medical Heart and West" said that "the reason why the heart and kidney intersect is actually dependent on the up and down passage of the spleen and stomach qi." Thus, it can be seen that the dysfunction of the spleen and stomach, as the pivot point of qi lifting and lowering, is another important pathogenesis of heart-kidney non-interaction insomnia. While inheriting the ancient academic experience, contemporary medical practitioners have advanced the understanding of insomnia of the heart-kidney disorder. The Second National Medical Master Wang Qi[6] The second National Medical Master, Wang Qi, built a clinical thinking model of Chinese medicine that combines body discernment - disease discernment - evidence discernment, and creatively combined Chinese medicine evidence discernment with the doctrine of body constitution to understand insomnia of the heart-kidney disorder, emphasizing the significant correlation between special body constitution and insomnia type. The Third National Medical Master Zhang Zhiyuan[7] Using the concept of Kan-water and Li-fire in the I Ching to describe the physiological relationship between the heart and kidney, he believes that the main axis of insomnia is the lack of intercourse between the heart and kidney, and clearly puts forward the symptom characteristics of insomnia in which the heart and kidney do not intercourse[8] (1) red tongue and dry mouth without great thirst for drinks; (2) restlessness, restlessness at night, short sleep, and difficulty in falling
asleep; (3) heat symptoms, with no dryness in the stool and no shortage of urine. The Fourth National Medical Master Wang Qingguo[9] Emphasizing the specificity of identifying and treating different main symptoms of insomnia, and using difficulty in falling asleep as the outline of the typological treatment, he divided the insomnia of the heart and kidney disorder into two types: (i) the loss of harmony between the yin and yang of water and fire; and (ii) the loss of smoothness of both water and fire. In summary, Chinese medicine has gradually enriched the understanding of insomnia of the heart-kidney disjunction type, and each generation has played its own role. The overall understanding of insomnia of the heart-kidney disjunction type is based on the deficiency of kidney water, the hyperactivity of heart fire and the disjunction of heart and kidney as the key pathogenesis of insomnia of the heart-kidney disjunction type. Chinese medicine emphasizes the holistic concept, and the normal functioning of the heart and kidneys is based on the coordination of the five organs and the harmonization of qi and blood. If the balance between heart and kidney is disrupted by various factors and the heart and kidney are out of sync, insomnia of the heart and kidney type will occur.

2. Traditional Chinese Medicine Internal Treatment

Chinese medicine internal treatment method for insomnia of the heart-kidney disorder is mainly based on the theory of internal organs. Under the physiological state, the heart is located on the top, endowed with the warmth of the five elements of fire, and the kidney is located on the bottom, with the moistening of the five elements of water, the heart yang is drawn down to the kidney by the heart yin, so that the kidney water is not cold, and the kidney yin is steamed up to the heart by the kidney yang, so that the heart yang is not hyperactive. The heart-kidney intersects with each other, and water and fire help each other, so that the gods can sleep peacefully. Based on the clear identification of the many causes of heart-kidney disorders - kidney-water deficiency and hyperactivity of heart-yang - the clinical practice is to use the biased nature of prescriptions and medicines to intermingle heart and kidney in order to achieve peaceful sleep at night. Su Wenli et al.[10] Based on the theory that insulin is related to the abnormal activity of transmitters[11] A randomized controlled clinical trial found that Liu Wei Di Huang Tang combined with Jiaotai Wan plus reduction (Shu Di Huang 20 g, Shan Yao 15 g, Shan Yu Fei 15 g, Ze Di 12 g, Fu Ling 12 g, Mudan Pi 12 g, Zao Zao Ren 20 g, Zhi Mu 12 g, Huang Lian 6 g, and Cinnamon (later) 4 g) can significantly enhance the levels of GABA and 5-HT transmitters in the body, exerting the effects of nourishing the liver and kidney, co-operating with water and fire, and tranquillizing the heart and calming the mind. It is effective for insomnia of the heart-kidney disorder. Wang Jing[12] Based on the theory that sleep is related to inflammatory factors and oxidative stress, Wang Jing et al.[13][14] The mechanism may be related to the inhibition of serum TNF-α and IL-6 levels and the improvement of the body's antioxidant capacity. Yan Xueli et al.[15] (15 g each of angelica, calamus and dragon bone, 10 g each of tortoise shell, maidenhair, menthol, raw earth, and farcical, 6 g each of Huanglian tablet and Aconite) has the efficacy of nourishing Yin and nourishing blood, tonifying the kidney and tranquilizing the heart, educating and calming the mind, and the efficiency of treating insomnia of the heart and kidney type (89.6%) was significantly higher than that of the control group taking eszopiclone orally (71.1%), and the incidence of adverse effects was low. The incidence of adverse effects was low. The mechanism may be related to the regulation of monoamine neurotransmitter levels in the body. Wang Taiyong et al.[16] It is believed that the key pathogenesis of insomnia of the heart-kidney disorder lies in the deficiency of kidney yin and hyperactivity of heart fire. By nourishing Yin and clearing heat, nourishing the heart and tranquilizing the mind, and communicating with the heart and kidney, the effective rate (89.5%) in the treatment of insomnia of the heart-kidney disorder was better than that of the control group
taking alprazolam orally (73.7%), and the adverse effects were less.

