

Research progress on hot flashes and insomnia in perimenopausal women

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Keywords: Perimenopausal insomnia, hot flushes, etiology and pathogenesis; Syndrome differentiation and treatment

Abstract: Insomnia caused by hot flashes can seriously affect the normal life and work of perimenopausal women, and it is easy to cause a variety of complications. How to prevent and treat insomnia related to hot flushes has become the focus of medical researchers. This paper combs the ancient medical books on the etiology, pathogenesis and treatment of insomnia caused by hot flashes in women during perimenopause, and summarizes the difference between deficiency and excess in the disease nature. In the pathogenesis, deficiency is often due to the deficiency of yin and blood, the Yin does not converge the Yang, and the Yang heat disturbs, so the Yang floats and moves and sleeps restlessly. Excess syndrome often turns into heat due to blood stasis, dry excrement and dampness, which disturbs the sleep and makes it difficult to sleep at night. In terms of treatment, according to different pathogenesis, methods such as nourishing yin and reducing fire, nourishing blood and clearing heat, regulating Ying and Wei, activating blood circulation and removing blood stasis, dredging the bowels and discharging heat, clearing heat and dampness, and calming the nerves and calming the mind are adopted.

Perimenopause refers to the period before and after menopause in women (around 45 years old to 1 year after menopause), during which a series of symptoms such as menstrual disorders, bone and joint pain, hot flashes and night sweats, and insomnia may occur due to the decline of ovarian function. Tidal fever refers to a fever with a certain temporal pattern, which occurs at a fixed time or increases in heat intensity on time. It is a very common symptom during the perimenopausal period and can start a few years before menopause, with a median duration of 7.4 years^[1]. Research has shown that hot flashes occur most frequently at night and are significantly associated with insomnia^[2]. They can lead to symptoms such as difficulty falling asleep, increased frequency of nocturnal awakening, early morning awakening, and difficulty falling asleep after waking up. Perimenopausal women not only face significant physiological and psychological changes, but also bear the dual burden of work and family^[3]. Prolonged hot flashes leading to insomnia can exacerbate daytime

fatigue, memory decline, emotional loss, etc., which in turn affects women's work performance, interpersonal relationships, and increases the risk of cardiovascular and cerebrovascular diseases ^[4] and bone loss ^[5]. At present, hormone replacement therapy (HRT) and sedative hypnotics are commonly used in western medicine to treat this disease, but long-term use of hormone will increase the risk of breast cancer and ovarian cancer ^[6], while long-term use of hypnotics is prone to drug dependence, leading to addiction, drug resistance, rebound insomnia, daytime activity disorders and a series of adverse reactions. Insomnia caused by perimenopausal hot flashes belongs to the categories of "premenopausal and perimenopausal symptoms", "internal injury fever", and "insomnia" in traditional Chinese medicine. Traditional Chinese medicine has a long history and unique characteristics in treating this disease, with many advantages such as high safety, definite therapeutic effect, and long-lasting effect, and has good application prospects. The following is a review of the etiology, pathogenesis, and medical treatment of insomnia in perimenopausal women related to hot flashes.

1. Etiology and pathogenesis

The etiology of this disease is mostly due to the deficiency of yin and yang in the body, congenital depression, or overthinking, often with chronic illnesses, and influenced by changes in family, social, and other environmental factors. The pathogenesis of the deficiency syndrome of this disease is in the seventh or seventh year, with the gradual depletion of Tiangui, the essence and qi in the kidney moving from fullness to deficiency, the deficiency and decline of the Chong and Ren meridians, the disharmony of qi and blood, the imbalance of camp and defense, the deficiency of yin and yang, the disturbance of yang heat, and the fluctuation of yang during hot flashes, causing restlessness in sleep at night; The pathological mechanism of empirical evidence is blood stasis, dampness suppression, and dryness and fecal stagnation leading to heat transformation, with intermittent hot flashes, heat disturbing the mind, and difficulty sleeping. This disease often involves a mixture of deficiency and excess. When seeking the cause based on syndrome differentiation, the treatment should adjust yin and yang, harmonize qi and blood, and supplement deficiency and reduce excess.

1.1 Yin Yang imbalance

Yin deficiency Zhang Nianshun ^[7] believes that Yin deficiency often leads to hot flashes at night, which is closely related to the rhythm of the rise and fall of the human body's day and night qi. Yin deficiency presents a relative yang prosperity, with yang winning leading to heat. In the evening, yang qi converges and falls into the body. Yin does not contain Yang, it will cause yang to move and heat up, making it difficult to sleep at night. Guo Weiqin ^[8] believed that this disease should distinguish between deficiency and excess, as well as the organs and determine why the organs are yin deficient. This viewpoint was recognized by Deng Ying ^[9], who believed that the treatment of insomnia caused by yin deficiency and hot flashes should be based on kidney yin deficiency. However, Tang Jun ^[10] believed that the liver and kidney should be equally important in this disease. Due to the homology of the liver and kidney, the essence and blood should be mutually transformed, and yin and yang should be mutually supplied. Ling Jiayan ^[11] believed that the disease of hot flashes and insomnia is located in the heart, where the heart governs the mind and is coordinated with the kidney's water and fire. If the kidney's water is deficient in the lower part and cannot regulate the heart's fire, and the heart's fire is excessive in the upper part and cannot regulate the kidney's water, then the water and fire are separated, the heart and kidney are not in harmony, and Yin Yang disharmony. If you sleep restlessly at night and you will lack energy during the day.

1.2 Dissonance of Qi and Blood

1.2.1 Blood Deficiency

Wei Xiangling ^[12] believes that excessive worry during menopause can consume heart and spleen energy, and lead to passive Qi and blood biochemistry. If blood does not nourish the heart, it can cause blood deficiency, hot flashes, and insomnia.

1.2.2 Disharmony between Ying Qi and Wei Qi

Cui Zhenbo ^[13] believe that the Wei Qi circulates in Yang during the day and enters Ying Yin at night. The two must be coordinated and orderly to maintain normal body temperature, causing "Good sleep at night and sufficient energy during the day". However, if the Ying and Wei is disharmonious and the Ying Qi is deficient inside, the Wei Qi will become excessive outside, and if the Yang is not strong enough, it will cause hot sweating and heat disturbance insomnia. This viewpoint is consistent with the understanding of Wang Jiawei ^[14], who also believes that abnormal sensations such as hot flashes on the skin during perimenopause can be caused by disharmony between Ying Qi and Wei Qi

1.3 Blockage of tangible objects

1.3.1 Blood stasis

Gao Zhi ^[15] pointed out that blood stasis is an important cause of intractable insomnia. It is the blood stasis in the pulse that blocks the yin-yang communication between Ying and Wei. After a long time, blood stasis turns into heat, heat disturbs the mind, and it is difficult to sleep. Fushuping ^[16] believes that the menopausal period is characterized by the lack of kidney essence, the deficiency of kidney yin, and the deficiency of fluid and blood metaplasia, which leads to fluid dryness and blood dryness, astringency and stagnation, resulting in blood stasis and hot flushes, and therefore insomnia.

1.3.2 Dry feces

Bu Huanyu ^[17] pointed if the Qi mechanism is obstructed by tangible solid evil and dry feces, the Qi stagnation will transform into heat, resulting in a high fever and high heat intensity, forcing the fluid to leak out, and visible sweating. Sweat can take away some of the hot flashes, and the fever is slightly relieved. However, due to the presence of dry feces caused by internal resistance, stagnation fever will occur again, leading to fluctuations in heat intensity, continuous circulation, and the generation of hot flashes, which can disturb the mind and cause restless sleep.

1.3.3 Damp heat

Chinese medicine master Wu Caibing ^[18] believed that the hot flash caused by the spread of dampness and evil in the Three Jiao system, which obstructed the expansion of Yang Qi and caused prolonged stagnation and heat. The positive energy was sometimes encouraged, leading to the appearance of dampness and heat, which disturbed the mind and caused restlessness in sleep.

2. Differential diagnosis and treatment

2.1 Adjusting Yin and Yang

Liu Ruifen ^[19] chose the formula Zhibai Dihuang Pill to treat hot flashes mainly caused by kidney yin deficiency and liver yang hyperactivity. For those with lower abdominal cold sensation and yin

loss and yang, a small amount of kidney warming and yang boosting drugs, Xianling Spleen, and radix dipsaci were added.

This formula has been clinically proven to be effective and effective.

Tang Jun ^[10] believes that perimenopausal women with hot flashes and insomnia are more common due to liver and kidney deficiency. He has developed a self-formulated Zishui Bagan Tang, which has a total effective rate of 85.3% (29/34) in clinical trials. The PSQI score, improved Kupperman score, traditional Chinese medicine syndrome score, and SAS score all show that it can improve patients' insomnia, hot flashes and sweating, while also improving anxiety and depression to a certain extent.