3. Traditional Chinese Medicine External Treatment

The external treatment of Chinese medicine for insomnia of the heart-kidney type is mainly based on the meridian theory (traditional meridian theory - meridian, meridian tendon and skin, modern meridian theory - neural theory, biological holography). The meridians are the channels for running qi and blood, linking the internal organs with the body surface and various parts of the body. The human body is connected to the internal organs, limbs and bones through the meridians to accomplish various physiological activities together, among which sleep is an important physiological activity. Insomnia of the heart-kidney type involves related meridians including the Heart meridian of Shaoyin, the Kidney meridian of Shaoyin, the Bladder meridian of the Sun, the Governor meridian, the Ren meridian, and the Yin-Yang Stilt meridian, etc. Most of the clinical evidence is also taken from the above meridian points to unblock the meridians to traffic the heart and kidney. He Xiuwen et al.[17] Through clinical research, we found that the efficacy of auricular acupressure pills (taking the points of heart, kidney, Shenmen, and sympathetic) combined with Chinese herbal compresses (Huang Lian 6 g, Cinnamon 3 g, Nightshade 3 g, Huxiang Pi 3 g, and mother of pearl 6 g powdered on bilateral Neiguan, Shenmen, Sanyinjiao, and Yongquan points) in treating insomnia of the heart-kidney disjunction type (88.89%) was significantly better than that of the control group with conventional Western medicine (eszopiclone 1 mg + alprazolam tablets 0.4 mg) with a high safety rate (66.67%). Li Xinwei et al.[18] Based on the umbilical holographic theory[19] The clinical study found that the efficiency of body acupuncture combined with umbilical acupuncture in treating insomnia of the heart-kidney disorder was higher (96.4%) than that of body acupuncture alone (Baihui, Sishencong, Shenmen, Sanyinjiao, Xin Yu, Kidney Yu and Zhaohai) (78.6%) and umbilical acupuncture alone (Kan position and Li position, refer to the 2016 edition of "Introduction to umbilical acupuncture" edited by Qi Yong) (92.9%), and more advantageous in short-term improvement of difficulty in falling asleep, sleep duration, and daytime dysfunction. Liu Bo et al.[21] Based on the advantages of shallow acupuncture and high safety, Liu Bo et al.[22] (98.18%) was significantly higher than the efficiency (70.91%) of the needle acupuncture group (the same acupuncture points as the lift acupuncture group), and it could effectively reduce patients' negative emotions such as anxiety and depression. The effective rate was 98.18% higher than that of the acupuncture group (70.91%). Lu Meijing et al.[23] found that the eight acupuncture points of the Spiritual Turtle Method (according to the quick checklist of the eight acupuncture points of the Spiritual Turtle Method)[24] The efficacy of acupuncture is better than that of acupuncture (Yin Tang, Si Shen Cong, An Men, Shen Men, Zhao Hai, Shen Wu, Tai Xi) in treating sleeplessness of the heart-kidney type with bird pecking moxibustion on the foot three li. It is more effective in promoting melatonin secretion, relieving patients' tension and anxiety and depression, shortening sleep time and increasing sleep duration. Fang Zefia et al.[25] Through clinical research, we found that the use of balanced fire cupping on top of general treatment[26] The efficacy of combining qi jiao moxibustion with general treatment for insomnia of the heart-kidney type (91.43%) was significantly better than that of the control group (65.71%). Lin Qinye et al.[27] Based on the treatment principle of tranquilizing the mind and tranquilizing the heart and transporting the heart and kidney, the clinical study found that the efficacy of applying the formula of tranquilizing the umbilical cord (Huang Lian, Wu Zhu Yu, Bing Pian, and Cinnamon) combined with massage at Shen Que point in the treatment of insomnia with non-interaction of the heart and kidney was higher (97.44%) than that of the control group with western medicine alone (82.05%), and the operation was simple, less irritating, safe, and easily accepted by patients. It is easy to accept. Yang Wei et al.[28] Through clinical research, it was found that the combination of
conventional treatment (glutamatergic tablets 20mg+sulepine 2mg) with internal organ massage (Yin Tang, Shenting, Qingming, Baihui, Fengchi, Zanzhu, Sun, Shoulder Well, Xin Yu, Kidney Yu, Zhonggu, Qihai, Guan Yuan points; using the methods of one-finger meditation pushing, finger pressing and kneading, holding, palm pressing, and kneading) and umbilical acupuncture (Kan position and Li position) was effective. The efficacy (93.02%) of treating insomnia in the heart and kidney was significantly better than that of conventional treatment in the control group, and the safety was better. (76.74%)

4. Combination of Internal and External Treatment in Chinese Medicine

Traditional Chinese medicine has always emphasized the holistic concept.