Zhong Guanghua ^[20] aimed at the characteristics of liver and kidney yin deficiency type, which is prone to depression and heat. He used Danzhi Xiaoyao Powder to transform and modify his own Zishui Qinggan Drink, nourishing the liver and kidney, soothing the liver and clearing heat. Clinical trials showed significant advantages in eliminating perimenopausal hot flashes. Among 108 clinical trials, 43 cases showed significant effects, 61 cases were effective, and 4 cases were ineffective, with an effective rate of 96.29%.

Ling Jiayan ^[11] selected the modified Huanglian ass hide glue Decoction for hot flashes and insomnia caused by heart kidney disjunction. After 40 clinical trials, 37 cases were proved effective, 3 cases were ineffective, and the total effective rate was 92.5%, successfully improving the objective sleep quality and hot flashes of perimenopausal women.

2.2 Harmony of Qi and Blood

2.2.1 Nourishing blood

Wei Xiangling et al. ^[12] believe that insufficient heart and spleen can cause blood deficiency, fever, restlessness, and insomnia. Therefore, the appropriate formula is Guipi Tang. Clinical research results show that the total effective rate of this formula is 91.5%, with 25 cases cured, 18 cases effective, and 4 cases ineffective. Du Fabin ^[21] believes that the main focus of this disease is to replenish qi and blood, and then relieve excess. Insomnia patients often have severe symptoms of restlessness and impatience. Therefore, the combination of Zhi Zi Chi Tang and Gui Pi Tang with modifications is recommended. This formula has good therapeutic effects on elderly insomnia or hypertensive insomnia.

2.2.2 Harmony between Ying Qi and Wei Qi

Cui Zhenbo ^[13] used cinnamon twig soup and dragon bone Oyster soup to reconcile the camp and Wei, and recovered from hot flashes, sweating, insomnia and other diseases. Forty patients with perimenopausal hot flashes and insomnia were screened for clinical efficacy observation, and 24 cases (60.0%) were cured, 12 cases (30.0%) improved, and 4 cases were ineffective. Huang Yanmei ^[22] uses Erxian Tang and Guizhi Tang to relieve hot flashes and sleep peacefully.

2.3 Remove the blockage of tangible objects

2.3.1 Promoting blood circulation and removing blood stasis

Li Boyu ^[23] targeted stubborn insomnia with the treatment of promoting blood circulation and removing stasis, unblocking collaterals and calming the mind, and selected Guizhi Fuling Pill with added flavor. Through 50 clinical trials, it has been proven that this prescription can reduce the scores of the Pittsburgh Sleep Quality Index Anxiety Self Rating Scale and Depression Self Rating Scale in patients. It is not only beneficial for improving the symptoms of hot flashes and insomnia in patients

with stubborn insomnia of blood stasis type, but also for alleviating their anxiety and depression.

Chinese medicine master Wang Qi ^[24] believes that for those with blood stasis, dark lips, dark eyes and eyes, and purple and dark tongue with bruises and insomnia, the Blood Mansion Zhuyu Tang should be selected to promote blood circulation, cool blood and nourish blood. Qi Cuiping ^[25] used the original formula to remove *Platycodon grandiflorus* and added *Leonurus heterophyllus* and Zelan to promote blood circulation and diuresis in order to prevent facial heat. A total of 40 patients with insomnia caused by blood stasis and hot flashes were observed, with 18 cured, 17 significantly improved, 3 effective, and 2 ineffective, with an effective rate of 95%.

2.3.2 Dredging the bowels and discharging heat

Chen Yifei ^[26] believes that perimenopausal women often suffer from constipation. If dry feces block, the main method is to dredging the bowels and discharging heat, so that the blockage can be eliminated and the heat evil can be eliminated. The clinical use of Da Cheng Qi Tang is better. Bu Huanyu ^[17] believes that this syndrome does not necessarily require the use of Cheng Qi, but can be treated with Bai Hu Tang to clear heat and lower Qi. Many cases are cured by taking Bai Hu Tang, which helps to clear the stool and relieve hot flashes, and sleep peacefully.

2.3.3 Clearing dampness and heat

Chinese medicine master Wu Caibing ^[18] believes that during the perimenopausal period, when there is insomnia caused by hot flashes, special attention should be paid to the pathogenic factors of dampness, mainly internal dampness. The focus should be on strengthening the spleen and tonifying qi, clearing and promoting dampness and heat. The formula is modified with Dongyuan Qingshu Yiqi Tang, which has been clinically proven to be effective.

Chen Yifei ^[26] believes that if the syndrome is severe in dampness and mild in heat, the formula should be Sanren Tang. For severe in heat and mild in dampness, the formula should be Haoqin Qingdan Tang. Jin Zhongyu ^[27] treated 63 menopausal women with Haoqin Qingdan Tang based on the differentiation of gallbladder heat to treat hot flashes and sweating. The results showed that 52 cases were cured, 5 cases were effective, and 6 cases were ineffective, with a total effective rate of 90.48%.

3. Discuss

In recent years, with the intensification of population aging, the proportion of women entering perimenopause has significantly increased, and research on perimenopausal diseases has received more and more attention. Although there are many symptoms at this stage, the vast majority of women have hot flashes, which often occur in the afternoon and at night, seriously affecting women's sleep quality. However, most studies currently separate perimenopausal hot flashes from insomnia, ignoring the close correlation between the two in terms of etiology, pathogenesis, and clinical practice. Therefore, this article starts from hot flashes to treat perimenopausal women's insomnia, sorting out the causes and pathogenesis of insomnia caused by hot flashes during perimenopause, and targeting different pathogenesis and treatment methods. Medicine summarizes that the nature of this disease is based on deficiency and excess, often mixed with deficiency and excess. Deficiency syndrome is based on kidney deficiency, and should also consider the heart, liver, and spleen. It is necessary to adjust yin and yang, harmonize qi and blood, Governance methods such as calming the mind; At the same time, special attention should be paid to the accumulation of pathological products caused by the imbalance of qi, blood, yin and yang, that is, the role of tangible solid pathogens such as blood stasis, dry feces, and damp heat in hot and humid insomnia. When both deficiency and excess are taken into account, supplementing deficiency and purging excess, and treating both symptoms and

symptoms.

However, there is currently insufficient experimental research on the treatment of perimenopausal insomnia caused by hot flashes using traditional Chinese medicine. The mechanism of action of insomnia caused by hot flashes is not fully understood, and the number of clinical studies is relatively small. There are many small sample observations, and more high-level evidence-based medicine research evidence is needed.