In the treatment of insomnia of the heart-kidney disorder type, the theory of internal organs is combined with the theory of meridians, and the synergistic effect is brought into play through the combination of internal and external treatment of Chinese medicine, which greatly improves the clinical efficacy of Chinese medicine. Qin Rui[29] et al. found through clinical trials that the use of Huang Lian Sheng Di Tang under the guidance of the "state target combination" theory[30] The efficacy of Huang Lian Sheng Di Tang (Huang Lian 12 g, Sheng Di Huang 15 g, Zao Zao Ren 30 g, Calcined Dragon Bone 30 g, Calcined Oyster 30 g, Sheng Bai Shao 12 g, Chen Pi 12 g, Dry Ginger 6 g) combined with ear acupressing dou was significantly higher (97.1%) than the efficacy of oral dextrazopiclone tablets (69.7%) in the control group under the guidance of the "combination of state and target" theory for insomnia with heart and kidney disorders, and the one-month relapse rate was low.

Sun Xiaoyuan et al.[31] In a clinical study, we found that the treatment of heart-kidney recurrence insomnia with the addition of lily of the valley soup (lily of the valley 25 g, heshou wu 25 g, roasted turtle board 25 g, sour dates 15 g, astragalus 15 g, rhemannia 15 g, keel bone 15 g, angelica 10 g, cypress seeds 10 g, fengshui 10 g, chenpi 6 g, dong quai zi 10 g, danshen 20 g, wu wei zi 6 g, magnet 20 g, mai dong 15 g) with magnetic bead pressure ear points (91.67%) was not different from that of the control group with oral eszolam tablets (90.0%). There was no significant difference in the efficacy of the treatment of insomnia of non-crossing type (91.67%) and the efficacy of oral eszopiclone tablets in the control group (90.00%), but the relapse rate in the treatment group (11.11%) was significantly lower than that in the control group (68.75%) after one month. The efficacy was significant, the recurrence rate was low, and the standard was balanced, so it is worth to be promoted in clinical practice. Zheng Ning et al.[32] The efficacy of scalp acupuncture in treating insomnia of the heart-kidney disorder (91.18%) was significantly higher than that of oral estradiol tablets (67.65%). Chen Qianqian et al.[33] found that the efficacy of the combination of up and down Liangji Dan (Shu Di Huang 30 g, Atractylodes Macrocephala and Ginseng 15 g each, Cornu Cervi Pantotrichium 9 g, Huang Lian 6 g, and Cinnamon 3 g) with transcranial magnetic stimulation was better than that of single transcranial magnetic stimulation in the control group (76.60%) in the treatment of chronic insomnia in the elderly with heart and kidney disjunction. The basic pathogenesis of insomnia in which the heart and kidneys are not intermingled is that the kidney water is insufficient and the kidney water cannot help the heart, and the heart fire is so hot that it cannot be intermingled with the kidneys. The clinical study found that the efficacy of Jiaotai formula (taking the points of Kidney Yu, Heart Yu, Sanyinjiao and Xingma) combined with Qingxin Anshin Tang (Chinese medicine granules, Sichuan New Green Pharmaceutical Technology Development Co., Ltd., formula composition: Shu Di Huang 20 g, Huang Lian 10 g, Sour Jujube Ren 20 g, Dragon Bone 20 g, etc.) in the treatment of insomnia of the heart-kidney disjunction type (97.06%) was better than the efficacy of Qingxin Anshin Tang in control group A (76.47%). The efficacy of Jiaotai formula (82.35%) was better than the efficacy of
Qing Xin An Shen Tang (76.47%) and Jiaotai formula (82.35%) in group A. The efficacy of Jiaotai formula was related to the increase of serum 5-HT level and decrease of serum NE level.

5. Discussion

To sum up, Chinese medicine has combined the identification of disease and evidence in the long-term treatment of insomnia of the heart-kidney disorder, forming the unique internal and external treatment methods with Chinese medicine characteristics. Many clinical studies have also proved its efficacy and safety. However, less clinical research has been done on how to standardize the treatment of insomnia of the heart-kidney disorder in a safer, more efficient and systematic clinical treatment plan. With the development of the times, the proportion of patients with insomnia of the heart-kidney disorder has increased, and the traditional one-person, individualized treatment model of traditional Chinese medicine cannot meet the needs of the majority of clinical patients, so it is significant to standardize the clinical guidelines of Chinese medicine for this disease. Different treatment modalities have enriched TCM theories from multiple perspectives, but in the clinical process, it is easy to stick to one end of the spectrum, and the lack of research on the commonality of different theories is not conducive to theoretical breakthroughs. Therefore, the author believes that standardizing the clinical guidelines of TCM for a certain disease type, summarizing the understanding of different physicians for the same disease, and exploring the commonality of theories should be the direction of clinical research in TCM in the future.

References