References

- [1] Samuel L, Antonio C, et al. Fezolinetant for treatment of moderate-to-severe vasomotor symptoms associated with menopause (SKYLIGHT 1): a phase 3 randomised controlled study. [J]. *Lancet* (London, England), 2023, 401(10382): 1091-1102.
- [2] Li Huihao, Wang Jieqiong, Gao Mingzhou et al. Progress in Traditional Chinese Medicine Research on Perimenopausal Heat Disorder [J]. *Chinese Journal of Basic Traditional Chinese Medicine*, 2019, 25 (03): 413-416
- [3] Zheng Yanwei, Tao Minfang. Research progress on sleep disorders in perimenopausal women [J]. *Journal of Shanghai Jiao Tong University (Medical Edition)*, 2016, 36 (07): 1088-1092
- [4] C , R T, E H V A, A C D, et al. Menopausal Vasomotor Symptoms and Risk of Incident Cardiovascular Disease Events in SWAN. [J]. *Journal of the American Heart Association*, 2021, 10(3).
- [5] Crandall CJ, Tseng CH, Crawford SL, et al. Association of menopausal vasomotor symptoms with increased bone turnover during the menopausal transition. [J]*Bone Miner Res* 2011; 26: 840
- [6] K J P .Neurokinin 3 receptor antagonists for menopausal vasomotor symptoms.[J].*Lancet* (London, England), 2023, 401(10382):1055-1058.
- [7] Zhang Nianshun. Diagnosis and treatment of hot flashes based on timing [J]. *Chinese Community Physician*, 1991 (01): 23-24
- [8] Xu Xinyan, Li Jun, Bao Xiaoxia, et al. Professor Guo Wei-qin's Experience in Treating Menopausal Insomnia [J]. *Grassroots Traditional Chinese Medicine*, 2023, 2 (03): 6-9
- [9] Deng Ying. Zishen Tang for the treatment of 50 cases of menopausal hot flashes and sweating [J]. *Shaanxi Traditional Chinese Medicine*, 2004 (05): 406-407
- [10] Mi Xiujian, Fang Junnan, Yu Xinyuan, et al. Clinical efficacy of Zishui Bagan Tang in the treatment of insomnia caused by liver and kidney deficiency during perimenopause [J]. *Chinese Journal of Experimental Formulas*, 2022, 28 (16): 116-122
- [11] Zhang Zhongyang, Ling Jiayan, Zhou Dun. Study on the clinical efficacy of modified Huanglian ass hide glue Decoction in treating insomnia of yin deficiency and fire hyperactivity syndrome and its effect on 5-hydroxytryptamine and dopamine levels [J]. *Chinese Journal of Traditional Chinese Medicine*, 2021, 39 (04): 167-171
- [12] Wei Xiangling, Sun Haijun. Modified Guipi Tang for the treatment of 47 cases of refractory insomnia [J]. *Chinese Journal of Basic Medicine of Traditional Chinese Medicine*, 2007 (09): 714
- [13] Cui Zhenbo, Yang Taiyin. Modified Guizhi Tang for the treatment of 40 cases of menopausal fever [J]. *Anhui Journal of Clinical Chinese Medicine*, 2003, 15 (6): 478
- [14] Liu Yaling, Wang Jiawei. Wang Jiawei's Experience in Treating Perimenopausal Syndrome [J]. *Journal of Traditional Chinese Medicine*, 2011, 52 (6): 524-525
- [15] Gao Zhili, He Juan. On Blood Stasis and Insomnia [J]. *Tianjin Traditional Chinese Medicine*, 2019, 36 (04): 371-373
- [16] Fu Shuping, Zhang Ronghua, Cai Yu, et al. Treatment of menopausal syndrome based on kidney deficiency and blood stasis [J]. *Shaanxi Traditional Chinese Medicine*, 2005, 26 (5): 435-436
- [17] Bu Huanyu. Analysis of Severe Heat in the Afternoon [J]. *Journal of Nanjing University of Traditional Chinese Medicine*, 2019, 35 (02): 127-129
- [18] Liu Tianping, Wu Jianguang. Experience of Chinese medicine master Wu Bingcai in treating perimenopausal hot flashes and sweating [J]. *Journal of Jiangxi University of Traditional Chinese Medicine*, 2023, 35 (04): 16-18+22
- [19] Li Hui, Jiang Qunqun. Clinical experience of Professor Liu Ruifen in treating perimenopausal hot sweating [J]. *Journal of Zhejiang University of Traditional Chinese Medicine*, 2013, 37 (07): 873-874
- [20] Zhong Guanghua. Modified Zishui Qinggan Yin for the treatment of 108 cases of perimenopausal hot flashes [J]. *Shaanxi Traditional Chinese Medicine*, 2004 (11): 977
- [21] Luo Chunhua, Yang Haiyu. Three medical cases of treating insomnia with the combination of Zhizi Black Bean Soup and Guipi Tang. [J]. *New Traditional Chinese Medicine*, 2020, 52 (13): 204-206
- [22] Huang Yanmei, Liu Yaqian, Zhou Ying. Study on the therapeutic effect of modified Erxian Huguizhi Tang on menopausal syndrome hot flashes and its impact on gut microbiota structure [J]. *New Chinese Medicine and Clinical*

Pharmacology, 2022, 33 (07): 970-976

[23] Li Boyu, Gao Baoyin. Clinical observation of 50 cases of stubborn insomnia with blood stasis type treated with integrated traditional Chinese and Western medicine [J]. *Clinical Research of Traditional Chinese Medicine*, 2020, 12 (28): 108-110

[24] Yao Haiqiang, Cui Hongsheng, Guo Gang et al. Wang Qi's use of Xuefu Zhuyu Tang for treatment [J]. *Journal of Traditional Chinese Medicine*, 2016, 57 (05): 375-378

[25] Qi Cuiping. Observation on the therapeutic effect of promoting blood circulation and removing stasis method on menopausal syndrome [J]. *Heilongjiang Traditional Chinese Medicine*, 2002, (04): 17-18

[26] Chen Yifei, Sun Meiling. Analysis and treatment of afternoon hot flashes based on syndrome differentiation [J]. *Shi Zhen, Traditional Chinese Medicine*, 2021, 32 (03): 689-690

[27] Jin Zhongyu, Zhang Guifang. 63 cases of menopausal syndrome treated by gallbladder differentiation [J]. *Zhejiang Journal of Traditional Chinese Medicine*, 2003, (04): 19